INAUGURAL ISCT ASIA 2026 REGIONAL MEETING

PROGRAM

SINGAPORE • SEPT 2-5, 2026

SUNTEC CONVENTION CENTRE

International Society
ISCT
Cell & Gene Therapy®
ASIA REGION

WWW.ISCT-ASIA2026.COM

Welcome from the Co-Chairs

Welcome to Singapore!

We are delighted to welcome you to the Inaugural ISCT Asia Regional Meeting, taking place from September 2–5, 2026, in one of the world's most dynamic centres for science, innovation, and healthcare. As a global crossroads connecting East and West, Singapore provides the ideal setting for the International Society for Cell & Gene Therapy (ISCT) to bring together our community to shape the future of advanced therapies across Asia and beyond.

Our theme for this meeting, "**Next Generation Cell & Gene Therapies**," reflects the extraordinary pace of innovation transforming our field. Asia has become a leading force in the global cell and gene therapy landscape, with groundbreaking advances in engineered cell therapies, gene editing technologies, regenerative medicine, and advanced manufacturing. This program has been designed to showcase these developments while creating opportunities for collaboration across disciplines and borders.

Whether your interests lie in fundamental discovery science, translational research, clinical development, manufacturing, regulatory science, commercialisation, or patient access, we have created a program that offers something for everyone. Through plenary lectures, concurrent scientific sessions, roundtable discussions, and interactive networking opportunities, we will explore the latest innovations that are shaping the next generation of cell and gene therapies.

We are honoured to welcome leading scientists, clinicians, manufacturers, industry innovators, and regulatory experts from across the Asia-Pacific region and around the world. As healthcare systems throughout Asia continue to evolve, our discussions will address some of the most important questions facing the field today: how we can accelerate the translation of new therapies, navigate increasingly complex regulatory landscapes, and improve patient access through innovative manufacturing and delivery models.

One of the defining conversations of this meeting will be the future of cell therapy manufacturing. Advances in automation and decentralized production are creating new opportunities for point-of-care manufacturing, while centralized manufacturing models continue to support global scalability. Asia's diversity of healthcare systems makes it uniquely positioned to lead the development of new approaches that balance quality, accessibility, and affordability for patients.

As the Inaugural ISCT Asia Regional Meeting, this gathering marks an important milestone for our Society and our community. It reflects the growing leadership of the region and our shared commitment to fostering scientific excellence, international collaboration, and the responsible advancement of transformative therapies.

Beyond the scientific program, we encourage you to experience everything Singapore has to offer. Renowned for its rich cultural heritage, world-class cuisine, and vibrant biomedical ecosystem, the city is home to leading research institutions, innovative biotechnology companies, and a thriving healthcare sector. Take time to explore its iconic gardens, diverse neighbourhoods, and celebrated culinary scene while reconnecting with colleagues and building new partnerships.

On behalf of the Organising Committee, we thank you for being part of this milestone event. Your participation helps establish a new platform for scientific exchange, collaboration, and innovation that will strengthen the cell and gene therapy community across Asia for years to come.

We invite you to make the most of your time together—engage in critical discussions, build new partnerships, and help shape the next generation of cell and gene therapies.

With best wishes,
William YK Hwang, Shin Kawamata and Sai Kiang Lim
ISCT Asia 2026 Regional Meeting Co-Chairs



William YK Hwang, MBBS, MMED, MRCP, FAMS, MBA
Immediate Past ISCT Asia Regional Vice President
National Cancer Center; Singapore General Hospital; REMEDIS, SingHealth
Singapore



Shin Kawamata, MD, PhD
Immediate Past ISCT Asia Regional Secretary
Kobe University
Japan



Sai Kiang Lim, PhD
ISCT Exosomes Committee Co-Chair
Paracrine Therapeutics
Singapore

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Organizing Committee Members

Program Co-Chairs

William YK Hwang
MBBS, MMed, FRCP, FAMS, MBA
Immediate Past ISCT Asia Regional Vice President
National Cancer Center; Singapore General Hospital; REMEDIS, SingHealth
Singapore

Shin Kawamata
MD, PhD
Immediate Past ISCT Asia Regional Secretary
Kobe University
Kobe, Japan

Sai Kiang Lim
PhD
ISCT Exosomes Committee Co-Chair
Paracrine Therapeutics Pte Ltd
Singapore

Organizing Committee Members

Sudipto Bari
PhD
ISCT Asia Regional ESP Subcommittee Co-Chair
Advanced Cell Therapy and Research Institute, Singapore (ACTRIS)
Singapore

Pawan Gupta
MBBS, MD, DNB, PhD
ISCT Asia Regional Vice President
Stempeutics Research
India

Suradej Hongeng
MD
Faculty of Medicine Ramathibodi Hospital
Mahidol University
Thailand

He Huang
MD, PhD
The First Affiliated Hospital—Zhejiang University School of Medicine
China

Srinivasan N. Kellathur
PhD
Roche
Singapore

Antonio Lee
PhD
ISCT APAC Industry Committee Co-Chair
MEDIPOST
South Korea

Natasha Hui Jin Ng
PhD
BetaLife
Singapore

Masayo Takahashi
MD, PhD
Vision Care Inc.
Japan

General Conference Information

Registration Desk Hours

Level 3 Foyer

Tuesday, Sept 1	16:00 - 19:00
Wednesday, Sept 2	07:00 - 18:30
Thursday, Sept 3	07:30 - 18:00
Friday, Sept 4	07:30 - 13:30

Exhibit Hours

Poster & Exhibit Hall

Wednesday, Sept 2	08:00 – 20:00
Thursday, Sept 3	08:00 – 19:30
Friday, Sept 4	08:00 – 16:00

Speaker Services Center

Level Room 323

Tuesday, Sept 1	16:00 – 19:00
Wednesday, Sept 2	07:00 – 18:30
Thursday, Sept 3	07:30 – 18:00
Friday, Sept 4	07:30 – 13:30

Wi-Fi

Network Name: FREE_WiFi@SuntecSingapore
No password required

Access & Security

Name badges must be worn at all times within the ISCT conference space to ensure entry to session rooms, partnering village, exhibit and poster hall.

Social & Networking Events

Events below are included for all registered delegates

WEDNESDAY, SEPT 2
08:00 - 08:30
Welcome Address
Summit 2

18:30 - 20:00
Welcome Reception
Poster and Exhibit Hall

18:30 - 20:00
Poster Reception 1
Supported by Sartorius
Poster Hall

THURSDAY, SEPT 3
18:00 - 19:30
Poster Reception 2
Supported by ScaleReady
Poster Hall

Conference App and Partnering System

Search 'ISCT' in your app store to download the conference app.

- Access the complete delegate list and company directory
- Request one-on-one meetings with delegates, speakers and sponsors
- Book your meetings in private, designated partnering tables on site at the conference venue
- Review the full agenda and build a personal schedule for the event days

Social Media

Join the conversation on LinkedIn, X, and Bluesky! #ISCTASIA2026

Questions?

Please stop by the Registration Desk on Level 3 or email meetings@isctglobal.org for assistance.

Venue Map

LEVEL 3, SUNTEC CONVENTION CENTRE

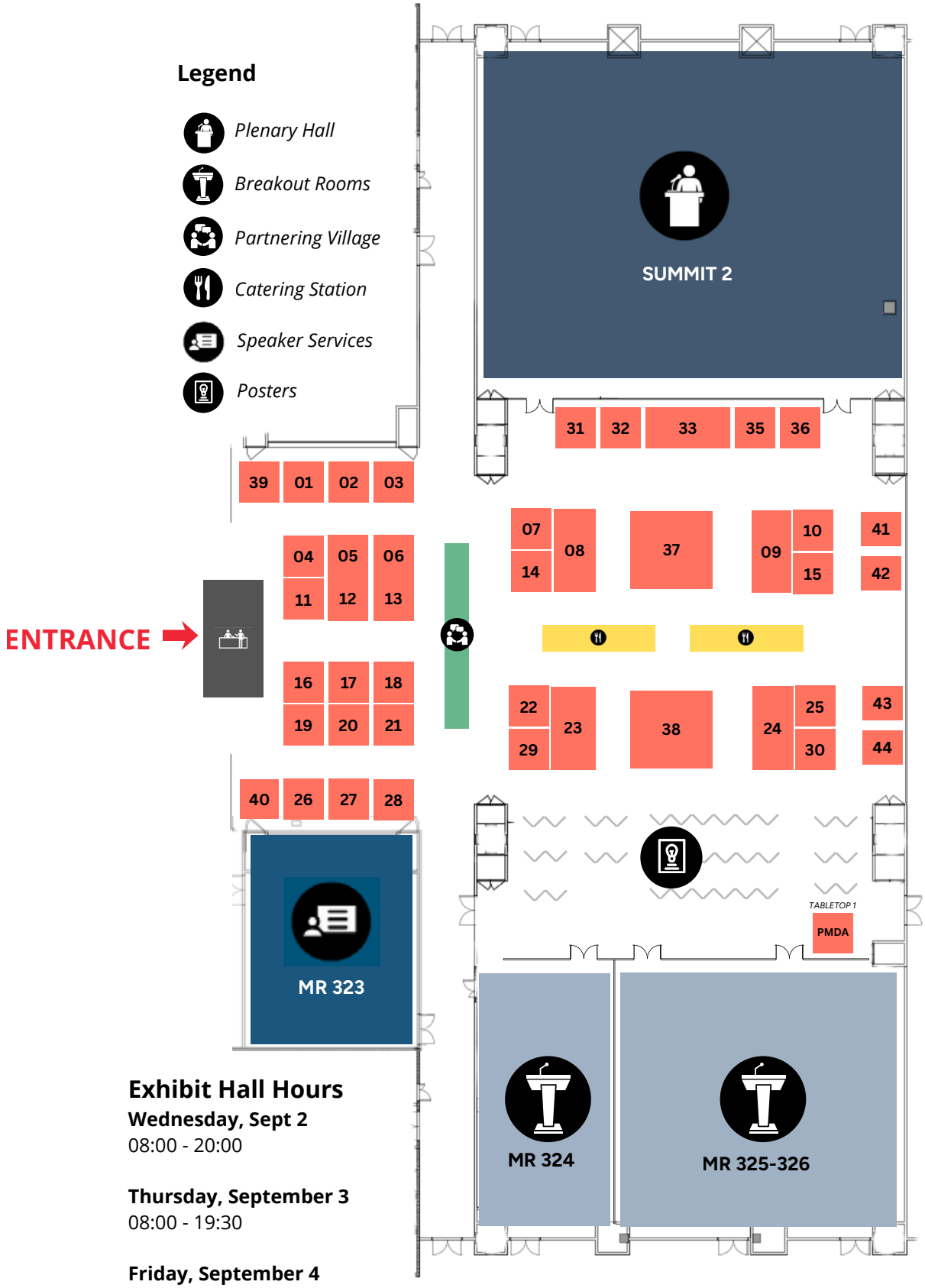


Exhibit Hall Hours

Wednesday, Sept 2
08:00 - 20:00

Thursday, September 3
08:00 - 19:30

Friday, September 4
08:00 - 16:00

Invited Chairs, Speakers, and Panelists

Eytan Abraham, *PhD, Minaris Advanced Therapies, United States*

Heedon Ahn, *MBA, Curiosis, Inc, South Korea*

Robert Ang, *MBBS, MBA, Vor Bio, Singapore*

Usanarat Anurathapan, *MD, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand*

Matias Ilmari Autio, *PhD, A*STAR; GIS; National University of Singapore, Singapore*

Sudipito Bari, *PhD, Advanced Cell Therapy and Research Institute, Singapore (ACTRIS), Singapore*

Antonio Bertoletti, *MD, Duke NUS Medical School, Singapore*

Lucas Chan, *PhD, Lucas Chan Consulting Pte Ltd; Yong Loo Lin School of Medicine, National University of Singapore, Singapore*

Alex H. Chang, *PhD, YaKe Biotech, China*

Yunxin Chen, *MBBS, Singapore General Hospital, Singapore*

Andre Choo, *PhD, National University of Singapore; A*STAR Bioprocessing Technology Institute (BTI), Singapore*

Kenon Chua, *MBBS, MRCSEd, MMed, MCI, FRCSEd, Singapore General Hospital, Singapore*

Riguo Fang, *PhD, Theia Therapeutics, China*

Michael Fehlings, *PhD, ImmunoScape, United States*

Miguel Forte, *MD, PhD, Kiji Therapeutics; mC4Tx, Belgium*

Qing-Ling Fu, *MD, PhD, The First Affiliated Hospital, Sun Yat-sen University, China*

Guanping Gao, *PhD, UMass Chan Medical School, United States*

Bernd Giebel, *PhD, University Hospital Essen (Universitätsklinikum Essen); University of Duisburg-Essen, Germany*

Pawan Gupta, *MBBS, MD, DNB, PhD, Stempeutics Research, India*

Hiroko Hanzawa, *PhD, Hitachi, Japan*

Mei Heng, *MD, PhD, Institute of Hematology, Union Hospital, Tongji Medical College, Huazhong University of Hematology, China*

Aloysius Ho, *MBBS, MMED, FRCP, FRCPath, Advanced Cell Therapy and Research Institute, Singapore (ACTRIS); Singapore General Hospital; National Cancer Centre Singapore, Singapore*

Sarah Ho, *PhD, AGeM Bio, Singapore*

Suradej Hongeng, *MD, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand*

Edwin M. Horwitz, *MD, PhD, Emory University School of Medicine, United States*

Masaki Hosoya, *PhD, Sinfonia Technology Co., Ltd, Japan*

Chia-Yi Hsu, *PhD, DrSignal BioTechnology Co., Ltd., Taiwan*

Chi-Ying Huang, *PhD, National Yang Ming Chiao Tung University, Taiwan*

William YK Hwang, *MBBS, MMED MRCP, FAMS, MBA, National Cancer Center; Singapore General Hospital; REMEDIS, SingHealth, Singapore*

Taruna Ikrar, *PhD, Indonesian Food and Drug Authority (BPOM), Indonesia, Indonesia*

Atsushi Inoue, *PhD, Cellafa Bioscience Inc, Japan*

Silviu Itescu, *MBBS, FRACP, Mesoblast, Australia*

Genny Jin, *PhD, MEDIPOST Korea, South Korea*

Ji Hyeon Ju, *MD, PhD, YiPSCELL, South Korea*

Genki N. Kanda, *PhD, Institute of Science Tokyo (Science Tokyo), Japan*

Shin Kawamata, *MD, PhD, Kobe University, Japan*

Srinivasan N. Kellathur, *PhD, Roche Singapore, Singapore*

Chaiyong Koaykul, *PhD, Faculty of Medicine, Chulalongkorn University, Thailand*

Maki Kumagai, *MSc, The University of Osaka Division of Stem Cell and Organoid Medicine, Japan*

Dinesh Kundu, *MBBS, MBA, East Ocyon Bio Private Limited, India*

Minh T. N. Le, *PhD, Department of Pharmacology, Institute for Digital Medicine, Yong Loo Lin School of Medicine; National University of Singapore, Singapore*

Antonio Lee, *PhD, MEDIPOST Co., Ltd, South Korea*

Kyung Jin Lee, *PhD, OrganoidSciences, South Korea*

Bruce Levine, *PhD, University of Pennsylvania, United States*

Nguyen Thanh Liem, *MD, PhD, Center for Regenerative Medicine and Cell Therapy, Vinmec Healthcare System, Vietnam*

Francesca Lorraine Lim, *MBBS, MMED, MRCP(UK), Singapore General Hospital, Singapore*

Sai Kiang Lim, *PhD, Paracrine Therapeutics, Singapore*

Thai-Yen Ling, *PhD, National Taiwan University, Taiwan*

Kai Yan Liu, *MD, PhD, Lu Daopei Hospital, China*

Chang Liu, *PhD, ASK Health Asia, Singapore*

Jonathan Yuin-Han Loh, *PhD, Institute for Molecular and Cell Biology (IMCB), A*STAR, Singapore*

Elena Maryamchik, *MD, MBA, Memorial Sloan Kettering Cancer Center, United States*

Takesi Matsuyama Hoyos, *PhD, Vision Care Inc., Japan*

Jod S Mehta, *MBBS, PhD, FRCOphth, FRCS (Ed), FAMS, FARVO, Singapore National Eye Centre, Singapore*

Keita Mori, *MBA, SanBio Co., Ltd., Japan*

Natasha Hui Jin Ng, *PhD, BetaLife, Singapore*

Atsushi Nishikawa, *MSc, Pharmaceuticals and Medical Devices Agency (PMDA), Japan*

Colin Lee Novick, *BA, Innovacell Inc., Japan*

Yusuke Nozaki, *MSc, Pharmaceuticals and Medical Devices Agency (PMDA), Japan*

Gabrielle O'Sullivan, *PhD, MPH (Hons), Sydney Local Health District, Australia*

Takahiro Ochiya, *PhD, Institute of Medical Science, Tokyo Medical University, Japan*

Steve Oh, *PhD, Independent Cell Therapy Consultant, Singapore*

Jolene Ooi, *PhD, EDBI Pte Ltd, Singapore*

YongKeun Park, *PhD, Tomocube Inc., South Korea*

Kim Png, *PhD, MBA, Polaris Partner, Singapore*

Changsong Qi, *PhD, Peking University Cancer Hospital, China*

Stanley Qi, *PhD, Stanford University, United States*

Nguyễn Ngô Quang, *Department of Science, Technology and Training, Vietnam*

Mahendra Rao, *MBBS, PhD, MD-Bio; NKURE, United States*

Yosef Refaeli, *PhD, Ascensus Therapeutics, Inc., United States*

Yoji Sato, *PhD, National Institute of Health Sciences (NIHS), Japan*

Jihye Shin, *PhD, Xcell Therapeutics, Inc., South Korea*

Jaichandran Sivaligam, *PhD, A*STAR Bioprocess Technology Institute, Singapore*

Yun-Kyoung Song, *PhD, College of Pharmacy, The Catholic University of Korea, South Korea*

Xinyi Su, *MBBChir, PhD, FAMS, Institute of Molecular and Cell Biology (IMCB), A*STAR, Singapore*

Masayo Takahashi, *MD, PhD, Vision Care Inc., Japan*

Eddie Tan, *PhD, EMBA, CABP, Centre of Regulatory Excellence, Duke-NUS Medical School, Singapore*

Pansakorn Tanratana, *MD, PhD, Mahidol University, Thailand*

Siok Tey, *MBBS, PhD, FRACP, FRCPA, QIMR Berghofer Medical Research Institute; Royal Brisbane; Women's Hospital, Australia*

James Khong Lek Then, *MSc, Cryocord, Malaysia*

Wei Seong Toh, *PhD, National University of Singapore, Singapore*

Kitipong Uaesoontrachoon, *PhD, Genepeutic Bio Co.,Ltd, Thailand*

Phil Vanek, *PhD, Redline Bioadvisors, United States*

Zlatibor Veličković, *PhD, Royal Perth Hospital; University of Western Australia, Australia*

Daniel J. Weiss *MD, PhD, University of Vermont, United States*

Yun Xia, *PhD, Institute for Molecular and Cell Biology (IMCB), A*STAR, Singapore*

Eng Soo Yap, *MBBS, MMED, MRCP (UK), FRCPath, Department of Laboratory Medicine, Ng Teng Fong General Hospital; Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore*

Lynn Yap, *PhD, Lee Kong Chian School of Medicine, NTU, Singapore*

Ying Zhang, *PhD, Health Sciences Authority, Singapore*

Yuchen Zhou, *PhD, Applied Cells, United States*

Oral Abstract Presenters

Toshikazu Araoka, *MD, PhD, Center for iPS Cell Research and Application (CiRA), Kyoto University, Japan*

Anupam Chhabra, *MD, MBA, Cartogene Therapeutics, India*

Lingyan Gong, *PhD, Nanyang Technological University, Singapore*

Luyan Jiao, *PhD, Nuwacell Biotechnologies Co., Ltd., China*

Hyejin Jo, *BEng, Dongguk University, South Korea*

Hsien-Yin Kao, *Westmead Institute for Medical Research, University of Sydney, Australia*

Srinivasan N. Kellathur, *PhD, Roche Singapore, Singapore*

Junjun Li,*PhD, Osaka University; EngiTissue Design Co., Ltd., Japan*

Arief Nurudhin, *MD, PhD, Medical Faculty Universitas Sebelas Maret; Moewardi General Hospital, Indonesia*

Weronika Ploch, *MD, Medical University of Warsaw, Poland*

Martin Rabel, *PhD, MPharm, Cytiva, Germany*

Jingjing Ruan, *Liangzhu Laboratory, Zhejiang University, China*

Lixia Sheng, *MD, PhD, The First Affiliated Hospital of Ningbo University, China*

Taro Takami, *MD, PhD, Yamaguchi University Graduate School of Medicine, Japan*

Amanda Tan, *PhD, Kids Research, Australia*

Wenjiao Tang, *MD, PhD, West China Hospital, Sichuan University, China*

Yue Zhang, *PhD, Zhejiang University, China*

Program Schedule

DAY 1 - Wednesday, September 2, 2026

07:00 - 18:30	**Registration Hours**
08:00 - 20:00	**Exhibit Hours**
10:00 - 20:00	**Partnering Village Hours**
08:00 - 09:00	**Welcome Address** Summit 2 **Keynote Presentation: The Next Chapter in the Fantastic Voyage of CAR T Cell Therapy: Potency, Access, and Delivery** Summit 2 Speaker: Bruce Levine, *PhD, University of Pennsylvania, United States*
09:15 - 10:15	**Breaking Through the Commercial Ceiling: Challenges and the Future of Approved Allogeneic MSCs** Summit 2 Chair: Daniel J. Weiss, *MD, PhD, University of Vermont, United States* Speakers: Silviu Itescu, *MBBS, FRACP, Mesoblast, Australia* Antonio Lee, *PhD, MEDIPOST Co., Ltd., South Korea* Keita Mori, *MBA, SanBio Co., Ltd., Japan*
	Oral Abstracts Session 1 MR 325-326 Abstract Presenters: **Longitudinal Urinary Extracellular Vesicle Profiling After CAR-T Cell Therapy: A Pilot Feasibility Study** Weronika Ploch, *MD, Medical University of Warsaw, Poland* **A 7-Day CAR-T Manufacturing Platform Delivering Three-Fold Faster Vein-to-Vein Time Through Negative Selection–Driven Cell Processing and GMP-Compliant Infrastructure** Anupam Chhabra, *MD, MBA, Cartogene Therapeutics, India* **Gene Therapy for MEF2C Haploinsufficiency Syndrome** Jingjing Ruan, *Liangzhu Laboratory, Zhejiang University, China* **Phase-Specific PD-1 Blockade During Early Contraction of IL-7/CCL19–Armored CD19 CAR-T Cells Promotes Response Deepening in High-Risk R/R LBCL: A First-in-Human Phase I Study** Lixia Sheng, *MD, PhD, The First Affiliated Hospital of Ningbo University, China* **Real-World Outcomes of BCMA-Targeted Car-T Cell Therapy in Relapsed/Refractory Multiple Myeloma** Wenjiao Tang, *MD, PhD, West China Hospital, Sichuan University, China*
	Cytiva Corporate Session **The Future-Ready CAR-T Playbook: Winning Across Ex Vivo and In Vivo Frontiers** MR 324 **Speakers:** Peiqing Zhang, *Scientific Director, Genomic Medicine, Cytiva, Singapore* Alan K. Smith, *PhD, Global Head of Innovation, Cell and Gene Therapy, Rose BioSolutions, Inc., United States* Martin Rabel, *Service Solution Specialist, Cytiva, Germany*

10:15 - 10:45	**COFFEE BREAK** **Supported by Cytiva** **Charles River Laboratories Company Presentation** **Principles in Viral Safety Testing for Cell and Gene Therapy Products** MR 324 | 10:15 - 10:45 **Speaker:** Colette Cote, *PhD, Executive Director and Scientific Advisor, Charles River, USA*
10:45 - 11:45	**Regenerative Medicine in Action: Translating Tissue-Specific Regeneration from Bench to Bedside** Summit 2 **Co-Chairs:** Pawan Gupta, *MBBS, MD, DNB, PhD, Stempeutics Research, India* Xinyi Su, *MBBChir, PhD, FAMS, Institute of Molecular and Cell Biology (IMCB), A*STAR, Singapore* **Speakers:** Kenon Chua, *MBBS, MRCSEd, MMed, MCI, FRCSEd, Singapore General Hospital, Singapore* Jod S Mehta, *MBBS, PhD, FRCOphth, FRCS (Ed), FAMS, FARVO, Singapore National Eye Centre, Singapore* Lynn Yap, *PhD, Lee Kong Chian School of Medicine, NTU, Singapore*
	Breaking the Code to CGT Access: Availability, Affordability, and Alignment MR 325-326 **Moderator:** Miguel Forte, *MD, PhD, Kiji Therapeutics; mC4Tx, Belgium* **Panelists:** Masayo Takahashi, *MD, PhD, Vision Care Inc., Japan* Phil Vanek, *PhD, Redline Bioadvisors, United States* Kitipong Uaesoontrachoon, *PhD, Genepeutic Bio Co.,Ltd, Thailand*
	Zheng Yang Biomedical Technology Company Presentation **Building a Regenerative Medicine Ecosystem in Asia: From CDMO to IDMO** MR 324 10:45 - 11:00 **Speaker:** Sean Chang, *CEO, Locus Cell Co., Ltd., Taiwan*
	ANEMOCYTE Company Presentation **AMCAP™ : The One-Pot Solution for Cell & Gene Therapies** MR 324 | 11:00 - 11:15 **Speaker:** Marco Pupo, *PhD, Innovation and Development Coordinator, Italy*
	Astraveus Company Presentation **Small Is Powerful: Streamlining And Improving Cell Therapy Economics With Lakhesys, The End-To-End Microfluidic Cell Factory** MR 324 | 11:15 - 11:30 **Speaker:** Jérémie Laurent, *CEO, Astraveus, France*
	Bio-Rad Laboratories Company Presentation **Droplet Digital PCR for Cell and Gene Therapy: Enabling Precision from Development to Quality Control** MR 324 | 11:30 - 11:45 **Speaker:** Dr. Lee Kee Wah, *Regional Marketing Manager, Bio-Rad Laboratories, Singapore*

11:45 - 13:00	**Lunch** **Poster and Exhibit Hall**
	Miltenyi Biotec Corporate Session **Advancing Clinical Cell Therapy: From Cell Separation to GMP Manufacturing** MR 324 | 12:00 - 13:00  **Speakers:** Ulf Bethke, *Executive Expert Cell and Gene Therapy Asia Pacific, Miltenyi Biotec B.V. & Co.KG, Germany* Caroline Blumer Toti, *Head of Clinical Marketing, Miltenyi Biotec B.V. & Co.KG, Germany* Ledio Bocova, *Global Product Manager CliniMACS Systems, Miltenyi Biotec B.V. & Co. KG, Germany*
	ScaleReady Corporate Session **SMART G-Rex®: An Introduction to Novel Integrated Process Analytic Technology for Intelligent Automation of CGT Manufacturing** MR 325-326 12:00 - 13:00  **Speaker:** Andrew Scheffler, *G-Rex Optimization Specialist, ScaleReady, United States*
13:00 - 14:00	**Bringing Cellular Immunotherapy to More Patients: Improving Potency While Controlling Cost** Summit 2 **Chair:** Sai Kiang Lim, *PhD, Paracrine Therapeutics, Singapore* **Speakers:** Jonathan Yuin-Han Loh, *PhD, Institute for Molecular and Cell Biology (IMCB), A*STAR, Singapore* Yosef Refaeli, *PhD, Ascensus Therapeutics, Inc., United States* Yuchen Zhou, *PhD, Applied Cells, United States*
	Navigating CGT Starting Material Requirements Across Asia: Harmonization and Cultural Compliance MR 325-326 **Chair:** Yoji Sato, *PhD, National Institute of Health Sciences (NIHS), Japan* **Speakers:** Taruna Ikrar, *PhD, Indonesian Food and Drug Authority (BPOM), Indonesia* Genny Jin, *PhD, MEDIPOST Korea, South Korea*

14:15 - 15:15	**Expanding the Reach of CAR-T Cell Therapy: Clinical Advances and Manufacturing Innovation** Summit 2 **Co-Chairs:** Bruce Levine, PhD, *University of Pennsylvania, United States* Francesca Lorraine Lim, *MBBS, BSc, MMED, MRCP(UK), Singapore General Hospital, Singapore* **Speakers:** Alex H. Chang, *PhD, YaKe Biotech, China* Kai Yan Liu, *MD, PhD, Lu Daopei Hospital, China* Changsong Qi, *PhD, Peking University Cancer Hospital, China*
	Beyond the Conventional Trials: Leveraging Plausible Mechanism and RWE to Accelerate CGT Development MR 325-326 **Chair:** Eddie Tan, *PhD, EMBA, CABP, Centre of Regulatory Excellence, Duke-NUS Medical School, Singapore* **Speakers:** Megha Kaushal, *MD, MSc, US Food and Drug Administration (FDA), United States* Chang Liu, *PhD, ASK Health Asia, Singapore* Yusuke Nozaki, *MSc, Pharmaceuticals and Medical Devices Agency (PMDA), Japan* Yun-Kyoung Song, *PhD, College of Pharmacy, The Catholic University of Korea, South Korea*
	Thermo Fisher Scientific Corporate Session **From Cell Expansion to Fill & Finish: Next-Generation Innovations for Scalable Cell Therapy Manufacturing** MR 324 **Speakers:** Ted Tish, *Vice President & General Manager, Cell Biology and Advanced Therapies (CBAT), Thermo Fisher Scientific, United States* Evan R. Zynda, *PhD, Senior Innovation Lead, Cell therapy R&D, Thermo Fisher Scientific, United States*
15:15 - 15:45	**COFFEE BREAK** **Supported by Cytiva**
	TEIJIN REGENET CO., LTD. Company Presentation **Development and FIH Trial for CGT in Japan Market** MR 324 | 15:15 - 15:30 **Speaker:** Akihiro Okano, *Pharmacist, MBA, Business Development Manager, TEIJIN REGENET CO., LTD., Japan*
	SPD Biomedia / Sony Corporation Company Presentation **CGX10 Cell Isolation System: Workflow Integration for Next Generation Cell Therapy Manufacturing** MR 324 | 15:30 - 15:45 **Speaker:** Marc-Aurele Brun, *Senior Manager, Cell Therapy Business, Sony Corporation, Japan*

15:45 - 16:45	**Emerging Cell & Gene Therapy Ecosystems in Asia: New Hubs, New Models, New Opportunities** Summit 2 Chair: Matias Ilmari Autio, *PhD, A*STAR; GIS; National University of Singapore, Singapore* Speakers: Chaiyong Koaykul, *PhD, Faculty of Medicine, Chulalongkorn University, Thailand* Dinesh Kundu, *MBBS, MBA, East Ocyon Bio Private Limited, India* Nguyễn Ngô Quang, *Department of Science, Technology and Training, Vietnam* James Khong Lek Then, *MSc, Cryocord, Malaysia*
	Potency Assays and Comparability: Navigating a Changing Landscape MR 325-326 Chair: Srinivasan N. Kellathur, *PhD, Roche Singapore, Singapore* Speakers: Lucas Chan, *PhD, Lucas Chan Consulting Pte Ltd; Yong Loo Lin School of Medicine, National University of Singapore, Singapore* Atsushi Nishikawa, *MSc, Pharmaceuticals and Medical Devices Agency (PMDA), Japan* Ying Zhang, *PhD, Health Sciences Authority, Singapore*
	Sartorius Company Presentation **Breaking Barriers in Immune Cell Therapy: Unlocking Scalable Manufacturing from Activation to Analytics** MR 324 Speaker: Patrick Carney, *Ph.D., Chief Business Officer & Chief Operating Officer, Nanotein Technologies* Rukmini Ladi, *Cell Culture Media Expert, Sartorius* Paul Cashen, *Process Expert Commercialisation & Optimisation, Sartorius*
17:00 - 18:30	**Plenary: Delivering Clinically Ready MSC-Exosomes for Real-World Use** Summit 2 Chair: **Chi-Ying Huang**, *PhD, National Yang Ming Chiao Tung University, Taiwan* Speakers: Bernd Giebel, *PhD, University Hospital Essen (Universitätsklinikum Essen); University of Duisburg-Essen, Germany* Sai Kiang Lim, *PhD, Paracrine Therapeutics, Singapore* Takahiro Ochiya, *PhD, Institute of Medical Science, Tokyo Medical University, Japan*
18:30 - 20:00	**Welcome Reception** Poster and Exhibit Hall
18:30 - 20:00	**Poster Reception 1** *Supported by Sartorius* Poster Hall

DAY 2 - Thursday, September 3, 2026

07:30 - 18:00	**Registration Hours**
08:00 - 19:30	**Exhibit Hours**
08:00 - 19:30	**Partnering Village Hours**
08:00 - 09:00	**Beyond the Hype: Re-Engineering the Promise of MSC Therapy** Summit 2 Chair: Pawan Gupta, *MBBS, MD, DNB, PhD, Stempeutics Research, India* Speakers: Miguel Forte, *MD, PhD, Kiji Therapeutics; mC4Tx, Belgium* Edwin M. Horwitz, *MD, PhD, Emory University School of Medicine, United States* Daniel J. Weiss, *MD, PhD, University of Vermont, United States*
	Oral Abstracts Session 2 MR 325-326 Abstract Presenters: **A Next-Generation Ionizable Lipid LNP Platform for Efficient In Vivo CAR T Cell Generation Across Species Through Passive and Active Immune Cell Targeting Strategies** Martin Rabel, *PhD, MPharm, Cytiva, Germany* **Hypoimmune iPSC-Derived Dopaminergic Progenitor Cell Therapy for Parkinson's Disease** Luyan Jiao, *PhD, Nuwacell Biotechnologies Co., Ltd, China* **Induced Pluripotent Stem Cell-Derived Mesenchymal Stromal Cell Extracellular Vesicles Ameliorate MASH-Related Liver Fibrosis in Mice** Taro Takami, *MD, PhD, Yamaguchi University Graduate School of Medicine, Japan* **On-Demand Microfluidic Automated Dissociation of iPSC Aggregates for Closed Bioreactor Culture Monitoring** Lingyan Gong, *PhD, Nanyang Technological University, Singapore* **Advanced Therapy Medicinal Products in ICH Member Countries: a Regulatory Landscape Analysis to Accelerate Convergence, Reliance and Patient Access** Srinivasan N. Kellathur, *PhD, Roche Singapore, Singapore* **A Dual Excitation-Contraction Platform for Functional Evaluation and Drug Safety Assessment of Human iPSC-Derived Cardiac Tissues** Junjun Li, *PhD, Osaka University; EngiTissue Design Co., Ltd., Japan*
	Broken String Biosciences Company Presentation **From Causes to Consequences: Decoding Off-Target Events in CRISPR Gene Editing** MR 324 | 08:15 - 08:30 Speaker: Claire Dacombe, *VP Sales APAC & EU, Broken String Biosciences, Dubai*
	10x Genomics Company Presentation **Access The Full Richness Of Biological Complexity With Single Cell And Spatial Multiomics** MR 324 | 08:45 - 09:00 Speaker: Benson Lim, *PhD, Senior Scientist & Technology Advisor*

09:15 - 10:15	**Uncovering the Preclinical Evidence Behind the Multi-Indication Therapeutic Promise of MSC Exosomes** Summit 2 **Chair:** Bernd Giebel, *PhD, University Hospital Essen (Universitätsklinikum Essen); University of Duisburg-Essen, Germany* **Speakers:** Qingling Fu, *PhD, The First Affiliated Hospital, Sun Yat-sen University, China* Thai-Yen Ling, *PhD, National Taiwan University, Taiwan* Wei Seong Toh, *PhD, National University of Singapore, Singapore*
	From Lab to Patient: Scaling CGT Manufacturing from Academic Programs to Broader Access MR 325-326 **Chair:** Aloysius Ho, *MBBS, MMED, FRCP, FRCPath, Advanced Cell Therapy and Research Institute, Singapore (ACTRIS); Singapore General Hospital; National Cancer Centre Singapore, Singapore* **Speakers:** Yunxin Chen, *MBBS, Singapore General Hospital, Singapore* Elena Maryamchik, *MD, MBA, Memorial Sloan Kettering Cancer Center, United States* Gabrielle O'Sullivan, *PhD, MPH (Hons), Sydney Local Health District, Australia*
	Terumo Blood and Cell Technologies Corporate Session **Roundtable Panel Discussion — Making CGT Manufacturing Work in Asia: Bridging Innovation and Reality** MR 324 **Speakers:** Wenyan Leong, *Director, APAC Commercial and Global Strategic Partnerships, Cell and Gene Therapies, Singapore* Cyrus Yang, *CEO, Taiwan Bio Therapeutics Inc., Taiwan* Sharon Sagnella, *Clinical Cell Therapies Processing Facility Director | Royal Prince Alfred Hospital, Director of Research & Development, Australia*
10:15 - 10:45	**COFFEE BREAK** **Supported by Terumo**
	Regenic Company Presentation **Session Details Forthcoming** MR 324 | 10:15 - 10:30
	Touchlight Company Presentation **Reimagining DNA Payloads: Enzymatic Circular DNA for the Next Generation of Cell and Gene Therapies** MR 324 | 10:30 - 10:45 **Speaker:** Daria Olijnyk-Dallis, *Head of Sales, Touchlight, USA*

10:45 - 12:15	**Plenary: From Journal Paper to Patients: Translating CAR-T, TCR and Gene Therapy Innovation** Summit 2 Chair **Suradej Hongeng**, *MD, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand* Speakers: **Antonio Bertoletti**, *MD, Duke NUS Medical School, Singapore* **Guanping Gao**, *PhD, UMass Chan Medical School, United States* **Bruce Levine**, *PhD, University of Pennsylvania, United States*
12:15 - 13:45	**Lunch** Poster and Exhibit Hall **Thermo Fisher Scientific Corporate Session** **Accelerating Clinical Translation of Treg & TIL Therapies Through Strategic Collaborations** MR 324 | 12:30 - 13:45 **Speakers:** Joshua Ooi, *PhD., Associate Professor, Head of Regulatory T cell Therapies Group, Monash University, Australia* Leon Brownrigg, *PhD., Senior Medical Scientist, Cell and Tissue Therapies (CTTWA), Royal Perth Hospital, Australia*
13:45 - 14:45	**Innovating the CGT Toolbox: NAMs and Ancillary Materials for More Efficient Manufacturing** Summit 2 Chair: Kunihiko Suzuki, *MBA, MEDINET Co., Ltd., Japan* Speakers: Heedon Ahn, *MBA, Curiosis, Inc, South Korea* YongKeun Park, *PhD, Tomocube Inc., South Korea* Jihye Shin, *PhD, Xcell Therapeutics, Inc., South Korea*
	From Regional Investment to Global Success: Commercializing CGT Pipelines in Asia, Europe, and the US MR 325-326 Moderator : Antonio Lee, *PhD, MEDIPOST Co., Ltd, South Korea* Panelists: Eytan Abraham, *PhD, Minaris Advanced Therapies, United States* Pawan Gupta, *MBBS, MD, DNB, PhD, Stempeutics Research, India* Colin Lee Novick, *BA, Innovacell Inc., Japan*
	Esco Aster Company Presentation **Linearly Scalable Fixed Packed Bed Bioreactors for Induced Pluripotent Stem Cells and Mesenchymal Stromal Cells with Closed Automated Single Use Harvester** MR 324 | 13:45 - 14:00 **Speaker:** XL Lin, *Founder, CEO, Esco Aster Pte Ltd, Singapore*

13:45 - 14:45	**EXODUS BIO Company Presentation** **Advancing EV Translation with an Automated, Scalable Isolation Platform** MR 324 | 14:00 - 14:15 **Speaker:** Viney Ying, *Product Application Manager, EXODUS BIO, USA*
	Lonza Company Presentation **A Non-Viral, Large-Scale Delivery of Gene Editing Tools for T Cell Manufacturing** MR 324 | 14:15 - 14:30 **Speaker:** Isaac Chen, *Channel Manager – SEA + Korea, Lonza Bioscience Singapore Pte Ltd., Singapore*
	ACROBiosystems Company Presentation **Advancing Cell and Gene Therapy: From Manufacturing Challenges to Integrated Solutions.** MR 324 | 14:30 - 14:45 **Speaker:** Li Yen Mah, *Technical Sales Manager (APAC), ACROBiosystems, Malaysia*
15:00 - 16:30	**Plenary: iPSC-Derived Therapies in Clinical Practice: Opportunities, Challenges, and Emerging Pathways** Summit 2 **Chair:** Masayo Takahashi, *MD, PhD, Vision Care Inc., Japan* **Speakers:** Riguo Fang, *PhD, Theia Therapeutics, China* Takesi Matsuyama Hoyos, *PhD, Vision Care Inc., Japan* Mahendra Rao, *MBBS, PhD, MD-Bio; NKURE, United States*
16:30 - 17:00	**COFFEE BREAK** **Supported by Terumo**
	BioCell Innovations Pte Ltd Company Presentation **Beyond Conventional CAR-T: Integrating Humanized CAR Designs and Advanced Manufacturing to Enhance Safety and Efficacy** MR 324 | 16:30 - 16:45 **Speaker:** Paula Lam, *Chief Scientific Officer, BioCell Innovations Pte. Ltd., Singapore*
	CellVec Pte Ltd Company Presentation **Enabling Scalable CAR-T Manufacturing: Advancing Lentiviral Vector Supply Through Robust and Scalable GMP Manufacturing** MR 324 | 16:45 - 17:00 **Speaker:** Ann Koay, *MSAT Lead, CellVec Pte Ltd., Singapore*

17:00 - 18:00	**Human Biology in a Dish: iPSC and Organoid Models Transforming Preclinical Testing and Therapeutics Development** Summit 2 Chair: Natasha Hui Jin Ng, *PhD, BetaLife, Singapore* Speakers: Maki Kumagai, *MSc, Osaka University Division of Stem Cell and Organoid Medicine, Japan* Kyung Jin Lee, *PhD, OrganoidSciences, South Korea* Yun Xia, *PhD, Institute for Molecular and Cell Biology (IMCB), A*STAR, Singapore*
	From Manufacturing to Market: Advancing Cell Therapies for Global Access MR 325-326 Chair: Antonio Lee, *PhD, MEDIPOST Co., Ltd., South Korea* Speakers: Pawan Gupta, *MBBS, MD, DNB, PhD, Stempeutics Research, India* Siok Tey, *MBBS, PhD, FRACP, FRCPA, QIMR Berghofer Medical Research Institute; Royal Brisbane; Women's Hospital, Australia* Zlatibor Veličković, *PhD, Royal Perth Hospital; University of Western Australia, Australia*
18:00 - 19:30	**Poster Reception 2** ***Supported by ScaleReady*** Poster Hall

DAY 3 - Friday, September 4, 2026	
07:30 - 13:30	**Registration Hours**
08:00 - 16:00	**Exhibit Hours**
08:00 - 16:00	**Partnering Village Hours**
08:00 - 09:00	**Scaling iPSC Mass Production Through Automated GMP Systems and Data Driven Quality Frameworks** Summit 2 Chair: Shin Kawamata, *MD, PhD, Kobe University, Japan* Speakers: Hiroko Hanzawa, *PhD, Hitachi, Japan* Masaki Hosoya, *PhD, Sinfonia Technology Co., Ltd, Japan* Atsushi Inoue, *PhD, Cellafa Bioscience Inc, Japan*
	Inside the Investor Mindset: What Makes a CGT Venture Fundable MR 325-326 Moderator: Natasha Hui Jin Ng, *PhD, BetaLife, Singapore* Panelists: Robert Ang, *MBBS, MBA, Vor Bio, Singapore* Jolene Ooi, *PhD, EDBI Pte Ltd, Singapore* Phil Vanek, *PhD, Redline Bioadvisors, United States*

08:00 - 09:00	**Elevator Pitch** MR 324 Abstract Presenters: **Autologous and Allogeneic Hematopoietic Stem Cell Transplantation in NK/T-Cell Lymphoma: a Long-Term Real-World Analysis** Jin Zhou, *Soochow University, China* **Engineering CRISPR/Cas12j8 System for Efficient Genome Editing Through A Novel Protein Engineering Strategy** Xiaoxiao Yu, *Zhejiang University; Liangzhu Laboratory, China* **Vortex-Actuated Cell Sorting Boosts Expansion of CRISPR-Edited Human Regulatory T Cells** Quan Yao Ho, *Singapore General Hospital; University of Oxford, Singapore* **Decentralized Point-of-Care CD19 CAR-T Manufacturing Enables Durable Responses in Relapsed/Refractory B-Cell Malignancies: Vietnam's First Clinical Experience** Van Hoang, *Vinmec Research Institute of Stem Cell and Gene Technology; Innnovation Health Sciences, VinUniversity, Vietnam* **Towards A Universal Lipid Nanoparticle (LNP) Platform for Multiplex Engineering of Next-Generation ex vivo Cell Therapies** Shaun Wen Zheng Lim, *Cytiva, Singapore* **From Blood to Treg Therapy in 10 Days: The Next-Generation Treg Manufacturing** Khai Loh, *Monash University, Australia* **Systems Biology Analysis of Oncolytic Virus-Mediated Tumor Priming for CAR NK Therapy in Head and Neck Cancer** Albeena Nisar, *Tata Memorial Centre, India* **Targeted Use of anti–CD19 and anti CD-22 CAR–T Cell Products For Dual–Antigen Targeting In B–ALL: A Feasible and Cost–Efficient Strategy from the Alacart Trial** Lee Bing Shen, *National University of Singapore, Singapore* **Tatmyctofusp (Tat-MYC) Fusion Protein Enhances T Cell Activation, Prevents Exhaustion, and Demonstrates Anti-Tumor Activity Across Multiple Solid Tumor Types** Lin Xiangliang, *Esco Aster Pte. Ltd., Singapore* **Sustained CD7 Expression Contributes to Improved Proliferation of Cord Blood Derived NK Cell by K562 Feeder Cell Expressing Membrane Bound IL-21** Yansong Zhu, *National Cancer Centre Singapore, Singapore* **Engineered HGF-Overexpressing iPSC-Derived Mesenchymal Stromal Cells Alleviate Lung Inflammation and Fibrosis** Ying Zhang, *Nuwacell Biotechnologies Co., Ltd, China* **A Novel Membrane-free in-line Microfluidics Media Exchanger for Continuous 3D iPSC Aggregates Manufacturing** Heesang Hong, *Nanyang Technological University; Agency for Science, Technology, and Research, Singapore* **Transcriptomic Analysis of Human Corneal Stromal Cells During ex vivo Expansion and Subsequent Fabrication of Stromal Tissue** Adaeze Ekwe, *Queensland University of Technology (QUT), Australia*
09:15 - 10:15	**From Ex Vivo to In Vivo: Reshaping Cell and Gene Therapy for Blood Disorders** Summit 2 Co-Chairs: Edwin M. Horwitz, *MD, PhD, Emory University School of Medicine, United States* Eng Soo Yap, *MBBS, MMED, MRCP (UK), FRCPath, Department of Laboratory Medicine, Ng Teng Fong General Hospital; Department of Medicine, Yong Loo Lin School of Medicine; National University of Singapore, Singapore* Speakers: Mei Heng, *MD, PhD, Institute of Hematology, Union Hospital; Tongji Medical College, Huazhong University of Hematology, China* Suradej Hongeng, *MD, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand* Tanratana Pansakorn, *MD, PhD, Mahidol University, Thailand*

09:15 - 10:15	**From Policy to Patient Bedside: How Regulatory Innovation in China, Japan, and Singapore Impacts Equitable Access to Decentralized CGT Manufacturing** MR 325-326 **Moderator:** Zlatibor Veličković, *PhD, Royal Perth Hospital; University of Western Australia, Australia* **Panelists:** Lisa Guan, *PhD, Miltenyi Biotec, China* Kunihiko Suzuki, *MBA, MEDINET CO., Ltd., Japan* Eddie Tan, *PhD, EMBA, CABP, Centre of Regulatory Excellence, Duke-NUS Medical School, Singapore*
10:15 - 10:45	**COFFEE BREAK** **Supported by Thermo Fisher Scientific** Shenzhen Cellbri Bio-Innovation Technology Co., Ltd Company Presentation **Bridging the Talent Gap: Enabling Robust, Multi-Site CGT Production Across Varied Expertise Levels** MR 324 | 10:15 - 10:45 **Speaker:** Anqi Li, *PhD, VP, Cellbri, Shenzhen Cellbri Bio-Innovation Technology Co.,Ltd, China*
10:45 - 12:15	**Plenary: Cutting Edge Technologies Transforming Cell Therapy Manufacturing** Summit 2 Chair: Steve Oh, ***PhD, Independent Cell Therapy Consultant, Singapore*** Speakers: Chia-Yi Hsu, *PhD, DrSignal BioTechnology Co., Ltd., Taiwan* Ji Hyeon Ju, *MD, PhD, YiPSCELL, South Korea* Shin Kawamata, *MD, PhD, Kobe University, Japan*
12:15 - 13:45	**Lunch** Poster and Exhibit Hall SciMed Asia, a PHC group & MaxCyte Company Presentation **Accelerating Cell Engineering with MaxCyte's High-Throughput Electroporation Platform** MR 324 | 12:30 - 12:45 **Speaker:** Leo He, *Field Application Scientist, MaxCyte, Inc., China* Tofflon Company Presentation **CGT Scale-up: Efficient Transition from Lab to Mass Production** MR 324 | 12:45 - 13:00 **Speaker:** Michael Wu, *Vice President of Tofflon Advanced Research Institute for Cell and Gene Therapy, Tofflon Group, China* Cell Signaling Technology Company Presentation **GMP-Grade Recombinant Monoclonal Antibody Conjugates for Cell Therapy Manufacturing & QC** MR 324 | 13:15 - 13:30 **Speaker:** Ryan Tay, *PhD, Commercial Lead APAC, Cell Signaling Technology, Singapore*

12:15 - 13:45	**Agilent Company Presentation** **Accelerating Cell & Gene Therapy Innovation with Agilent Cell Biology and Genomics Solutions** MR 324 | 13:30 - 13:45 **Speakers:** Lee Chee Yang, *PhD, Senior Field Application Scientist, Diagnostics and Genomics Group, South Asia Pacific, Agilent Technologies Singapore (Sales) Pte Ltd., Singapore* Federica Tomay, *PhD, Field Application Scientist, South Asia Pacific, APAC Technical Specialization & Solutions, Singapore*
13:45 - 14:45	**Bending the Cost Curve in CGT: Viral Vectors, GMP Cell Banks, and Early Technology Adoption** Summit 2 **Chair:** Sudipto Bari, *PhD, Advanced Cell Therapy and Research Institute, Singapore (ACTRIS), Singapore* **Speakers:** Lucas Chan, *PhD, Lucas Chan Consulting Pte Ltd; Yong Loo Lin School of Medicine, National University of Singapore, Singapore* Sarah Ho, *PhD, AGeM Bio, Singapore* Jaichandran Sivaligam, *PhD, A*STAR Bioprocess Technology Institute, Singapore*
	Accelerating the CGT Translational Pathway: Integrating AI and Autonomous Systems MR 325-326 **Chair:** William YK Hwang, *MBBS, MMed, FRCP, FAMS, MBA, National Cancer Center; Singapore General Hospital; REMEDIS, SingHealth, Singapore* **Speakers:** Michael Fehlings, *PhD, ImmunoScape, United States* Genki N. Kanda, *PhD, Institute of Science Tokyo (Science Tokyo), Japan*
15:00 - 16:00	**Centralized or Point-of-Care? The Models Shaping Asia's Next Wave of CGT Manufacturing** Summit 2 **Chair:** Gabrielle O'Sullivan, *PhD, MPH (Hons), Sydney Local Health District, Australia* **Speakers:** Usanarat Anurathapan, *MD, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand* Shin Kawamata, *MD, PhD, Kobe University, Japan* Nguyen Thanh Liem, *MD, PhD, Center for Regenerative Medicine and Cell Therapy, Vinmec Healthcare System, Vietnam*
	Nucleic Acid Therapeutics: From Delivery Innovation to Clinical Translation MR 325-326 **Chair:** Jonathan Yuin-Han Loh, *PhD, Institute for Molecular and Cell Biology (IMCB), A*STAR, Singapore* **Speakers:** Andre Choo, *PhD, National University of Singapore; A*STAR Bioprocessing Technology Institute (BTI), Singapore* Minh T. N. Le, *PhD, Department of Pharmacology, Institute for Digital Medicine, Yong Loo Lin School of Medicine; National University of Singapore, Singapore* Stanley Qi, *PhD, Stanford University, United States*

15:00 - 16:00	**Oral Abstracts Session 3 - Early Stage Professionals (ESP)** MR 324 Abstract Presenters: **AAV-Mediated Dual-Gene Therapy Restores Metabolism and Mitochondrial Structure in Propionic Acidemia** Yue Zhang, *PhD, Zhejiang University, China* **Precision Correction of a Nonsense Mutation Using Base Editing and Prime Editing** Hsien-Yin Kao, *Westmead Institute for Medical Research, University of Sydney, Australia* **Functional efficacy of EphA2 CAR T-cells generated from paediatric osteosarcoma patients** Amanda Tan, *PhD, Kids Research, Australia* **Development of Next-Generation iPSC-Derived Nephron Progenitor Cells (INPCS) for Advanced CKD Toward Clinical Translation** Toshikazu Araoka, *MD, PhD, Center for iPS Cell Research and Application (CiRA), Kyoto University, Japan* **Umbilical Cord Mesenchymal Stem Cell-Derived Secretome as a Potential Treatment for Systemic Lupus Erythematosus: a Double-Blind Randomized Controlled Trial** Arief Nurudhin, *MD, PhD, Medical Faculty Universitas Sebelas Maret/Moewardi General Hospital, Indonesia* **Multifunctional Chitosan/Tannic Acid Cryogels as a Charge-Selective BMP-4 Delivery Platform for Bone Regeneration** Hyejin Jo, *B.Eng, Dongguk University, South Korea*

Keynote Session

The Next Chapter in the Fantastic Voyage of CAR T Cell Therapy: Potency, Access, and Delivery

Wednesday, September 2, 2026 | 8:30 - 9:00

Summit 2

Bruce Levine, PhD, University of Pennsylvania, United States

With a history of first-in-human clinical trials, Dr. Levine's work has consistently focused on what it takes to make engineered cell therapies reliable, manufacturable, and accessible. Drawing on insights from more than 200 scientific articles and book chapters, and co-invention of over 30 U.S. patents, his keynote will explore how the field can responsibly broaden patient impact by improving cell potency and production while maintaining the quality systems that advanced therapies require.

Key Topics

1. Next-Gen Manufacturing: Automation, closed systems, analytics, and standardization to improve scalability and consistency across centralized and hybrid models.

2. Expanding Horizons: Progress and remaining barriers in applying cell therapy to solid tumors and autoimmune diseases.

3. Beyond Autologous: Realistic paths forward for in vivo strategies, including the hurdles that continue to shape adoption.

Join us to engage with one of the field's pioneers and explore what it will take to translate innovation into dependable therapies for patients across the region.

Plenary Sessions

Delivering Clinically Ready MSC-Exosomes for Real-World Use

Wednesday, September 2, 2026 | 17:00 - 18:30

Summit 2

Chair: Chi-Ying Huang, PhD, National Yang Ming Chiao Tung University, Taiwan

Clinical Potential of MSC-Derived Extracellular Vesicles: Challenges in Production and Characterization

Bernd Giebel, PhD, University Hospital Essen (Universitätsklinikum Essen); University of Duisburg-Essen, Germany

From Discovery to Translation: Advancing MSC-sEVs as Regenerative Biologics

Sai Kiang Lim, PhD, Paracrine Therapeutics, Singapore

First-in-Human Study of GMP-Compliant UC-MSC EVs in Japan

Takahiro Ochiya, PhD, Institute of Medical Science, Tokyo Medical University, Japan

MSC-derived exosomes are rapidly moving toward clinical and commercial application, particularly within Asia's fast-growing regenerative medicine ecosystem. This session provides practical insights into solving core challenges in MSC-exosome development, including MSC source heterogeneity, scalable GMP manufacturing, and defining meaningful potency and identity CQAs. Speakers will present emerging evidence on mechanisms of action and outline regulatory pathways that support consistent, clinically deployable products. Attendees will gain clear, actionable guidance for advancing MSC-exosome therapies from innovation to real-world clinical use.

From Journal Paper to Patients - Translating CAR-T, TCR and Gene Therapy Innovation

Thursday, September 3, 2026 | 10:45 - 12:15

Summit 2

Chair: Suradej Hongeng, MD, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand

mRNA Based T cell Engineering for HBV-related Hepatocellular Carcinoma

Antonio Bertoletti, MD, Duke NUS Medical School, Singapore

In Vivo Gene Therapy for Genetic Diseases - Moving from Fundamental to Translational Science

Guanping Gao, PhD, UMass Chan Medical School, United States

The Patient Product Persistence Perplexity and Pivot

Bruce Levine, PhD, University of Pennsylvania, United States

Recent high-impact research in CAR-T engineering, TCR therapy, and gene therapy platforms is now driving real clinical translation across the Asia-Pacific region. This session highlights evidence-based advances that expand indications beyond oncology, improve durability and persistence, and strengthen vector design and manufacturability. Speakers will present practical insights to help regional programs translate cutting-edge research into scalable, regulator-ready therapies.

iPSC-Derived Therapies in Clinical Practice: Opportunities, Challenges, and Emerging Pathways

Thursday, September 3, 2026 | 15:00 - 16:30

Summit 2

Chair: Masayo Takahashi, MD, PhD, Vision Care Inc., Japan

Translational Advances and Clinical Development of iPSC-Derived Therapies in China

Riguo Fang, PhD, Theia Therapeutics, China

iPSC-Derived Therapies in Clinical Practice: Opportunities, Challenges, and Emerging Pathways

Takesi Matsuyama Hoyos, PhD, Vision Care Inc., Japan

iPSC Derived Cells for Therapy

Mahendra Rao, MBBS, PhD, MD-Bio; NKURE, United States

Asia has become a global leader in iPSC-derived cell therapy development and clinical translation, supported by unique regulatory pathways and real-world implementation frameworks. This session presents the latest clinical progress in Asia and beyond, featuring first-hand trial experience and evolving regulatory strategies. While challenges in scalability, long-term safety, and cost remain, participants will gain forward-looking insights into the scientific and policy foundations needed for sustainable commercialization.

Cutting-Edge Technologies Transforming Cell Therapy Manufacturing

Friday, September 4, 2026 | 10:45 - 12:15

Summit 2

Chair: Steve Oh, PhD, Independent Cell Therapy Consultant, Singapore

iCellPro: AI-Powered Automated Cell Manufacturing System

Chia-Yi Hsu, PhD, DrSignal BioTechnology Co., Ltd., Taiwan

Strategic Diversification in the Development of iPSC-based Chondroprotective Therapies

Ji Hyeon Ju, MD, PhD, YiPSCELL, South Korea

Agent-AI-Based Cell and Gene Product Manufacturing and Digital Twin

Shin Kawamata, MD, PhD, Kobe University, Japan

Asia is rapidly adopting advanced cell manufacturing technologies to support the expansion of cell and gene therapies, driven by innovations in AI, automation, and QbD-based manufacturing. This session will highlight practical approaches for automated production, selection of scale-up and scale-out strategies, and regulatory considerations for implementing new technologies. Speakers will provide insights to help regional programs build efficient, compliant, and scalable manufacturing systems.

Concurrent Sessions

Breaking Through the Commercial Ceiling: Challenges and the Future of Approved Allogeneic MSCs

Wednesday, September 2, 2026 | 09:15 - 10:15

Summit 2
Chair: Daniel J. Weiss MD, PhD, University of Vermont, United States

Title Forthcoming
Silviu Itescu, MBBS, FRACP, Mesoblast, Australia

Commercial-stage Allogeneic MSC Product CARTISTEM® : Market-Access Experience and Strategy in Korea, Japan and the U.S.
Antonio Lee, PhD, MEDIPOST Co., Ltd, South Korea

The Journey to Developing and Securing Approval for the World's First Cell Therapy for TBI
Keita Mori, MBA, SanBio Co., Ltd., Japan

Launching an allogeneic MSC therapy requires navigating divergent regulatory pathways and reimbursement landscapes. This session provides a comparative look at approved products across the U.S., Japan, and South Korea. Drawing on first-hand corporate case-sharing, speakers will address the hard realities of localized hurdles, evolving payer expectations, and industrial manufacturing frameworks needed to sustain cross-border success and future expansion.

Regenerative Medicine in Action: Translating Tissue-Specific Regeneration from Bench to Bedside

Wednesday, September 2, 2026 | 10:45 - 11:45

Summit 2
Co-Chairs:
- Pawan Gupta, MBBS, MD, DNB, PhD, Stempeutics Research, India
- Xinyi Su, MBBChir, PhD, FAMS, Institute of Molecular and Cell Biology (IMCB), A*STAR, Singapore

Title Forthcoming
Kenon Chua, MBBS,MRCSEd, MMed, MCI, FRCSEd, Singapore General Hospital, Singapore

Regenerative Therapy for the Corneal Endothelium
Jod S Mehta, MBBS, PhD, FRCOphth, FRCS (Ed), FAMS, FARVO, Singapore National Eye Centre, Singapore

Decoding Cardiac Progenitors: Unraveling the Path to Heart Regeneration
Lynn Yap, PhD, Lee Kong Chian School of Medicine, NTU, Singapore

Moving past proof-of-concept, tissue-specific regenerative platforms across musculoskeletal, ocular, and cardiovascular systems are now demonstrating meaningful clinical impact. This cross-disciplinary session explores how these emerging cell, gene, and biologic therapies are reshaping chronic disease management, highlighting key translational milestones, regional regulatory progress, and pivotal clinical outcomes.

Bringing Cellular Immunotherapy to More Patients: Improving Potency While Controlling Cost

Wednesday, September 2, 2026 | 13:00 - 14:00

Summit 2
Chair: Sai Kiang Lim, PhD, Paracrine Therapeutics, Singapore

Title Forthcoming
*Jonathan Yuin-Han Loh, PhD, Institute for Molecular and Cell Biology (IMCB), A*STAR, Singapore*

Clinical Development of a Rescue Protein Based Novel Cell Immunotherapy for the Reversal of Immune Exhaustion and Treatment of Solid Tumors
Yosef Refaeli, PhD, Ascensus Therapeutics, Inc., United States

Democratizing CAR-T Therapy: Low-Cost, GoFast™ Manufacturing on a Scalable Platform
Yuchen Zhou, PhD, Applied Cells, United States

This session examines emerging strategies to make cellular immunotherapy more clinically and economically accessible. It brings together advances that extend cellular therapies beyond oncology, enhance cell function without permanent genetic modification, and streamline manufacturing to reduce cost and shorten vein-to-vein time. By integrating clinical experience, molecular innovation, and process optimization, the session highlights practical pathways to deliver potent therapies at a scale and cost that support broader patient access.

Navigating CGT Starting Material Requirements Across Asia: Harmonization and Cultural Compliance

Wednesday, September 2, 2026 | 13:00 - 14:00

MR 325 - 326

Chair: Yoji Sato, PhD, National Institute of Health Sciences (NIHS), Japan

Title Forthcoming

Taruna Ikrar, PhD, Indonesian Food and Drug Authority (BPOM), Indonesia

Asia-Specific Challenges in CGT Starting Material Requirements: Case Study on Allogeneic Cord Blood in Korea vs. Japan vs. US

Genny Jin, PhD, MEDIPOST Korea, South Korea

Achieving regulatory alignment for CGT starting materials is critical for global supply chain scaling, yet Asia's regional landscape demands highly customized CMC strategies. This session maps starting material regulations across major Asian jurisdictions and will dissect technical and regulatory solutions for specialized regional mandates, specifically the operational execution of Halal requirements for autologous cell products.

Expanding the Reach of CAR-T Cell Therapy: Clinical Advances and Manufacturing Innovation

Wednesday, September 2, 2026 | 14:15 - 15:15

Summit 2

Co-Chairs:

- Bruce Levine, PhD, University of Pennsylvania, United States
- Francesca Lorraine Lim, MBBS, BSc, MMED,MRCP(UK), Singapore General Hospital, Singapore

CAR-T Cell Therapy: Breaking Boundaries from Hematology to Solid Tumors and Autoimmunity

Alex H. Chang, PhD, YaKe Biotech, China

Outcomes of CD19 CAR-T Therapy for Relapsed/ Refractory B-cell Acute Leukemia in China

Kai Yan Liu, MD, PhD, Lu Daopei Hospital, China

CLDN18.2 Targeted CAR-T Cell Therapy in Gastric Cancer

Changsong Qi, PhD, Peking University Cancer Hospital, China

Gain a rare, end-to-end view of China's CAR-T landscape, spanning real-world clinical outcomes and manufacturing innovation. This session connects advances in addressing CAR-T durability and safety with scalable manufacturing approaches and emerging indications, including solid tumors, offering practical lessons that extend beyond publications for teams operating in Asia and globally.

Beyond the Conventional Trials: Leveraging Plausible Mechanism and RWE to Accelerate CGT Development

Wednesday, September 2, 2026 | 14:15 - 15:15

MR 325 - 326

Chair: Eddie Tan, PhD, EMBA, CABP, Centre of Regulatory Excellence, Duke-NUS Medical School, Singapore

Title forthcoming

Megha Kaushal, MD, MSc, US Food and Drug Administration (FDA), United States

Title Forthcoming

Chang Liu, PhD, ASK Health Asia, Singapore

Real-World Evidence in Cell and Gene Therapy Development: PMDA Perspective

Yusuke Nozaki, MS, Pharmaceuticals and Medical Devices Agency (PMDA), Japan

Beyond Conventional Trials: Leveraging Advanced Regenerative Medicine Clinical Research to Accelerate Cell and Gene Therapy Development in South Korea

Yun-Kyoung Song, PhD, College of Pharmacy, The Catholic University of Korea, South Korea

This session breaks down the core operational implications of this framework and explores how sponsors can merge adaptive trial designs with robust Real-World Evidence (RWE) to accelerate clinical timelines. Bringing together regulatory experts, the discussion highlights practical evidence-generation strategies across the product lifecycle to streamline the path to market.

Emerging Cell & Gene Therapy Ecosystems in Asia: New Hubs, New Models, New Opportunities

Wednesday, September 2, 2026 | 15:45 - 16:45

Room: Summit 2

Chair: Matias Ilmari Autio, PhD, A*STAR; GIS; National University of Singapore, Singapore

From Bench to Bedside to Handoff: A Translational Development Center Model for ATMP Ecosystem Building in Emerging Economies

Chaiyong Koaykul, PhD, Faculty of Medicine, Chulalongkorn University, Thailand

Cell & Gene Therapy Landscape in India; Understanding the Regulations and Partnering Opportunities

Dinesh Kundu, MBBS, MBA, East Ocyon Bio Private Limited, India

Title Forthcoming

Nguyễn Ngô Quang, Department of Science, Technology and Training, Vietnam

Evolving Cell & Gene Therapy Ecosystem In Asia: The Malaysia Experience

James Khong Lek Then, MSc, Cryocord, Malaysia

Discover how emerging CGT ecosystems across South and Southeast Asia are rapidly building credible advanced therapy capabilities. Through four country-specific perspectives, this session offers a regional view of progress from laboratory innovation to clinical translation. Discussions will spotlight manufacturing advances and the regulatory reforms reshaping how CGTs are developed, delivered, and expanded for broader global patient access.

Potency Assays and Comparability: Navigating a Changing Landscape

Wednesday, September 2, 2026 | 15:45 - 16:45

MR 325 - 326

Chair: Srinivasan N. Kellathur, PhD, Roche Singpaore, Singapore

Comparability Strategies for Cell and Gene Therapies - Manufacturing Perspective

Lucas Chan, PhD, Lucas Chan Consulting Pte Ltd; Yong Loo Lin School of Medicine, National University of Singapore, Singapore

Comparability Assessment and Potency Assays: The Japanese Regulatory Perspective

Atsushi Nishikawa, MSc, Pharmaceuticals and Medical Devices Agency (PMDA), Japan

Comparability Considerations of Cell and Gene Therapy Products Subjected to Manufacturing Changes

Ying Zhang, PhD, Health Sciences Authority, Singapore

Manufacturing modifications are inevitable across the CGT lifecycle, making scientifically robust potency assays and comparability frameworks non-negotiable. This session examines how the new ICH Q5E ATMP annex reshapes process validation and matrix strategies for advanced therapeutics. Speakers will discuss practical approaches to aligning functional characterization with clinical relevance, providing developers with clear strategies to withstand international regulatory scrutiny.

Beyond the Hype: Re-Engineering the Promise of MSC Therapy

Thursday, September 3, 2026 | 08:00 - 09:00

Summit 2

Chair: Pawan Gupta, MBBS, MD, DNB, PhD, Stempeutics Research, India

Optimizing MSCs: iPSC Sourcing and Gene Engineering

Miguel Forte, MD, PhD, Kiji Therapeutics; mC4Tx, Belgium

MSC for Immune Mediated Disorders: The Right Cell in the Right Place at the Right Time

Edwin M. Horwitz, MD, PhD, Emory University School of Medicine, United States

Future of MSCs in Therapeutic Application: Sciences and Clinical Development

Daniel J. Weiss MD, PhD, University of Vermont, United States

Mesenchymal stromal cells (MSCs) have demonstrated broad therapeutic potential, yet clinical outcomes have often been inconsistent across indications. This session examines the biological and translational factors underlying MSC performance, explores how disease context and treatment timing influence therapeutic activity, and highlights emerging strategies to enhance efficacy through genetic engineering and iPSC-derived MSC platforms. Together, these perspectives offer a roadmap for improving the consistency, potency, and clinical impact of MSC-based therapies.

Uncovering the Preclinical Evidence Behind the Multi-Indication Therapeutic Promise of MSC Exosomes

Thursday, September 3, 2026 | 09:15 - 10:15

Summit 2

Chair: Bernd Giebel, PhD, University Hospital Essen (Universitätsklinikum Essen); University of Duisburg-Essen, Germany

The Effects of MSCs and Their sEV in Allergic Airway Inflammation

Qing-Ling Fu, MD, PhD, The First Affiliated Hospital, Sun Yat-sen University, China

Title Forthcoming

Thai-Yen Ling, PhD, National Taiwan University, Taiwan

Immunomodulatory Mechanisms and Potency Attributes of MSC Exosomes in Joint Repair

Wei Seong Toh, PhD, National University of Singapore, Singapore

Assess the state of MSC-derived exosomes as cell-free biologics with multi-indication potential. This session will discuss the scientific rationale underlying the pleiotropic activity of MSC-derived exosomes, linking mechanistic insights and preclinical validation to potency assessment strategies required for successful clinical translation

From Lab to Patient: Scaling CGT Manufacturing from Academic Programs to Broader Access

Thursday, September 3, 2026 | 09:15 - 10:15

MR 325 - 326

Chair: Aloysius Ho, MBBS, MMed, FRCP, FRCPath, Advanced Cell Therapy and Research Institute, Singapore (ACTRIS); Singapore General Hospital; National Cancer Centre Singapore, Singapore

Title Forthcoming

Yunxin Chen, MBBS, Singapore General Hospital, Singapore

Strategic Growth of a Cell Therapy Laboratory: A Data-Driven Framework for Staffing, Quality Assurance, and Workforce Development

Elena Maryamchik, MD, MBA, Memorial Sloan Kettering Cancer Center, United States

An Overview of Global Regulatory Frameworks Governing Cell and Gene Therapy Development Programs

Gabrielle O'Sullivan, PhD, Royal Prince Alfred Hospital, Australia

Building a sustainable CGT program demands more than scientific excellence — it requires operational rigor, regulatory foresight, and access-conscious development from the outset. This session delivers an integrated, practical roadmap across three pillars: data-driven academic manufacturing scale-up covering workload forecasting, staffing algorithms, QA resourcing, training capacity, and enterprise planning; a comparative overview of global regulatory frameworks governing GMP, CMC, and lifecycle expectations; and a start-up CAR-T case study examining how construct innovation and manufacturing strategy can be aligned to broaden patient access across Asia.

Innovating the CGT Toolbox: NAMs and Ancillary Materials for More Efficient Manufacturing

Thursday, September 3, 2026 | 13:45 - 14:45

Summit 2

Chair: Kunihiko Suzuki, MBA, MEDINET Co., Ltd., Japan

A New Approach to Image-Based Process Monitoring and Quality Control in Cell Therapy Manufacturing

Heedon Ahn, MBA, Curiosis, Inc, South Korea

Holotomography and Artificial Intelligence: Label-free Prediction of Pluripotency and Virtual Staining of iPSC Colonies

YongKeun Park, PhD, Tomocube Inc., South Korea

Defined by Design: Unlocking the Full Potential of CGT with Chemically Defined Media

Jihye Shin, PhD, Xcell Therapeutics, Inc., South Korea

This session showcases how New Approach Methodologies (NAMs) and advanced ancillary materials are enabling greater efficiency, consistency, and quality in cell therapy development. Case studies from leading innovators will highlight solutions addressing key bottlenecks, offering practical insights to accelerate development, improve CMC performance, and support scalable, high-quality CGT production.

Human Biology in a Dish: iPSC and Organoid Models Transforming Preclinical Testing and Therapeutics Development

Thursday, September 3, 2026 | 17:00 - 18:00

Summit 2

Chair: Natasha Hui Jin Ng, PhD, BetaLife, Singapore

Development of an Extracorporeal Liver Support System Using iPSC-derived Liver Organoids

Maki Kumagai, MSc, The University of Osaka Division of Stem Cell and Organoid Medicine, Japan

Clinical Translation of Colon Organoid Regenerative Medicine (ATORM-C)

Kyung Jin Lee, PhD, OrganoidSciences, South Korea

Establishing Macrophage-Kidney Assembloids to Unravel Context-Dependent Immune Modulation in Kidney Disease

*Yun Xia, PhD, Institute for Molecular and Cell Biology (IMCB), A*STAR, Singapore*

Explore how iPSC derived organoids and multicellular

tissue models are reshaping preclinical testing and therapeutics development by re-creating complex human organ systems, reducing reliance on animal studies and improving translational predictability. This session reviews scientific maturity, emerging applications, and the evolving regulatory landscape, while candidly addressing current limitations and gaps in developing and producing human relevant iPSC and organoid based systems.

From Manufacturing to Market: Advancing Cell Therapies for Global Access

Thursday, September 3, 2026 | 17:00 - 18:00

MR 325 - 326

Chair: Antonio Lee, PhD, MEDIPOST Co., Ltd, South Korea

Path to Achieve MSC Products Approval in India

Pawan Gupta, MBBS, MD, DNB, PhD, Stempeutics Research, India

Place-of-Care Manufacturing of CAR T Cells in Australia

Siok Tey, MBBS, PhD, FRACP, FRCPA, QIMR Berghofer Medical Research Institute; Royal Brisbane; Women's Hospital, Australia

Access by Design: A Connected Place-of-Care Manufacturing Framework for Advanced Therapies in APAC and Beyond

Zlatibor Veličković, BSc (Hons), PhD, Royal Perth Hospital; University of Western Australia, Australia

This session brings together three critical pillars of cell therapy—innovative delivery models, scalable production, and real-world regulatory success. It will examine how novel production approaches can be integrated with regulatory pathways to enable accessible therapies in the Asia-Pacific region, addressing key challenges including decentralized versus centralized models, GMP compliance, cost reduction, and regulatory complexity.

Scaling iPSC Mass Production Through Automated GMP Systems and Data Driven Quality Frameworks

Friday, September 4, 2026 | 08:00 - 09:00

Summit 2

Chair: Shin Kawamata, MD, PhD, Kobe University, Japan

Bridging Research and Regulated Manufacturing: Flexible Automation with an Automated Cell Culture Platform

Hiroko Hanzawa, PhD, Hitachi, Japan

Fully Automated and Closed iPSC Expansion Platform with Process Monitoring

Masaki Hosoya, PhD, Sinfonia Technology Co., Ltd, Japan

Building a Digital Manufacturing Platform for iPSC-Based Cell Therapy Products Through Robotics, AI, and Quality Analytics

Atsushi Inoue, PhD, Cellafa Bioscience Inc, Japan

Accelerating the next generation of iPSC-based cell therapies requires shifting from manual laboratory processes to automated, large-scale GMP manufacturing. This session evaluates latest automation technologies and critical regulatory frameworks, contrasting QbD and non-QbD approaches to secure critical quality attributes. Panelists will also explore the integration of AI and advanced IT systems to optimize production beyond the factory floor.

From Ex Vivo to In Vivo: Reshaping Cell and Gene Therapy for Blood Disorders

Friday, September 4, 2026 | 09:15 - 10:15

Summit 2

Co-Chairs:

- Edwin M. Horwitz, MD, PhD, Emory University School of Medicine, United States
- Eng Soo Yap, MBBS, MMED, MRCP (UK), FRCPath, Department of Laboratory Medicine, Ng Teng Fong General Hospital; Department of Medicine, Yong Loo Lin School of Medicine; National University of Singapore, Singapore

Progress and Prospects of In Vivo CAR-T

Mei Heng, MD, PhD, Union Hospital, Huazhong University of Science and Technology, China

Point of Care for Gene Therapy in Hemoglobinopathies

Suradej Hongeng, MD, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand

Title Forthcoming

Pansakorn Tanratana, MD, PhD, Mahidol University, Thailand

Asia is emerging as a significant contributor to in vivo cell and gene therapy, with active clinical programs across the region advancing rapidly. This session moves beyond established ex vivo approaches to spotlight next-generation in vivo platforms, CAR-T cells, gene editing, andMRNA therapeutics applied to hematological conditions—including multiple

myeloma, inherited blood disorders, and hemophilia. Attendees will gain first-hand insights into the regional clinical progress reshaping how blood diseases are treated.

Bending the Cost Curve in CGT: Viral Vectors, GMP Cell Banks, and Early Technology Adoption

Friday, September 4, 2026 | 13:45 - 14:45

Summit 2

Chair: Sudipto Bari, PhD, Advanced Cell Therapy and Research Institute, Singapore (ACTRIS), Singapore

In Vivo and Ex Vivo Vector Development and Manufacture - Key Considerations

Lucas Chan, PhD, Lucas Chan Consulting Pte Ltd; Yong Loo Lin School of Medicine, National University of Singapore, Singapore

Rethinking Cost of Goods in Cell and Gene Therapy: Non-Viral Engineering for Scalable Off-the-Shelf MSC Manufacturing

Sarah Ho, PhD, AGeM Bio, Singapore

Developing GMP-ready Scalable Manufacturing Workflows for Immune Cell Therapy Pipelines

*Jaichandran Sivaligam, PhD, A*STAR Bioprocess Technology Institute, Singapore*

Transform COGS from a barrier into a competitive advantage. This practical session identifies the primary cost drivers in CGT manufacturing and connects them to actionable levers: high-yield viral vector production, optimized GMP cell banking, and data-driven automated process development. Leave with a prioritized playbook to reduce costs, accelerate time-to-clinic, and ensure your process remains fully GMP-compliant and comparability-ready.

Accelerating the CGT Translational Pathway: Integrating AI and Autonomous Systems

Friday, September 4, 2026 | 13:45 - 14:45

MR 325 - 326

Chair: William YK Hwang, MBBS, MMED, MRCP, FAMS, MBA, National Cancer Center; Singapore General Hospital; REMEDIS, SingHealth, Singapore

Building Next-Generation T Cell Therapies for Solid Tumors: From AI-Driven T Cell Receptor Discovery to Addressing Therapeutic Challenges

Michael Fehlings, PhD, ImmunoScape, United States

Toward Full Automation of Cell and Gene Therapy Research

Genki N. Kanda, PhD, Institute of Science Tokyo (Science Tokyo), Japan

This session examines the critical role of artificial intelligence and automation in bridging the gap between discovery and clinical delivery. Experts will discuss the transition toward autonomous, robotic closed-loop manufacturing, AI-augmented prognostic modeling for clinical decision support, and the digital infrastructure required to scale next-generation therapies. By evaluating the Asia-Pacific landscape, the session provides a roadmap for operationalizing precision-built advanced therapies on a global scale.

Centralized or Point-of-Care? The Models Shaping Asia's Next Wave of CGT Manufacturing

Friday, September 4, 2026 | 15:00 - 16:00

Summit 2

Chair: Gabrielle O'Sullivan, PhD, MPH (Hons), Sydney Local Health District, Australia

Point-of-Care CGT Manufacturing System in Thailand

Usanarat Anurathapan, MD, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand

Centralized, Point-of-Care and Hybrid Manufacturing - A New Modality for CGT from Therapy Accessibility

Shin Kawamata, MD, PhD, Kobe University, Japan

Safety and Efficacy of Allogeneic Umbilical Cord-Derived Mesenchymal Stem Cell Infusion for Frailty: A Phase II Randomized Controlled Trial

Nguyen Thanh Liem, MD, PhD, Center for Regenerative Medicine and Cell Therapy, Vinmec Healthcare System, Vietnam

Compare centralized and PoC manufacturing through the lenses of cost, safety, release timelines, and system readiness in diverse Asian healthcare settings. Learn where each model excels, what standardization and training require, and how programs are navigating approvals and operational realities to expand patient access.

Nucleic Acid Therapeutics: From Delivery Innovation to Clinical Translation

Friday, September 4, 2026 | 15:00 - 16:00

MR 325 - 326

Chair: Jonathan Yuin-Han Loh, PhD, Institute for Molecular and Cell Biology (IMCB), A*STAR, Singapore

Title Forthcoming

*Andre Choo, PhD, National University of Singapore; A*STAR Bioprocessing Technology Institute (BTI), Singapore*

RNA Delivery Using Extracellular Vesicles: A Natural Solution for Gene Therapy

Minh T. N. Le, PhD, Department of Pharmacology, Institute for Digital Medicine; Yong Loo Lin School of Medicine; National University of Singapore, Singapore

Title Forthcoming

Stanley Qi, PhD, Stanford University, United States

This session explores the rapid evolution of nucleic acid therapeutics, including siRNA,MRNA, and gene editing, with a focus on how advances in delivery technologies are enabling clinical translation. Bringing together leaders across national strategy, platform development, and disease applications, it will examine how overcoming tissue-specific delivery challenges is expanding impact beyond rare diseases into oncology, immunology, and regenerative medicine.

Roundtable Sessions

Breaking the Code to CGT Access: Availability, Affordability, and Alignment

Wednesday, September 2, 2026 | 10:45 - 11:45

Room: MR 325 - 326
Moderator: Miguel Forte, MD, PhD, Kiji Therapeutics; mC4Tx, Belgium

Panelists:
- Masayo Takahashi, MD, PhD, Vision Care Inc., Japan
- Kitipong Uaesoontrachoon, PhD, Genepeutic Bio Co.,Ltd, Thailand
- Phil Vanek, PhD, Redline Bioadvisors, United States

This roundtable explores the three interdependent pillars shaping CGT access in Asia—availability, affordability, and alignment. Panelists will discuss how access pathways and infrastructure influence availability, why conventional affordability models often fall short in heterogeneous markets, and how aligning development, regulatory, and commercialization strategies with local healthcare systems, stakeholders, and patient needs is essential to enabling sustainable and meaningful access.

From Regional Investment to Global Success: Commercializing CGT Pipelines in Asia, Europe, and the US

Thursday, September 3, 2026 | 13:45 - 14:45

Room: MR 325 - 326
Moderator: Antonio Lee, PhD, MEDIPOST Co., Ltd, South Korea

Panelists:
- Eytan Abraham, PhD, Minaris Advanced Therapies, United States
- Pawan Gupta, MBBS, MD, DNB, PhD, Stempeutics Research, India
- Colin Lee Novick, BA, Innovacell Inc., Japan

CGT investment landscape in Asia is different to that of North America & Europe. Commercial and late-stage CGT developers from India and Japan will share their journey through local and international investments reaching to successful commercialization of their pipelines. A perspective from global CGT CDMO with presence in United States, Japan and Europe will add additional insights into how investments to and from Asia is shaping the CGT industry in APAC region.

Inside the Investor Mindset: What Makes a CGT Venture Fundable

Friday, September 4, 2026 | 08:00 - 09:00

Room: MR 325 - 326
Moderator: Natasha Hui Jin Ng, PhD, BetaLife, Singapore

Panelists:
- Robert Ang, MBBS, MBA, Vor Bio, Singapore
- Jolene Ooi, PhD, EDBI Pte Ltd, Singapore
- Phil Vanek, PhD, Redline Bioadvisors, United States

Engage with corporate venture, public, and private investors to uncover the critical factors that make CGT companies fundable in today's market. Panelists will unpack how they evaluate platform technologies, translational readiness, regulatory strategy, and IP—alongside the mounting pressures of scalability and manufacturing. Gain practical guidance to strengthen fundraising, strategic partnerships, and company design within Asia's fast-evolving ecosystem as it advances in lockstep with global therapeutic development.

From Policy to Patient Bedside: How Regulatory Innovation in China, Japan, and Singapore Impacts Equitable Access to Decentralized CGT Manufacturing

Friday, September 4, 2026 | 09:15 - 10:15

Room: MR 325 - 326
Moderator: Zlatibor Veličković, BSc (Hons), PhD, Royal Perth Hospital; University of Western Australia, Australia

Panelists:
- Lisa Guan, PhD, Miltenyi Biotec, China
- Kunihiko Suzuki, MBA, MEDINET CO., Ltd., Japan
- Eddie Tan, PhD, EMBA, CABP, Centre of Regulatory Excellence, Duke-NUS Medical School, Singapore

Thank you to our ISCT Asia 2026

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Corporate Program

Access The Full Richness Of Biological Complexity With Single Cell And Spatial Multiomics

10x Genomics Company Presentation

MR 324

Thursday, September 3, 2026 | 08:45 - 09:00

Speakers:

- Benson Lim, PhD, Senior Science and Technology Advisor, 10x Genomics, Singapore

The vast complexities of cancer are characterized by heterogeneity across samples, from tumor cells and tumor microenvironments to therapeutic responses. Elucidating disease mechanisms requires a deep understanding of these complexities. Join 10x Genomics to learn how researchers are using our single cell assays and spatial tools to gain a multidimensional view of cancer.

The Future-Ready CAR-T Playbook: Winning Across Ex Vivo and In Vivo Frontiers

Cytiva Corporate Session

MR 324

Wednesday, September 2, 2026 | 09:15 - 10:15

Speakers:

- Peiqing Zhang, Scientific Director, Genomic Medicine, Cytiva, Singapore
- Alan K. Smith, PhD, Global Head of Innovation, Cell and Gene Therapy, Rose BioSolutions, Inc., United States
- Martin Rabel, Service Solution Specialist, Cytiva, Germany

CAR-T is moving fast and the next wave will demand more than one winning formula.

This session brings together two powerful frontiers shaping the future of CAR-T: flexible ex vivo manufacturing and in vivo T cell reprogramming.

The ex vivo talk will share real-world experience with the SefiaTM manufacturing platform, highlighting how flexible, modular manufacturing can support diverse CAR-T workflows beyond fixed, fully integrated systems.

The in vivo talk will spotlight targeted LNP technology as a non-viral path to CAR-T - shifting CAR-T manufacturing to inside the body. A case study will show how targeted LNPs can drive precise and potent T cell reprogramming in vivo, offering a potential route to overcome some of the toughest barriers of ex vivo CAR-T: complexity, time, scale, and access.

Join us for a practical, forward-looking discussion on how to build CAR-T strategies that are adaptable, scalable, and future-ready across ex vivo and in vivo frontiers.

Session Objectives:

1. See where CAR-T is heading next – across flexible ex vivo manufacturing and in vivo reprogramming
2. Learn how modular platforms can unlock workflow flexibility beyond fixed, fully integrated systems
3. Explore targeted LNPs as a non-viral route to in vivo CAR-T, shifting cell engineering inside the body
4. Walk away with a sharper playbook for building adaptable CAR-T strategies across ex vivo and in vivo frontiers

Principles in Viral Safety Testing for Cell and Gene Therapy Products

Charles River Laboratories Company Presentation

MR 324

Wednesday, September 2, 2026 | 10:15 - 10:45

Speaker:

Colette Cote, PhD, Executive Director and Scientific Advisor, Charles River, USA

The manufacturing processes of innovative cell and gene therapy products have no or only limited viral clearance capacities. Therefore, virus safety testing is key for the used starting materials and raw materials to prevent that viral contaminants are introduced into the manufacturing process. In addition to or as an alternative to traditional viral detection methods, next-generation sequencing (NGS) can be utilized for the detection of viral contaminants.

Session Objectives:

1. Viral contamination risk mitigation strategy for biologics
2. Viral contamination risk mitigation strategy for CGT
3. Traditional adventitious virus detection methods & limitations
4. Virus detection by NGS
5. Adventitious agent test strategy for HEK293 cells
6. Replication competent viral vectors

Building a Regenerative Medicine Ecosystem in Asia: From CDMO to IDMO

ZHENG YANG Biomedical Technology Co., Ltd. Company Presentation

MR 324

Wednesday, September 2, 2026 | 10:45 - 11:00

Speaker:

Sean Chang, CEO, Locus Cell Co., Ltd., Taiwan

This session explores how regenerative medicine products move from clinical development to manufacturing readiness, and how Taiwan is emerging as a key hub within Asia's regenerative medicine ecosystem. Through insights from advanced therapy manufacturing and a regenerative ophthalmology case study involving collaboration between Taiwan and Australia, attendees will learn how clinical, regulatory, and manufacturing capabilities can be integrated to accelerate the development and delivery of regenerative medicine products.

Session Objectives:

1. Explore the role of CDMO infrastructure, quality systems, and digital manufacturing in advanced therapy development
2. Learn how Taiwan is building integrated capabilities across clinical, regulatory, and manufacturing domains to support regenerative medicine
3. Examine how cross-border partnerships can accelerate the development and commercialization of regenerative medicine products

AMCAP™ : The One-Pot Solution for Cell & Gene Therapies

ANEMOCYTE Company Presentation

MR 324

ANEMOCYTE
Manufacturing Biotech Innovation

Wednesday, September 2, 2026 | 11:00 - 11:15

Speaker:

Marco Pupo, PhD, Innovation and Development Coordinator, Italy

Anemocyte is a leading Italian Biotech Manufacturing Organization (BMO) with extensive experience in the field of Cell and Gene Therapies (CGTs) and nucleic acid research, development and manufacturing.

Anemocyte's core capabilities lie in two specific areas of expertise:
- pDNA (Plasmid DNA);
- mRNA (messenger RNA).

The company leverages over twenty-five years of experience to address the continuously evolving needs of the advanced therapies market. A key innovation differentiating Anemocyte is its proprietary, patent-pending technology, AMCAP™ .

AMCAP™ is a game-changing one-pot technology for mRNA synthesis that intelligently merges the crucial steps of transcription and capping into a single, seamless reaction resulting in different key advantages such as increase in efficacy and speed, cost-effectiveness, flexibility and scalability. AMCAP™ enables the rapid synthesis of high-performance mRNA, positioning Anemocyte at the forefront of the enzymatic capping evolution in mRNA manufacturing.

Session Objectives:

1. pDNA and mRNA development and manufacturing solutions
2. Custom and off-the-shelf products
3. Innovative capping technology: AMCAP™
4. Analytical services for pDNA and mRNA needs

Small Is Powerful: Streamlining and Improving Cell Therapy Economics with Lakhesys, the End-to-end Microfluidic Cell Factory

Astraveus Company Presentation

MR 324

ASTRAVEUS

Wednesday, September 2, 2026 | 11:15 - 11:30

Speaker:

Jérémie Laurent, CEO, Astraveus, France

Increasing throughput and decreasing the cost of cell therapy manufacturing are imperatives. While automation helps it does not suffice, the complexity and reagent intensity of current processes requires deeper innovation in manufacturing processes to bring cell therapy to all patients.

Lakhesys is the world first microfluidic cell factory, an integrated and parallelized cell manufacturing platform streamlining cell therapy footprint, labor and reagent consumption. It is currently being tested by leading cell therapy developers.

Session Objectives:

1. Introduce microfluidic end-to-end cell manufacturing working principles and reagent saving characteristics, particularly for cell selection and genetic engineering steps
2. Introduce Lakhesys capabilities, early validation data and perspectives.

Droplet Digital PCR for Cell and Gene Therapy: Enabling Precision from Development to Quality Control

Bio-Rad Laboratories Company Presentation

MR 324

Wednesday, September 2, 2026 | 11:30-11:45

Speaker:
Lee Kee Wah, Regional Marketing Manager, Bio-Rad Laboratories, Singapore

Cell and gene therapy workflows require robust analytical tools that can support confident decision-making from early development through manufacturing and quality control. This 15-minute session will introduce how Droplet Digital PCR, or ddPCR, can help address key analytical challenges in cell and gene therapy, including viral vector quantification, vector copy number assessment, residual DNA testing, genome editing analysis, and cell therapy monitoring.

By partitioning each sample into thousands of droplets, ddPCR enables absolute nucleic acid quantification without the need for a standard curve, supporting high precision and reproducibility in complex biological samples. The presentation will highlight practical examples relevant to CGT development, including viral titer measurement, CAR-T and TCR vector copy number analysis, and monitoring of engineered cells. Attendees will gain a concise overview of where ddPCR can fit into translational research, process development, and QC workflows to improve confidence in advanced therapy development.

Session Objectives:

5. Understand the value of ddPCR for cell and gene therapy analytics.
6. Learn key applications of ddPCR in CGT workflows.
7. Explore how absolute quantification improves data confidence and reproducibility.
8. Identify opportunities to implement ddPCR in development and quality control.

Advancing Clinical Cell Therapy: From Cell Separation to GMP Manufacturing

Miltenyi Biotec Corporate Session

MR 324

Miltenyi Biotec

Wednesday, September 2, 2026 | 12:00 - 13:00

Speakers:

- Ulf Bethke, Executive Expert Cell and Gene Therapy Asia Pacific, Miltenyi Biotec B.V. & Co.KG, Germany
  Caroline Blumer Toti, Head of Clinical Marketing, Miltenyi Biotec B.V. & Co.KG, Germany
- Ledio Bocova, Global Product Manager CliniMACS Systems, Miltenyi Biotec B.V. & Co. KG, Germany

As cell and gene therapy manufacturing evolves, there is an increasing need for integrated solutions that support efficient, standardized, and GMP-compliant manufacturing solutions. This symposium highlights three key aspects of advancing clinical cell therapy manufacturing.

- The first part introduces the new CliniMACS Plus® Instrument to improve operations and expand capabilities. A new design, validated applications, new software and services set the new bar for reliable clinical-scale cell separation workflows.
- The second part explores the latest advancements in T cell engineering and digitalization of cell manufacturing and QC, and how we accelerate customers on their journey to accelerate the path to CAR T cell therapy manufacturing.
- The third part shares Miltenyi's practical experience in designing modular GMP facilities for CAR T cell therapy manufacturing. Through real-world case studies, attendees will gain insights into facility planning, implementation, scalability, and regulatory considerations - from brown-field and small-scale manufacturing sites to commercial-scale facilities.

Together, these sessions demonstrate how innovations in cell processing technologies, digitalization and manufacturing infrastructure can help accelerate the translation of advanced therapies from development to clinical practice.

Session Objectives:

1. Explore the latest advancements in clinical cell separation technologies and their role in enabling standardized, GMP-compliant cell therapy manufacturing.
2. Gain insights into TCT applications, digitalization and acceleration programs to speed up the path to cell therapy manufacturing.
3. Understand practical approaches to designing and implementing standardized, modular GMP facilities for autologous CAR-T cell therapy manufacturing.

SMART G-Rex®: An Introduction to Novel Integrated Process Analytic Technology for Intelligent Automation of CGT Manufacturing

ScaleReady Corporate Session

MR 325 - 326

Wednesday, September 2, 2026 | 12:00 - 13:00

Speaker:

Andrew Scheffler, ScaleReady, United States

SMART G-Rex® represents a novel evolution of the G-Rex® platform, integrating process analytical technology directly into closed-system cell expansion while preserving the simplicity and scalability that define G-Rex® manufacturing.

Attendees will learn how SMART G-Rex® and SensoRex™ use passive resonant sensor technology to generate real-time, non-invasive information about cell expansion without disrupting the culture or requiring burdensome manual sampling. The presentation will explore how SMART-enabled workflows can support harvest timing, preserve closed-system manufacturing, and reduce operator intervention. This approach adds useful process intelligence while preserving a simple manufacturing workflow.

The session will also look ahead to how these capabilities could evolve over time toward intelligent automation, illustrating a broader vision for engineering unnecessary complexity out of CGT manufacturing rather than automating it.

Session Objectives:

1. How can PAT be integrated directly into closed-system G-Rex® manufacturing without adding the complexity CGT teams are trying to avoid?
2. How do SMART G-Rex® and SensoRex™ use passive resonant sensor technology to generate real-time, non-invasive insight into cell expansion?
3. Where can SMART-enabled G-Rex® workflows create value today, and how could they evolve toward intelligent automation and process control

From Cell Expansion to Fill & Finish: Next-Generation Innovations for Scalable Cell Therapy Manufacturing

Thermo Fisher Scientific Corporate Session

MR 324

Wednesday, September 2, 2026 | 14:15 - 15:15

Speakers:

- Ted Tish, Vice President & General Manager, Cell Biology and Advanced Therapies (CBAT), Thermo Fisher Scientific, United States
- Evan R. Zynda, PhD., Senior Innovation Lead, Cell therapy R&D, Thermo Fisher Scientific, United States

This session introduces next-generation technologies and proce ss innovations that support allogeneic cell therapy manufacturing—from engineered T-cell therapies to iPSC-derived regenerative medicines.

Discover how the new Gibco™ CTS™ DynaXS™ single-use bioreactor platform, featuring flexible operating parameters and an automation-ready architecture, enables controlled, cGMP-ready T-cell expansion and scale-up. Downstream, learn how the Gibco™ CTS™ Compleo™ Fill and Finish System automates formulation and fill-finish operations in a functionally closed workflow. Through protocol-driven execution, automated calculations, in-process checks, and flexible batch-size handling, the CTS Compleo system helps improve consistency and quality in final drug product preparation for engineered cell therapies, including CAR-T, CAR-NK, and iPSC-derivatives.

The session concludes with a real-world case study from BetaLife, demonstrating how integrated manufacturing solutions support scalable production of iPSC-derived pancreatic islet cell therapies for insulin-dependent diabetes. Leveraging a proprietary 3D suspension manufacturing process and advanced genome engineering to insert multiple transgenes at safe harbour loci, BetaLife is advancing off-the-shelf allogeneic islet replacement therapies without long-term immunosuppression, with the potential to broaden patient access to a transformative treatment for diabetes.

Session Objectives:

1. The Gibco Cell Therapy System (CTS) portfolio of products is cGMP manufactured, safety tested, and backed by regulatory documentation
2. Learn how to streamline, integrate and scale manufacturing workflows with closed modular instruments, from cell expansion to fill-finish
3. Identify and harness key process control and flexibility benefits for therapy process development while maintaining scalability across diverse cell types
4. Discover real-world case study of how integrated workflow technologies can accelerate the translation of innovative regenerative therapies

Development and FIH Trial for CGT in Japan Market

TEIJIN REGENET CO., LTD. Company Presentation

MR 324

TEIJIN REGENET CO.,LTD.

Wednesday, September 2, 2026 | 15:15 - 15:30

Speaker:

Akihiro Okano, Pharmacist, MBA, Business Development Manager, TEIJIN REGENET CO., LTD., Japan

Teijin Regenet Co., Ltd. is a CDMO providing contract development and manufacturing services for cell therapy and regenerative medicine products. Through its Kashiwa-no-ha Facility and Iwakuni Factory, Teijin Regenet offers flexible support tailored to each stage of development, from products for clinical research and clinical trials to commercial manufacturing.

This presentation will introduce Teijin Regenet's capabilities, including the quality and production technologies cultivated by the Teijin Group in the pharmaceutical and medical device fields, as well as practical know-how in the commercialization of regenerative medicine products through collaboration with J-TEC. The presentation will also highlight Teijin Regenet's experience with various cell therapy modalities, including CAR-T cells, MSCs, and iPSCs.

In addition, the session will describe how Teijin Regenet supports academia, startups, and biotech companies from research and development through commercialization, market launch, and stable supply, leveraging the Kashiwa-no-ha regenerative medicine platform and partnerships in Japan and overseas.

Session Objectives:

1. Understand the value Teijin Regenet provides as a regenerative medicine CDMO
2. Learn about Teijin Regenet's support framework from early-stage development to commercial manufacturing of cell therapy and regenerative medicine products
3. Understand the roles and features of the Kashiwa-no-ha Facility and Iwakuni Factory
4. Gain insight into Teijin Regenet's manufacturing, quality, and regulatory capabilities for modalities such as CAR-T cells, MSCs, and iPSCs
5. Understand how startups and biotech companies can leverage CDMO support to advance commercialization
6. Explore the potential of regenerative medicine development support networks in Japan and the APAC region

CGX10 Cell Isolation System: Workflow Integration for Next Generation Cell Therapy Manufacturing

Sony Corporation Company Presentation

MR 324

Wednesday, September 2, 2026 | 15:30 - 15:45

Speaker:

Marc-Aurele Brun, Sony Corporation, Japan

After a quick review of the CGX10 Cell Isolation System key features, we will present some use cases of integration into closed workflows for the manufacturing of next generation cell therapies, e.g. CAR-T, Treg, TIL, iPSC-based cell therapies.

These will highlight the flexibility of CGX10 to adapt to a variety of innovative cell therapies and requirements thereof such as speed, purity or recovery. Some examples of closed workflow integration with up/downstream processing solutions will also be discussed.

Session Objectives:

1. Rationale for multiparameter selection
2. Type of next generation cell therapies enabled by CGX10
3. Key features of CGX10
4. Key considerations for the integration of CGX10 in a manufacturing workflow: adjustment to critical quality attributes requirements and up/downstream processing solutions

Breaking Barriers in Immune Cell Therapy: Unlocking Scalable Manufacturing from Activation to Analytics

Sartorius Corporate Session

MR 324

Wednesday, September 2, 2026 | 15:45 - 16:45

Speaker:

- Patrick Carney, Ph.D., Chief Business Officer & Chief Operating Officer, Nanotein Technologies
- Rukmini Ladi, Cell Culture Media Expert, Sartorius
- Paul Cashen, Process Expert Commercialisation & Optimisation, Sartorius

Immune cell therapies such as CAR-T hold tremendous promise for previously incurable diseases; however, their broader clinical impact is limited by manufacturing and analytical challenges. Producing T cells at scale while maintaining viability, potency, resistance to exhaustion and long-term persistence remain constant hurdles. This is further compounded by the need for robust assays to consistently measure identity, purity and functional activity across batches. At the same time, CAR-T therapies depend on the supply of high-quality lentiviral vectors, where yield and efficient downstream purification are persistent bottlenecks.

This session will present integrated strategies to overcome these challenges, including the use of novel next-generation immune cell activators, the development of scalable manufacturing processes using stirred-tank bioreactors and DOE-driven process optimization, and advanced analytical approaches such as high-throughput live-cell imaging and cytometry. In addition, key aspects of lentiviral vector purification, such as chromatography and tangential flow filtration, will be discussed. Together, these approaches aim to enable more efficient, reproducible, and accessible manufacturing of immune cell therapies.

Session Objectives:

1. Assess how next-generation soluble immune cell activators can generate more potent immune cells while simplifying workflows and eliminating the need for beads.
2. Examine a case study demonstrating how stirred-tank bioreactors and Design of Experiments (DOE) methodologies were used to identify critical process parameters and develop scalable manufacturing processes while preserving cell functionality.
3. Explore integrated analytical and downstream solutions, including live-cell imaging with high-throughput cytometry for rapid product characterization and scalable lentiviral vector purification strategies to increase process yield of infectious lentiviral vector.

From Causes to Consequences: Decoding Off-Target Events in CRISPR Gene Editing

Broken String Biosciences Company Presentation

MR 324

Thursday, September 3, 2026 | 08:15 - 08:30

Speaker:

Claire Dacombe, VP Sales APAC & EU, Broken String Biosciences, Dubai

Advances in genome editing are enabling cell and gene therapies that offer curative treatment for many diseases. However, unintended off-target DNA breaks remain a key safety concern, as they can drive genomic instability and malignant transformation in edited cells. Comprehensive genome-wide characterisation of on- and off-target breaks is therefore critical across discovery and preclinical development. This need is reinforced by the FDA's April 2026 draft guidance, which recommends NGS-based methods for evaluating off-target editing risk and loss of genome integrity in support of IND applications.

Despite this, sensitive, unbiased methods for therapeutically relevant cells have been limited, relying on indirect readouts, distorted by PCR amplification bias, and an inability to distinguish editing-induced breaks from background damage. These constraints make off-target data difficult to interpret, standardise, and scale.

INDUCE-seq® is a scalable, genome-wide, cell-based platform addressing these limitations through direct, PCR-free mapping of editing-induced DNA breaks, using a novel in situ break-labelling approach coupled with next-generation sequencing. It delivers a sensitive, unbiased, single-nucleotide-resolution readout that characterises on- and off-target sites simultaneously.

This talk presents data linking editing-induced breaks to downstream mutational outcomes, showing why direct detection is essential for safety assessment. We also demonstrate broad applicability across cell types, nuclease systems, and base editing modalities within one standardised workflow.

Session Objectives:

1. Why direct break detection matters: editing-induced DNA breaks link to downstream mutational outcomes, making direct DSB detection essential for safety assessment.
2. Why current methods fall short: indirect readouts, no therapeutic cell context, PCR bias, and an inability to separate editing-induced breaks from background damage.
3. How INDUCE-seq® solves this: PCR-free, in situ break-labelling with NGS for a sensitive, unbiased, single-nucleotide-resolution readout of on- and off-target sites directly in any therapeutically relevant cell.
4. One workflow, full landscape: works across cell types, nuclease systems, and base editing modalities.
5. Regulatory alignment: INDUCE-seq supports the FDA's April 2026 draft guidance on NGS-based off-target assessment for IND applications.

Roundtable Panel Discussion: Making CGT Manufacturing Work in Asia: Bridging Innovation and Reality

Terumo Corporate Session

MR 324

Thursday, September 3, 2026 | 09:15 - 10:15

Speakers:

- Wenyan Leong, Director, APAC Commercial and Global Strategic Partnerships, Cell and Gene Therapies, Singapore
- Cyrus Yang, CEO, Taiwan Bio Therapeutics Inc., Taiwan
- Sharon Sagnella, Clinical Cell Therapies Processing Facility Director | Royal Prince Alfred Hospital, Director of Research & Development, Australia

This 60-minute roundtable panel discussion will bring together cell and gene therapy leaders from across Asia to explore the practical manufacturing challenges that emerge as CGT programs move from early innovation toward clinical implementation. While scientific progress continues to accelerate, many therapy developers still face difficult questions around process complexity, scalability, cost, consistency, automation adoption, and operational readiness.

The discussion will examine whether these challenges differ in Asia compared with the US and Europe, and what makes the regional context unique. Panelists will share perspectives on where automation and closed-system processing can create the greatest value, how the industry can improve standardization while preserving manufacturing flexibility, and what ecosystem support is needed beyond equipment alone.

By connecting clinical, technical, and operational viewpoints, the session aims to provide practical insights for hospitals, biotech companies, and manufacturing teams seeking to build more reliable, scalable, and accessible CGT manufacturing workflows across Asia.

Session Objectives:

1. Identify key manufacturing challenges as CGT programs move toward clinical implementation
2. Discuss what makes CGT manufacturing in Asia unique
3. Explore how automation and closed systems can improve reliability and scalability
4. Understand the support needed to enable practical adoption beyond equipment alone

The UCMSC Secretome: A Cell-Free Gel Promoting Angiogenesis and Tissue Regeneration in Chronic Wounds

Regenic Company Presentation

MR 324

Thursday, September 3, 2026 | 10:15 - 10:30

1. Breaking the Chronic Inflammation Cycle with Dual-Action Bioactivity
Unlike single-growth-factor treatments, our UCMSC secretome gel addresses the root cause of chronic wounds—the failure to progress past the inflammatory stage. Our in-vitro data confirms ~50% anti-inflammatory activity (comparable to triamcinolone) by polarizing macrophages away from the pro-inflammatory M1 state, while simultaneously demonstrating 20–30% anti-fibrotic activity by reducing □-SMA expression, preventing pathological scarring.

2. Clinical Proof-of-Concept: Rapid Epithelialization in Days
The therapeutic efficacy is not just theoretical. In a documented case, topical application of the secretome gel achieved 100% epithelialization of a 64 cm^2 wound in just 5 days, compared to only 87.5% in the control. This dramatic acceleration—reducing raw surface area from 64 cm^2 to 0 cm^2—highlights its potent ability to drive keratinocyte migration and wound closure.

3. A Practical, Off-the-Shelf Solution with a Stable Formulation
We have overcome the logistical barriers of live-cell therapies. Our product is a sterile, serum-free, antibiotic-free biological solution with an 18-month shelf life at -20°C. Critically, our proprietary hydrogel formulation allows for storage in a standard freezer without ice crystal formation, enabling easy handling and consistent, sustained release upon topical application or intralesional injection.

4. Comprehensive Mechanism Beyond Just Growth Factors
While many therapies focus on a single cytokine (like FDA-approved PDGF), our secretome provides a physiologically balanced cocktail of over 100 proteins, cytokines, and chemokines. This holistic "cell-free" approach not only promotes angiogenesis but also modulates the entire wound microenvironment, offering a more robust and safer strategy than growth-factor monotherapy, with reduced malignancy risk.

Reimagining DNA Payloads: Enzymatic Circular DNA for the Next Generation of Cell and Gene Therapies

Touchlight Company Presentation

MR 324

TOUCHLIGHT
DNA is our DNA™

Thursday, September 3, 2026 | 10:30 - 10:45

Speakers:

Daria Olijnyk-Dallis, Touchlight, USA

Enzymatically produced circular DNA formats offer an alternative to conventional plasmids, allowing high sequence complexity, secondary structures, and elimination of bacterial or phage-derived sequences. These studies aimed to evaluate enzymatic circular DNA formats as flexible templates for gene editing and expression.

We evaluated mbDNA™ , a circular single-stranded DNA containing a defined double-stranded stem loop, as a donor template for homology-directed repair (HDR) in immune and stem cell populations using an ex vivo CAR T-cell workflow. DNA from a GMP-representative manufacturing process was electroporated into cells, with knock-in efficiency, viability, proliferation, and functional phenotype assessed. mbDNA demonstrated minimal toxicity and achieved impressive 75% knock-in efficiency, while maintaining cell counts (like the DNA-free control) over a concentration range.

To extend applicability beyond HDR, additional custom circular DNA formats (sscDNA, hsscDNA, & dscDNA) incorporating user-defined single- and double-stranded regions were developed for compatibility with recombination, transposition, and homology-independent targeted integration (HITI) editing platforms.

Collectively, these data demonstrate that enzymatically produced circular DNA formats can support multiple gene editing and expression modalities while being compatible with a variety of delivery techniques such as electroporation and lipid nanoparticle (LNP) delivery, providing a flexible and scalable DNA payload platform for cell and gene therapies.

Session Objectives:

1. Enzymatically produced circular DNA formats provide a scalable, non-viral alternative to plasmids for delivering large and complex gene editing payloads.
2. mbDNA™ achieves ~75% HDR knock-in efficiency in CAR T-cell workflows, ~40% in CD34+ HSCs with 10-15x better engraftment in vivo
3. Additional engineered DNA formats (sscDNA, hsscDNA, dscDNA) expand compatibility beyond HDR to recombination, transposition, and HITI-based editing
4. The platform is compatible with multiple delivery methods, including electroporation and lipid nanoparticles (LNPs)

Accelerating Clinical Translation of Treg & TIL Therapies Through Strategic Collaborations

Thermo Fisher Scientific Corporate Session

MR 324

Thursday, September 3, 2026 | 12:30 - 13:45

Speakers:

- Joshua Ooi, Ph.D., Associate Professor, Head of Regulatory T cell Therapies Group, Monash University, Australia
- Leon Brownrigg, PhD., Senior Medical Scientist, Cell and Tissue Therapies (CTTWA), Royal Perth Hospital, Australia

The next wave of cell therapies will depend not only on breakthrough biology, but also on manufacturing strategies that enable safe, scalable and accessible clinical translation. This session brings together leading clinical and translational researchers to discuss how strategic partnerships are accelerating the development of next-generation Treg and TIL therapies.

Our invited experts will explore emerging approaches including TCR-engineered antigen-specific Tregs for autoimmune disease, clinically applicable suppressor T-cell platforms for transplantation, and point-of-care manufacturing of autologous TIL therapies for advanced melanoma. Drawing on real-world clinical and manufacturing experience, they will share lessons from developing robust, cost-effective and clinically deployable workflows, including the integration of advanced cell processing technologies to support manufacturing consistency and scalability.

Through collaborations spanning academia, hospitals and industry, the discussion will highlight how scientific innovation, process development and enabling technologies are converging to overcome translational bottlenecks and accelerate the path from discovery to clinical impact for next-generation cell therapies.

Session Objectives:

1. Discover how strategic partnerships can accelerate cell therapy commercialization
2. Gain valuable insights on building effective research-industry collaborations to overcome manufacturing and translational challenges
3. Explore how closed, modular Cell Therapy Systems (CTS) solutions support scalable manufacturing and clinical translation of Treg and TIL therapies

Linearly Scalable Fixed Packed Bed Bioreactors for Induced Pluripotent Stem Cells and Mesenchymal Stromal Cells with Closed Automated Single Use Harvester

Esco Aster Pte Ltd Company Presentation

MR 324

Thursday, September 3, 2026 | 13:45 - 14:00

Speaker:

XL Lin, Founder, CEO, Esco Aster Pte Ltd, Singapore

3D single use fixed packed bed bioreactors are widely used for commercial manufacture of biologics, including viral vectors, oncolytic viruses, secretomes, extracellular vesicles and exosomes. However, there is limited adoption for therapies where the final product is harvested cells. This is due to challenges associated with seed train expansion, which is generally less efficient than microcarrier-based suspension culture with tank-to-tank microcarrier transfer, as well as the complexities of downstream cell harvesting and processing.

We present the use of 3D Tide Motion packed-bed bioreactor technology for whole-cell manufacturing. Human induced pluripotent stem cells (iPSCs) were successfully cultured in the 50 mL MiniTide® bioreactor. Mesenchymal stromal cells (MSCs) were expanded in 0.1 L bioreactor for ~1 billion cells. The process is integrated with an automated closed-system single use cell harvester and downstream processing workflow, addressing one of the key historical limitations of fixed-bed bioreactors for stem cell therapy manufacturing.

This breakthrough has the potential to significantly reduce cost of goods (COGs) compared with multilayer cell culture systems, providing a scala ble, closed, and automated manufacturing platform for allogeneic cell therapies. Such technology is particularly timely given the recent U.S. FDA approval of allogeneic MSCs for GVHD, which are expected to drive demand for other MSCs therapies.

Session Objectives:

1. Fixed-bed bioreactors are well established for manufacturing secreted biologics such as viral vectors, oncolytic viruses, secretomes, and extracellular vesicles (EVs/exosomes), but have been underutilized for whole-cell therapies.
2. Proof-of-concept demonstrated successful expansion of:
    - Human induced pluripotent stem cells (iPSCs) in a 50 mL MiniTide® 3D bioreactor.
    - Mesenchymal stromal cells (MSCs) in a 0.1 L packed-bed bioreactor producing approximately 1–3 billion cells.
3. Integrated automated closed-system cell harvesting addresses a key bottleneck in fixed-bed bioreactor manufacturing.
4. Offers a scalable, automated, and closed manufacturing platform for allogeneic cell therapies.
5. Potential to significantly reduce cost of goods (COGs) compared with conventional multilayer cell culture systems.
6. Demonstrates the feasibility of packed-bed bioreactors as a next-generation manufacturing platform for large-scale stem cell therapy production.

Advancing EV Translation with an Automated, Scalable Isolation Platform

EXODUS BIO Company Presentation

MR 324

Thursday, September 3, 2026 | 14:00 - 14:15

Speaker:

Viney Ying, Product Application Manager, EXODUS BIO, USA

Extracellular vesicles (EVs) are increasingly important in cell therapy, regenerative medicine, biomarker discovery, and therapeutic translation. However, EV isolation remains a major workflow bottleneck because many conventional methods are manual, time-consuming, difficult to standardize, or challenging to scale. This session will introduce EXODUS as an automated EV isolation platform designed to improve recovery, purity, reproducibility, and workflow efficiency while maintaining EV integrity and downstream biological activity. Using application examples from biofluid EV isolation, cell culture medium EV preparation, engineered EV regenerative medicine, and large-volume process development, the presentation will show how automated, gentle isolation can support functional readouts and translational decision-making. The session will also discuss how the EXODUS platform family can support research-scale workflows, multi-channel process screening, and larger-volume EV preparation for cell therapy and regenerative medicine programs.

Session Objectives:

1. Understand key EV isolation bottlenecks in cell therapy and regenerative medicine translation
2. Learn how automated EXODUS workflows improve consistency, purity, recovery, and hands-on efficiency
3. Review application examples across biofluid EVs, cell culture EVs, engineered EVs, and functional EV readouts

A Non-Viral, Large-Scale Delivery of Gene Editing Tools for T Cell Manufacturing

Lonza Company Presentation

MR 324

Thursday, September 3, 2026 | 14:15 - 14:30

Speaker:

Isaac Chen, Channel Manager – SEA + Korea, Lonza Bioscience Singapore Pte Ltd., Singapore

The 4D-Nucleofector® LV Unit PRO is the new generation advanced electroporation platform enabling efficient, non-viral delivery of complex cargos for scalable T cell engineering and cell therapy manufacturing. Built on established Nucleofector® technology, the system supports versatile transfection of DNA, mRNA, and CRISPR-based components with high efficiency and cell viability. Process conditions developed at small scale are seamlessly translated to large volumes, allowing reliable modification of up to 1×10^9 cells using fixed-volume and flow-through cartridge formats. Robust performance is demonstrated across multiple donors, cargo types, and applications, including gene knockout, knock-in, and transposon-based integration, while maintaining stable editing efficiency, high cell recovery (>95%), and strong expansion capacity. The platform also supports closed, GMP-compatible workflows with validated consumables and compliant software, facilitating transition from research to manufacturing. Overall, LV Unit PRO provides a scalable, reproducible, and regulatory-aligned solution for non-viral cell and gene therapy production.

Session Objectives:

1. Non-viral technologies are now viable alternatives to viral methods for cell therapy manufacturing - delivering clinically relevant cargos efficiently while reducing complexity and risk.
2. LV Unit PRO maintains efficiency, viability, and reproducibility from R&D to large-scale manufacturing.
3. Strong strategic fit for cell therapy manufacturing by providing a reliable, flexible, and regulatory-aligned solution for commercial-scale production.

Advancing Cell and Gene Therapy: From Manufacturing Challenges to Integrated Solutions

ACROBiosystems Company Presentation

MR 324

Thursday, September 3, 2026 | 14:30 - 14:45

Speaker:

Li Yen Mah, Technical Sales Manager (APAC), ACROBiosystems, Malaysia

Cell and gene therapies leave no room for error. Unlike traditional biologics, every reagent decision in manufacturing directly impacts patient outcomes — yet CGT workflows bring unique complexity: variable matrices, tight IND timelines, and evolving regulatory expectations that traditional reagent portfolios weren't built to meet.

Our solution: a comprehensive portfolio spanning the full CGT continuum — GMP-grade cytokines and CAR target proteins, validated cell line models, and recombinant factor C endotoxin detection. Purpose-built for CGT's demands, this end-to-end offering gives researchers and manufacturers the precision and reliability to strengthen lot release decisions, accelerate IND timelines, and confidently bridge the gap between cutting-edge research and safe, scalable delivery of life-changing therapies.

Session Objectives:

1. Recap of CGT challenges
2. Fit for purpose tool at every stage of CGT
3. Choosing the right QC solutions

Beyond Conventional CAR-T: Integrating Humanized CAR Designs and Advanced Manufacturing to Enhance Safety and Efficacy

BioCell Innovations Pte. Ltd. Company Presentation

MR 324

Thursday, September 3, 2026 | 16:30 - 16:45

Speaker:

Paula Lam, Chief Scientific Officer, BioCell Innovations Pte. Ltd., Singapore

Chimeric antigen receptor (CAR)-T cell therapy has demonstrated remarkable clinical efficacy in hematologic malignancies; however, challenges remain including limited CAR persistence, antigen escape, manufacturing complexity, high production cost and treatment-associated toxicities. Emerging advances in synthetic biology, cellular engineering, and bioprocess development are creating new opportunities to overcome these limitations and redefine the next generation of adoptive cell therapies. In this presentation, BioCell Innovations will present its integrated strategy that combines rational CAR engineering with advanced and scalable manufacturing technologies to optimize therapeutic performance outputs.

Session Objective:

1. Addressing critical CAR-T manufacturing bottlenecks through integrated process innovation.

Enabling Scalable CAR-T Manufacturing: Advancing Lentiviral Vector Supply Through Robust and Scalable GMP Manufacturing

CellVec Pte. Ltd. Company Presentation

MR 324

Thursday, September 3, 2026 | 16:45 - 17:00

Speaker:

Ann Koay, MSAT Lead, CellVec Pte Ltd., Singapore

The rapid growth of CAR-T therapies and clinical trials has increased demand for high-quality lentiviral vectors (LVVs) across all stages of development. Early-phase studies require flexible small-batch GMP production, while late-stage programs demand scalable, high-volume supply. CellVec is addressing these challenges through the development of robust and scalable LVV manufacturing platforms. This presentation will highlight key considerations in balancing early clinical supply with long-term scalability, and discuss strategies to improve process robustness, reproducibility, and GMP readiness. Experience from CellVec's LVV manufacturing platform across multiple CAR transgenes will be shared to illustrate key technical challenges and practical hurdles encountered in process development and manufacturing.

Session Objectives:

1. Flexible, scalable manufacturing platforms are essential to bridge small-batch clinical needs and commercial-scale requirements
2. Process robustness and reproducibility are critical to ensuring reliable GMP vector supply
3. Practical manufacturing experience highlights key technical hurdles in translating LVV processes across diverse CAR constructs
4. Explore flexible, scalable manufacturing platforms that are essential to bridge small-batch clinical needs and commercial-scale requirements
5. Understand why process robustness and reproducibility are critical to ensure reliable GMP vector supply
6. Highlight key technical hurdles in translating LVV processes across diverse CAR constructs through practical manufacturing experience

Bridging the Talent Gap: Enabling Robust, Multi-Site CGT Production Across Varied Expertise Levels

Shenzhen Cellbri Bio-Innovation Technology Co.,Ltd Company Presentation

MR 324

Friday, September 4, 2026 | 10:15 - 10:45

Speaker:

Anqi Li, PhD, VP, Cellbri, Shenzhen Cellbri Bio-Innovation Technology Co.,Ltd, China

Cellbri is dedicated to making cell therapy accessible to all. Automation is one of the key strategies to enable cost reduction and seamless tech transfer. Previously, our modular platforms streamlined CAR-T processing, achieving automated closed processing in Class C clean room. However, we observed only a mild reduction in labor cost, as operators were still required to intervene across multiple discrete steps.

To address this, the CellFab integrated series was first launched in 2025. By consolidating modular processes into a single, unified workflow, CellFab enables true "1-click" manufacturing. This dramatically reduces hands-on time and significantly cuts operational costs. Importantly, the CellFab series retains full flexibility for process design. Process development teams can customize the "1-click" workflow by selecting suitable hardware modules, such as nanobead sorting and bag culturing, and by programming the overall process using steps from our comprehensive SOP library.

This highly simplified manufacturing process reduces the dependency on highly specialized staff. This also shortens training time while the robust manufacturing process could be transferred to multiple sites. The ease of technology transfer proved most valuable for point of care decentralized manufacturing in hospitals and for technology transfer in developing countries. This flexibility also enables continuous process improvement and collaboration with different reagent developers.

Session Objectives:

1. Modular automation closes the processing loop, but cost savings remain limited without an integrated solution.
2. The CellFab series consolidates multiple steps into a true "1-click" workflow, dramatically cutting hands-on time and operational costs.
3. Simplified processes reduce reliance on highly specialized staff and shorten training time.
4. Seamless tech transfer is now achievable across multi-site networks, hospital point-of-care settings, and manufacturing facilities in developing countries.

Accelerating Cell Engineering with MaxCyte's High-Throughput Electroporation Platform

SciMed Asia, a PHC group & Maxcyte Company Presentation

MR 324

Friday, September 4, 2026 | 12:30 - 12:45

Speaker:

Leo He, Field Application Scientist, MaxCyte, Inc., United States

As demand for advanced therapies accelerates, developers face mounting pressure to innovate despite high costs, long development timelines, and inconsistent gene editing outcomes. The ExPERT DTx™ Electroporation Platform was designed to address these challenges by delivering rapid, scalable, and customizable electroporation of up to 96 samples in under three minutes, offering high-throughput efficiency, reproducible results, and compatibility with diverse cell types. Importantly, optimized conditions on the DTx™ can be directly transferred to other MaxCyte systems, enabling seamless scale-up from small-scale discovery to GMP-compliant manufacturing. Here, we applied the DTx™ to a high-throughput CRISPR screening workflow to evaluate guide RNA performance for T cell knockout across a range of RNP concentrations. Collectively, these findings establish the DTx™ Electroporation Platform as a powerful and versatile solution for high-throughput gene-editing optimization, delivering reliable results and seamless scalability to streamline the transition from early discovery to clinical manufacturing.

Session Objectives:

1. Understand how high-throughput electroporation can address key barriers, such as accelerating timelines and high cost.
2. Explore the capabilities of MaxCyte's new electroporation platform, including rapid sample processing and customizable energy delivery.
3. Gain practical insights into high-throughput CRISPR screening workflows.

CGT Scale-up: Efficient Transition from Lab to Mass Production

Tofflon Company Presentation

MR 324

Friday, September 4, 2026 | 12:45 - 13:00

Speaker:

Michael Wu, Vice President of Tofflon Advanced Research Institute for Cell and Gene Therapy, Tofflon Group, China

Cell and gene therapy (CGT) is at a pivotal stage of transitioning from laboratory research to industrial-scale production. However, challenges such as process scale-up, cost control, supply chain stability, and cross-border regulatory compliance remain critical bottlenecks limiting the global accessibility of innovative therapies. Grounded in Tofflon's full-industry-chain capabilities, this topic systematically explores efficient CGT industrialization pathways across four key dimensions—engineering, equipment, reagents, and consumables—centered around the three core objectives of "rapid factory construction, rapid production launch, and rapid application." Leveraging over three decades of deep expertise in the pharmaceutical equipment sector, Tofflon provides customers with comprehensive engineering design and process solutions spanning from R&D pilot-scale to commercial manufacturing, covering a complete supply system that includes core pharmaceutical equipment, critical production reagents, and single-use consumables. Notably, Tofflon has established a robust overseas service network, offering one-stop support for cross-border technology transfer, domestic and international regulatory alignment, overseas facility setup, and localized operational guidance. This enables Chinese CGT innovations to reach global markets while simultaneously bringing international advanced process concepts into China. This topic aims to provide CGT practitioners with an actionable roadmap from bench to mass production, accelerating the safe, compliant, and efficient delivery of innovative therapies to patients worldwide.

Session Objectives:

1. Understand Tofflon's systematic capabilities across engineering, equipment, reagents, and consumables
2. Learn how modular factory solutions shorten construction timelines and enable scalable capacity investment
3. Explore ways to accelerate the full journey from lab to commercial manufacturing through integrated services
4. Gain insights into Tofflon's one-stop overseas technology transfer and global deployment support
5. Develop initial ideas for your own project industrialization

GMP-Grade Recombinant Monoclonal Antibody Conjugates for Cell Therapy Manufacturing & QC

Cell Signaling Technology Company Presentation

MR 324

Friday, September 4, 2026 | 13:15 - 13:30

Speakers

Ryan Tay, PhD, Commercial Lead APAC, Cell Signaling Technology

Chimeric Antigen Receptor (CAR)-T cell therapy is a highly innovative form of immunotherapy that has proven to be successful in treating hematologic malignancies. As this therapeutic modality continues to evolve toward the targeting of novel combinations of tumor antigens and the development of more efficacious CAR-T cells, there is a need for tools that can be leveraged to selectively manipulate CAR-T cells in preclinical research workflows. Here, we report on a novel and highly versatile recombinant monoclonal antibody raised against the Gly4Ser (G4S) peptide linker, which is commonly integrated into single-chain variable fragment (scFv)-based CARs. Our data demonstrate the utility of an anti-G4S linker monoclonal antibody for the isolation of CAR T cells, which eliminates the need for a co-expressed marker for selection. Furthermore, this antibody can be leveraged in flow cytometry assays to provide a direct measure of the surface expression of G4S-linker-containing CARs, independent of CAR specificity. The versatile attributes of the anti-G4S linker monoclonal antibody warrant further investigation aimed at the development of more standardized CAR-T workflows, thereby eliminating custom reagent development across multiple programs with unique CAR designs.

Session Objectives:

1. The anti-G4S antibody represents a platform-enabling tool for CAR-T workflows rather than a program-specific reagent.
2. Adoption of this strategy can streamline the development of CAR-T therapies, reducing variability and operational burden.
3. Development of GMP-grade antibody conjugates supports standardized, regulatory-compliant processes for cell therapy production.
4. This approach eliminates custom reagent development for each new CAR construct, saving time and cost.
5. Broad applicability across CAR designs positions this tool as a scalable solution for next-generation and multiplexed CAR-T therapies.

Accelerating Cell & Gene Therapy Innovation with Agilent Cell Biology and Genomics Solutions

Agilent Company Presentation

MR 324

Agilent
Trusted Answers

Friday, September 4, 2026 | 13:30 - 13:45

Speakers

- Lee Chee Yang, PhD, Senior Field Application Scientist, Diagnostics and Genomics Group, South Asia Pacific, Agilent Technologies Singapore (Sales) Pte Ltd., Singapore
- Federica Tomay, PhD, Field Application Scientist, South Asia Pacific, APAC Technical Specialization & Solutions, Singapore

Cell and gene therapy (CGT) development demands workflows that enable rapid discovery, robust process development, and reliable analytical characterization. In this session, Agilent will showcase its comprehensive portfolio of cell biology and genomics solutions designed to support researchers and biopharma innovators across the CGT continuum. From advanced cellular imaging, automation, and sample preparation to next-generation sequencing, genomics analysis, and quality control workflows, Agilent's technologies help accelerate research while improving data confidence and reproducibility.

The session will also feature Agilent's latest product launches and innovations aimed at addressing emerging challenges in CGT, including higher-throughput workflows, enhanced cellular characterization, and streamlined genomic analysis

Session Objectives:

1. Understand current trends and challenges shaping the Cell & Gene Therapy landscape
2. Explore Agilent's Cell Biology and Genomics portfolio for CGT research and development
3. Learn how advanced cellular imaging, automation, genomics, and molecular analysis technologies support CGT workflows
4. Gain insights into recent Agilent product launches and innovations relevant to cell and gene therapy applications
5. Explore opportunities for implementing scalable solutions from discovery through manufacturing support
6. Engage with Agilent experts to discuss emerging applications and future directions in CGT research

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LEVEL 3, SUNTEC CONVENTION CENTRE

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Exhibitors and Sponsors

10x Genomics Booth #40

10x Genomics was founded on the vision that this century will bring advances in biomedicine and transform the way we understand and treat disease. We deliver powerful, reliable tools that fuel scientific discoveries and drive exponential progress to master biology to advance human health. Our end-to-end single cell and spatial solutions include instruments, consumables, and intuitive software, letting you unravel highly intricate biological systems, while bringing into focus the details that matter most.

ACROBiosystems Booth #17

ACROBiosystems aims to become a cornerstone enterprise of the global biopharma and healthcare industries. We offer and develop a wide array of products and services. This encompasses proteins, antibodies, and kits, as well as analytical and testing services. Each of these products is specially designed to be used throughout the discovery to commercialization studies for novel therapeutics combating cancer, autoimmune, cardiovascular, infectious, and neurological diseases.

Agilent Booth #18

Agilent is a leader in life sciences, diagnostics, and applied chemical markets, delivering innovative technology solutions that provide trusted answers to researchers' most challenging scientific questions. The company generated revenue of $5.34 billion in fiscal year 2020 and employs 16,400 people worldwide.

Information about Agilent is available at www.agilent.com. To receive the latest Agilent news, please subscribe to the Agilent Newsroom. Follow Agilent on LinkedIn, Twitter, and Facebook.

ANEMOCYTE Booth #11

Anemocyte could significantly support your programs offering a range of services and products that includes:

AMCAP™ (mRNA Synthesis): Our high-yield 5' CAP-1 "one-pot" process. Designed for less complexity and higher integrity. anemocyte.com/amcap/

AMCLARITY (Visual Inspection Defect Kits): Advanced automated quality control solutions for uncompromising consistency. anemocyte.com/amclarity/

pDNA and mRNA Development & Manufacturing Platforms: Scaling your innovation from lab to commercial, leveraging more than 25 years of GMP experience. anemocyte.com

For a quick preview of our ecosystem, you can also visit: shop.anemocyte.com | AMCAP™

Astraveus

Astraveus is pioneering a new paradigm in cell therapy manufacturing with Lakhesys™ , a fully automated benchsize platform that streamlines end-to-end CAR-T production using advanced microfluidics while reducing manufacturing costs and infrastructure requirements.

Biomass Sensor Pte. Ltd. Booth #39

Biomass Sensor is in the business of distributing and supplying high-technology equipment for the Bioprocessing Industry & Cell Gene Therapy in Singapore and Southeast Asia.

Established in 2010, Biomass Sensor helps companies achieve process consistency through its expertise in process automation, making it easier to make key process

decisions with the help of a fully digitized information and state-of-the-art inline sensors and other equipment imported worldwide.

We represent instruments like CarT Cell Activation & Separation, Bioreactor (Conventional/ Custom), Cell Sensor (Capacitance/ NIR), Gas Sensor (CO2/O2), Autosampler, Aseptic Filling, pH/DO/Cond/ORP.

BioMed Linkage Tech Co., Ltd. Booth #25

BioMed Linkage provides comprehensive, one-stop CRO and CDMO solutions in China. We collaborate with leading CDMOs, pharmacology CROs, and GLP-certified institutions to deliver integrated support across drug manufacturing, pharmacology, DMPK, and toxicology studies, covering both IND- and NDA-enabling programs.

Our key strengths include:

1. IND- and NDA-Enabling Studies
2. We have extensive experience in DMPK and toxicology studies across multiple species, including non-human primates (NHPs), supporting regulatory submissions from IND through NDA.
3. Strong NHP Capabilities in China
4. Leveraging robust NHP resources, we support a broad range of studies, including:
5. Disease models for efficacy evaluation
6. PK and efficacy studies in both naïve and non-naïve NHPs
7. Pre-toxicology and GLP toxicology studies for IND/NDA-enabling programs

Our experienced, China-based project management team ensures efficient communication, high-quality execution, and strict timeline control.

If you are seeking reliable and cost-effective CRO or CDMO services in China, BioMed Linkage is well positioned to be your trusted partner.

Bio-Rad Laboratories, Inc. Booth #27

Trusted partner in life science and clinical diagnostics

At Bio-Rad, we support researchers and clinicians working to improve lives through science. From life science research to clinical diagnostics, our tools help move science and healthcare forward with confidence and precision.

For more than 70 years, we've delivered trusted solutions and meaningful advances that help turn possibilities into progress—every day, everywhere.

Bluecord Booth #7

Bluecord is a software company helping cell and gene therapy organizations digitize and connect their quality and manufacturing operations. Our cloud-based platform brings together Quality Assurance, Manufacturing, Inventory, and Quality Control into one integrated system built specifically for GMP environments.

Developed in partnership with leading academic and clinical centers, Bluecord streamlines how teams manage documentation, deviations, batch records, and supplies. Every module is designed with regulatory readiness in mind, supporting HIPAA, 21 CFR Part 11, GAMP 5, and global data integrity standards.

Today, Bluecord supports facilities across North America, Europe, and Asia-Pacific. Our mission is to make advanced therapy manufacturing simpler, safer, and faster so that life-changing treatments can reach patients sooner.

Broken String Biosciences Booth #10

Broken String Biosciences technology platform, INDUCE-seq®, supports the development of cell and gene therapies that are safer by design. INDUCE-seq® is an NGS-based DNA break mapping platform that enables companies developing cell and gene therapies to measure and quantify the specificity of off-target genetic edits and evaluate the associated genetic outcomes. The platform provides data-driven, actionable insights across the discovery, pre-clinical and clinical development stages to advance gene editing programs.

Cell Signaling Technology Booth #19

Doing good science is important. So is just doing good.

Cell Signaling Technology (CST) is a different kind of life science company—one founded, owned, and led by active research scientists, with the highest standards of product and service quality, technological innovation, and scientific rigor for over 20 years. We consistently provide fellow scientists around the globe with best-in-class antibody products and services to fuel their quests for discovery. Founded in 1999 and headquartered in Danvers, Massachusetts, USA, CST employs over 600 people worldwide.

Helping researchers find new solutions is our main mission every day—but it's not our only mission. We're also dedicated to helping identify solutions to other problems facing our world. We believe that all businesses must be responsible and work in partnership with local communities, while seeking to minimize their environmental impact. That's why we joined 1% for the Planet as its first life science member, and have committed to achieving net-zero emissions by 2029.

At CST, we believe in the power and promise of science to solve the challenges we face as a global community. We're a company of caring people driven by a devotion to facilitating good science—a company committed to doing the right thing for our customers, our communities, and our planet.

Cellvec Pte. Ltd. Booth #30

CellVec is a certified GMP gene therapy Contract Development and Manufacturing Organisation (CDMO) that is a specialist provider of custom viral vectors for pre-clinical and clinical applications. With the use of our lentivirus-based CellVec Vector Platform, we set ourselves apart through the ability to overcome current technological bottlenecks in the upscale production of viral vectors and develop novel gene transfer technologies for advanced therapies in order to facilitate the advancement of our client's products from bench-to-bedside for clinical applications

Charles River Laboratories Booth #13

Charles River provides essential products and services to support pharmaceutical and biotechnology companies, government agencies, and leading academic institutions worldwide in accelerating research and drug development. As a leader in scientific innovation, we are deeply committed to pioneering alternative methods that drive discovery while reducing reliance on traditional models. By embracing cutting-edge technologies and forward-thinking approaches, we enhance preclinical and clinical research. Our dedicated employees focus on delivering precisely what our clients need to improve, innovate, and expedite the discovery, early-stage development, and safe manufacture of new therapies for patients, because every moment matters.

• Biologics Testing Solutions
With 50+ years of experience and over 40,000 tests run annually at the GMP biologics testing facilities, we provide comprehensive testing services for a wide range of modalities.

• Cell and Gene Therapy CDMO
We have supported the development of 20 FDA-approved cell and gene therapies and have conducted more than 1,000 studies in this field over the past year.

ChemoMetec Booth #42

ChemoMetec develops and manufactures advanced cell counting and analysis instruments for research, bioprocessing, and clinical applications. Our solutions help scientists and healthcare professionals obtain fast, accurate, and reliable cell data, supporting innovation in life sciences and improving decision-making across laboratories worldwide.

Cytiva Booth #9

At Cytiva, our mission is to advance and accelerate the development of therapeutics. With 15,000 associates in more than 40 countries, we're driven to use our expertise and talent to achieve better flexibility, capacity, and efficiency for our customers. Our broad and deep portfolio of tools and technologies, global scale, and best-in-class service provides critical support from discovery to delivery, for customers spanning researchers, emerging biotech, large-scale biopharma and contract manufacturers. Learn more at Cytiva.com
Cytiva is proud to be part of Danaher. Visit https://www.danaher.com/ to learn more about Danaher, a leading life sciences and diagnostics innovator committed to accelerating the power of science and technology to improve human health.

CytoNiche Biotech Pte. Ltd. Booth #14

CytoNicheTM is revolutionizing the cell and gene therapy (CGT) industry with its scalable 3D FloTrixTM technology, offering comprehensive solutions for CGT manufacturing. Our product portfolio includes GMP-grade dissolvable microcarriers, serum-free media for mesenchymal stromal/stem cells, and a complete suite of GMP-compliant equipment and consumables. These solutions support every stage of cell production—from expansion and harvesting to processing and filling.

Driven by a vision to ignite a new era in industrial cell development, we are empowering CGT advancements through intelligent, 3D cellular mass manufacturing technology. This innovation not only reduces production time and costs but also improves scalability, making it possible to produce billions of high-quality cells more efficiently than traditional methods.

By reducing facility footprint, labor costs, and contamination risks, our technology is helping shape the future of sustainable biomanufacturing, bringing us closer to benefiting more patients around the world.

Esco Aster Pte. Ltd. Booth #16

Esco Aster is a vertically-integrated contract research (CRO), contract development and manufacturing organization (CDMO) founded and deeply rooted by scientists enabling fellow scientists to translate their benchwork into life-saving diagnostics, medicines, therapies, cosmeceuticals, and cellular agriculture, at affordable prices for self-sufficiency of the country. We make complex manufacturing simple via our proprietary best-in-class continuous manufacturing platforms providing a reliable and linearly scalable outcome with a track record of being used in 7 commercial human and animal health vaccines. We continuously invest in meeting unmet clinical needs by unlocking manufacturing bottlenecks for current and new platform modalities. Together, we are working on an interconnected one health approach to bring your next molecule into the clinic and life. Join us for the world we are making redefining food and medicine for the current and future generations to come.

Esco Aster. One World. One Health.

EXODUS BIO — Booth #21

EXODUS is an automatic, label-free, and highly efficient exosome isolation system. With EXODUS, you can easily and quickly isolate high-quality, intact exosomes with excellent yield and purity from a variety of bio-fluids and sample volumes. Experience the efficiency of EXODUS for yourself and take your research to the next level.

InnoCellular — Booth #40

InnoCellular Tech Pte. Ltd. is a Singapore-based biotechnology company dedicated to advancing the scalable and reproducible manufacturing of cell and gene therapy products. As a spin-off from A*STAR, Singapore's national research agency, InnoCellular bridges cutting-edge research with commercial manufacturing by delivering integrated solutions for cell expansion and bioprocess development.

Our portfolio combines advanced bioreactor technologies with high-performance, regulatory-compliant cell culture media to support research, process development and GMP manufacturing. Through strategic collaborations with leading research institutes, technology partners and clinical innovators, we help accelerate the translation of promising cell therapies from laboratory discovery to clinical and commercial applications.

InnoCellular is the exclusive distributor of Applitech's advanced bioreactor platforms across multiple Asia-Pacific markets, providing comprehensive support in process optimization, scale-up, technology integration and technical training. Complementing our bioreactor solutions, we develop and supply chemically defined and serum/xenofree media designed to enhance consistency, scalability and regulatory readiness.

With a commitment to innovation, quality and long-term partnerships, InnoCellular empowers researchers, biotechnology companies and therapy developers to overcome manufacturing challenges and accelerate the delivery of next-generation regenerative medicines to patients worldwide.

Lonza — Booth #5

Lonza is one of the world's largest contract development and manufacturing organizations (CDMOs), dedicated to serving the healthcare industry. We work alongside a broad range of customers – from emerging biotechs to global pharmaceutical companies – to transform their therapeutic discoveries into life-saving and life-enhancing treatments for their patients. Our vision is to be the pioneer and world leader in the CDMO industry, setting the pace with cutting-edge science, smart technology and lean manufacturing.

Founded in 1897 in the Swiss Alps, our business has embraced innovation and kept pace with a fast-changing world for more than 125 years. As the first and the original CDMO, we have been manufacturing medicines for more than four decades. Today we offer one of the largest Western CDMO networks with a global team of approximately 20,000 colleagues working across more than 30 sites in five continents. Our people are united by a common purpose: to turn our customers' breakthrough innovations into viable therapies and manufacture the medicines of tomorrow.

Our business is structured to meet our customers' complex needs across three synergistic Business Platforms: Integrated Biologics, Advanced Synthesis and Specialized Modalities. Our services span from early development to drug substance and drug product manufacturing, and we lead in both established and emerging technologies including mammalian biologics, small molecules, highly potent active pharmaceutical ingredients (APIs), bioconjugates, mRNA, microbial, and cell and gene. Across technologies, we deliver integrated solutions to meet our customers' needs throughout the entire treatment lifecycle.

MedChemExpress Booth #12

MedChemExpress (MCE) is a leading global supplier of research chemicals and bioactive compounds, serving prestigious research institutes, labs, biotech, and pharmaceutical companies worldwide. Our extensive portfolio includes 100,000+ small molecules (specific inhibitors/agonists, isotope-labeled compounds, reference standards), 36,000+ oligonucleotides, and 25,000+ life science products (recombinant proteins, peptides, antibodies, fluorescent dyes, kits). We also offer a one-stop screening library service for drug discovery. Backed by an experienced team, we are dedicated to providing friendly and expert service to meet your unique research needs.

Miltenyi Biotec Booth #8

Miltenyi Biotec is a global leader in innovating technologies and services for patient-specific cell and gene therapies, turning scientific discoveries into practical treatments for personalized medicine. Having pioneered a groundbreaking method of cell separation, Miltenyi Biotec continues to set industry standards today. With over 35 years of expertise, it supports customers in biomedical discoveries, translating them into clinical applications to enable access to new therapies for patients. Miltenyi Biotec focuses on providing integrated, advanced solutions to address complex challenges in the treatment of cancers, autoimmune diseases, and inherited disorders. Through its Miltenyi Bioindustry division, it provides expert guidance to therapy developers, helping them efficiently and cost-effectively navigate the path from process development to commercialization. Miltenyi Biotec is headquartered in Bergisch Gladbach and has a global team of 4,700 employees across 24 countries.

Minerva Biolabs GmbH Booth #20

Minerva Biolabs GmbH is a Berlin-based biotech company developing PCR-based tests and reagents for detecting, controlling, and eliminating microbial contamination in cell cultures and biopharmaceutical production.

MP Biomedicals Booth #1

MP Biomedicals is dedicated to giving scientists and researchers innovative, quality tools and superior service to aid them in their quest for ground-breaking discovery and turning the hope for life-changing solutions into a reality.

The company manufactures and sells more than 55,000 products and is one of the only companies in the industry to offer a comprehensive line of life science, fine chemical and diagnostic products.

MP Biomedicals is a worldwide corporation, with ISO-certified and FDA-approved manufacturing and distribution facilities throughout the globe and headquartered in Southern California. A vast network of global distributors and satellite facilities and offices throughout Europe, Asia, Australia and the Americas assures customers top quality products delivered when and where needed.

No matter how dynamic the evolution of the life science and biotechnology markets, we remain committed to supporting our customers in their efforts to make new discoveries. From basic research, through scale-up, to full-scale production and diagnostic testing, MP Biomedicals serves every industry need – from specialized areas of research to supplying large scale quantities of fine chemicals.

Our customers partner with us because they want a long-time player and reliable colleague in the fields of life science research and diagnostics. MP Biomedicals will never rest in our odyssey to remain at the forefront of discovery in the ever-changing biomedical industry.

Promega Corporation Booth #22

Promega is a global leader in innovative life science technologies, offering more than 4,000 products that accelerate research, drug discovery and development, and manufacturing. Promega provides a variety of solutions to meet the fast-growing demands in cell and gene therapy development. Our solutions enable sensitive, automation-friendly, quantitative analysis of AAV and Lenti genome titer, cell identity and purity, cell health, and potency—critical parameters for ensuring safety, consistency, and regulatory compliance in advanced therapy manufacturing. Our automated nucleic acids extraction and qPCR/ddPCR-based solutions help streamline analytical workflows for vector copy number and in vivo biodistribution studies.

Promega partners closely with academic groups, industry leaders, and biomanufacturers to help standardize methods, improve analytical rigor, and accelerate the path from discovery to clinical impact.

To learn more about how Promega supports cell and gene therapy development, visit: https://www.promega.com/applications/cell-and-gene-therapy/

Regenic Booth #6

Regenic is Indonesia's first cGMP-certified stem cell manufacturing facility, dedicated to advancing healthcare through innovative stem cell and secretome therapies. With state-of-the-art technology and a commitment to quality, safety, and ethics, we develop solutions for orthopedic conditions, chronic diseases, and more. Collaborating with hospitals and institutions, Regenic is driving the future of regenerative medicine, offering hope and new possibilities for improved health and quality of life. Headquartered at the Kalbe Business Innovation Centre (KBIC) in Jakarta, Regenic was founded in 2013 as a stem cell manufacturing and education center under PT Bifarma Adiluhung, a subsidiary of PT Kalbe Farma, Tbk. Regenic holds the distinction of being the first in Indonesia to achieve GMP certification from BPOM and an Operating License from the Ministry of Health (Kementerian Kesehatan), enabling us to manufacture clinical-grade stem cells and their metabolites products. Regenic aims to provide new hope for patients with unmet medical needs. In line with this vision, our mission is to consistently produce and deliver high-quality cell therapy products with integrity, prioritizing patient safety, product quality, and patient well-being. Our scope of business includes Research and Development Centre for innovation cell therapy products, GMP manufacturing of allogenic stem cells and its derivatives, stem cell processing for autologous purposes, education center for stem cell.

Sartorius Booth #37

Sartorius is a global leader in life sciences research and the biopharmaceutical industry, headquartered in Göttingen, Germany. It operates through two main divisions: Lab Products & Services, which supports research and quality control in pharmaceutical and academic labs, and Bioprocess Solutions, which offers single-use solutions for biotech medication, vaccine, and cell and gene therapy production. With approximately 60 production and sales sites worldwide, Sartorius employs around 13,500 people. The company is known for expanding its portfolio through strategic acquisitions and reported a sales revenue of approximately 3.4 billion euros in 2024.

ScaleReady Booth #38

ScaleReady is advancing the future of cell and gene therapy manufacturing through the G-Rex® platform and integrated process innovations designed to maximize efficiency at scale. Trusted by therapy developers worldwide, G-Rex technology supports programs from early research through clinical development and large-scale commercial manufacturing.

Through continuous innovation and close collaboration with industry partners, ScaleReady is constantly evolving its platform to improve manufacturing performance, scalability, and reliability. This FutureReady approach enables therapy developers to streamline production and bring transformative therapies to patients faster.

ScaleReady partners with organizations around the world to build the next generation of scalable, efficient cell therapy manufacturing.

Learn more at scaleready.com.

SciMed Asia, a PHC Group & Maxcyte Booth #33

SciMed, a PHC Group is dedicated to advancing the future of medicine through a comprehensive portfolio of cell and gene therapy solutions that empower innovation, scalability, and clinical impact.

At the heart of our portfolio is MaxCyte, a global leader in cell engineering providing advanced flow electroporation technology that empowers the development and commercialization of next generation cell and gene therapies. With unmatched scalability, reproducibility, and versatility, MaxCyte enables seamless transition from research to clinical and commercial manufacturing. Its proven platform has supported hundreds of programs worldwide, driving breakthroughs in gene editing, immuno oncology, regenerative medicine, and other transformative fields. Trusted by leading pharmaceutical and biotechnology companies, MaxCyte continues to accelerate innovation and deliver solutions that advance the future of medicine by enabling engineered cells to reach their full therapeutic potential.

In addition, our portfolio includes Applied Cells GoFast platform which delivers breakthrough cell separation technology that accelerates workflows while dramatically lowering manufacturing costs. By enabling efficient, high purity isolation of target cells, GoFast reduces COGs to below USD10K per batch, empowering scalable, cost effective cell therapy production and supporting broader patient access to transformative treatments.

Finally, our PHCbi LicellGrow provides advanced cell culture systems optimized for consistency and scalability. PHCbi LicellGrow's innovative bioprocessing solutions ensure that engineered cells thrive in controlled environments, reducing variability and supporting reproducible outcomes across development pipelines.

Together, these platforms position SciMed as a trusted partner in the cell and gene therapy ecosystem—empowering innovation, enabling scalability, and driving the future of medicine.

Shenzhen Cellbri Bio-Innovation Technology Co.,Ltd Booth #15

CellBri is redefining what's possible in cell therapy manufacturing. As a pioneer in automated cell processing systems, we empower therapy developers and CDMOs to reduce cost, streamline timelines, and minimize risk without sacrificing flexibility or control – and without having to disrupt your existing processes. With deep roots in engineering and regulatory insight, we've created a cell therapy platform that grows with your needs, from early development to commercial scale.

SPD Biomedia / SONY — Booth #31

As part of Biomedia Holdings, SPD Scientific delivers integrated solutions across In-Vitro Diagnostics, Life Science & Translational Research, Microbiology, and Laboratory & Industrial Essentials. We provide high-quality products and technologies that support clinical diagnostics, advanced research, microbial testing, and day-to-day laboratory operations across healthcare, academic, and industrial sectors.

With a strong regional presence and cross-functional expertise, we serve customers throughout Asia with tailored solutions and dedicated support. From consultation to implementation and post-sales service, our teams ensure reliable performance, regulatory compliance, and exceptional value at every stage.

STEMCELL Technologies — Booth #36

As a company of Scientists Helping Scientists, STEMCELL Technologies is committed to enabling cell and gene therapy research around the world with high-quality services and solutions. Whether you're editing CD34+ cells, differentiating PSCs, or expanding immune cells, we have the specialized cell isolation products, cell culture media, and reagents you need. Through our Services for Cell Therapy Program, we can help you qualify our products for use as ancillary materials. Learn more at www.STEMCELL.com.

TEIJIN REGENET — Booth #29

In accordance with the commitment, TEIJIN group offers Contract Development and Manufacturing Organization (CDMO) services through the group companies TEIJIN REGENET and J-TEC.

We specialize in Cell and Gene Therapies including tissue-engineered products, with the aim of supporting the process development and manufacturing of CGT products in Japan - taking innovative science from concept to patient treatment.

Terumo Blood and Cell Technologies — Booth #24

Terumo Blood and Cell Technologies is a global medical technology company offering products, software, and services that enable the collection and preparation of blood and cells to treat challenging diseases.
Within this organization, the Global Therapy Innovations delivers automated, closed-system solutions that support the entire vein-to-vein journey of cell and gene therapies — from cell collection and expansion to fill and finish.

Trusted by biotech companies, hospitals, and research institutions worldwide, we combine deep cell therapy insight with automation expertise to empower developers and manufacturers with GMP-compliant platforms that enhance consistency, reduce manual steps, and accelerate timelines from early research to commercialization.

We believe in the power of blood and cells to do more for patients. This belief drives our innovation, fuels collaboration, and strengthens our commitment to expanding access to transformative therapies.

We partner. We innovate. We accelerate.

Thermo Fisher Scientific Booth #23

Thermo Fisher Scientific Inc. is the world leader in serving science, with annual revenue over $40 billion. Our Mission is to enable our customers to make the world healthier, cleaner and safer. Whether our customers are accelerating life sciences research, solving complex analytical challenges, increasing productivity in their laboratories, improving patient health through diagnostics or the development and manufacture of life-changing therapies, we are here to support them. Our global team delivers an unrivaled combination of innovative technologies, purchasing convenience and pharmaceutical services through our industry-leading brands, including Thermo Scientific, Applied Biosystems, Gibco, Invitrogen, Fisher Scientific, Patheon and PPD.

Tofflon Booth #28

Tofflon is a leading provider of integrated pharmaceutical and biotechnology solutions, serving customers in over 50 countries worldwide. With comprehensive capabilities spanning process development, equipment manufacturing, automation, and engineering services, Tofflon supports the full lifecycle of biologics and advanced therapies manufacturing.

For the cell and gene therapy sector, Tofflon offers scalable solutions including single-use technologies, bioprocess equipment, aseptic fill-finish systems, isolators, lyophilization technologies, and modular manufacturing facilities. Our global manufacturing footprint and strong engineering expertise enable us to deliver flexible, compliant, and cost-effective solutions for both clinical and commercial production.

At ISCT Singapore, we look forward to connecting with industry partners and exploring innovative approaches to accelerate the development and manufacturing of advanced therapies.

Touchlight Booth #4

Touchlight is an innovation-driven leading CDMO pioneering enzymatic GMP DNA production to enable the genetic medicine revolution. As pioneers, with an FDA Drug Master File accepted in 2022 followed in 2025 by the world's first cell-free DNA GMP license, Touchlight's enzymatic DNA technology is on the cutting edge of AAV, mRNA, DNA vaccine, and gene editing technology with its state-of-the-art facility recognised by ISPE's Facility of the Year Awards (FOYA) for Innovation.

With multiple client products already in the clinic, Touchlight's evidence-based, synthetic DNA manufacturing solutions offer a scalable, sustainable alternative to plasmid DNA (pDNA) for all stages of pre-clinical, clinical and commercial development. The company and technology are built on the conviction that DNA is fundamental to the future of medicine. Traditional methods, based on bacterial fermentation, are slow, costly, and unable to meet the growing demands of genetic medicine due to limited scalability and speed. Founded in 2007, Touchlight's team is inspired by breakthroughs in genetic medicine, recognising the urgent need for innovative DNA production techniques to support the future of genetic therapies.

VectorBuilder Booth #32

VectorBuilder Revolutionizing Gene Delivery from Research to Therapy

VectorBuilder is a leading gene delivery solutions provider offering an integrated suite of products and services for the global research and therapeutic community. Through its industry-leading online platform, VectorBuilder enables scientists to design, customize, and order vectors with unmatched ease and efficiency — with free expert design support included.

VectorBuilder's comprehensive service offerings span the full gene delivery workflow, including custom vector design and cloning, recombinant virus packaging (Lentivirus, AAV, Adenovirus, Retrovirus and more), recombinant protein expression, stable cell line engineering, CRISPR-based genome editing, library screening and therapeutic IVT RNA and LNP production. With a commitment to consistent quality, rapid turnaround, and competitive pricing, VectorBuilder serves thousands of research institutions, biotechnology companies, and pharmaceutical organizations worldwide.

Waters Biosciences Booth #44

At Waters Biosciences, formerly BD Biosciences, we take pride in our innovative history. From the invention of the first fluorescence activated cell sorter (FACS) in the 1970s to pioneering monoclonal antibody development in the 1990s to the industry-changing invention of polymer fluorochromes, we continue to be at the forefront of discovery, shaping the future with new innovations in single-cell sequencing, genomics, proteomics and informatics. True to our mission of advancing the world of health™, we proudly offer a large and extensive portfolio of products to address your research and clinical needs, along with many new research innovations:

- A family of spectrally optimized fluorochrome reagents
- Monoclonal antibodies for novel immunological targets
- The latest in data analysis software
- The new BD Rhapsody™ HT Xpress System that enables high-throughput single-cell sequencing studies
- And, the first real-time imaging, spectral flow cytometer that combines advanced spectral flow cytometry with real-time spatial and morphological insights using BD CellView™ Image Technology, a novel high-speed image-enabled sorting technology. Now as we enter a new chapter as Waters Biosciences, we continue our dedication to supporting the scientific community with total workflow solutions throughout their journey in basic to translational and clinical research clear through to clinical diagnostics.

Wise Formula Limited Booth #44

Established in 2025 and headquartered in Hong Kong, WISE FORMULA is a premier life science solutions provider and a trusted partner in scientific innovation and scalable industrial application worldwide. WISE FORMULA is more than a distributor, WISE FORMULA specializes in bridging the gap between novel technology and industry-scale operation. If you are looking for a reliable supply of reagents, media, or all-in-one workflow solution, WISE FORMULA is your trusted partner.

Xcell Therapeutics Inc. Booth #35

Xcell Therapeutics is a biotechnology company specializing in the development and manufacturing of serum-free, chemically defined media. The company supports cell therapy, regenerative medicine, and biopharmaceutical production by providing high-quality, consistent, and scalable culture solutions. With a strong focus on innovation and regulatory compliance, Xcell Therapeutics aims to enhance cell growth, productivity, and safety across various applications, enabling advanced research and commercialization in the life sciences industry.

ZHENG YANG Biomedical Technology Co., Ltd.
Booth #3

We are a Taiwan-based biotech company specializing in exosome R&D and production.

With ExoYoung, we aim to bring biotech excellence into the world of beauty.

Pharmaceuticals and Medical Devices Agency
Tabletop #1, Located outside MR 325-326

Pharmaceuticals and Medical Devices Agency (PMDA) is the regulatory authority of Japan. PMDA provides consultation services to support the development of cell and gene therapy (CGT) products in Japan, primarily for academia and start-up companies, with the objective of facilitating the development of CGT products in Japan by providing an overview of the regulatory framework and consultation services to those considering for the Japanese market.

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Abstracts

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

LONGITUDINAL URINARY EXTRACELLULAR VESICLE PROFILING AFTER CAR-T CELL THERAPY: A PILOT FEASIBILITY STUDY

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KEYWORDS: CAR-T, Extracellular vesicles, Urinary biomarkers.

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Background & Aim

Chimeric antigen receptor (CAR)-T cell therapy has revolutionized the treatment of B-cell malignancies; however, relapse remains common and may be associated with T-cell exhaustion and senescence. Standard assessment of circulating lymphocytes may not fully reflect immune-cell activity within tissues. Activated and senescent T cells release extracellular vesicles (EVs) carrying biomarkers involved in immune regulation. We evaluated the feasibility of longitudinal urinary EVs profiling after CAR-T cell therapy and explored changes in EVs populations expressing T-cell-associated, activation- and exhaustion-related markers.

Methods, Results & Conclusion

Clinical data was prospectively collected from 6 patients treated with anti-CD19 CAR-T cells (tisagenlecleucel) for diffuse large B-cell lymphoma or B-cell acute lymphoblastic leukemia. Urine samples were obtained on days −7, 0, 7, 14 and 21 post infusion. Urinary EVs were isolated by size-exclusion chromatography analyzed by flow cytometry for TCR, CD27, lymphocyte-activation gene (LAG), and CD81 expression. Urinary EVs profiling was feasible in 23 longitudinal samples. Samples were available at day −7 (n=6), day 0 (n=3), day 7 (n=4), day 14 (n=6) and day 21 (n=4).

Median LAG+ EVs counts were 44.7×10³/ml at baseline, 25.6×10^3/ml at day 0, 13.5×10³/ml at day 7, 34.0×10³/ml at day 14 and 29.3×10³/ml at day 21. CD27+ EVs count decreased immediately after infusion (5.6×10³/ml vs 9.3×10³/ml at baseline) and subsequently increased to 12.5×10³/ml at day 14 and 16.8×10³/ml at day 21. TCR+ EVs showed the most consistent increase, rising from 2.4×10³/ml at baseline to 7.9×10³/ml at day 0, 9.3×10³/ml at day 14 and 8.4×10³/ml at day 21. CD81+ EVs demonstrated a biphasic pattern, decreasing from 40.6×10³/ml at baseline to 7.0×10³/ml at day 14 and rebounding to 35.0×10³/ml at day 21 (Fig. 1). Individual trajectories were heterogeneous. The highest LAG+ EVs level (421×10³/ml) was observed in a patient who developed immune effector cell-associated neurotoxicity syndrome (ICANS) at day 5, whereas a marked increase in CD27+ EVs (185×10³/ml) occurred in a patient who achieved only partial response at day 30.

Longitudinal urinary EVs profiling after CAR-T cell therapy is feasible and reveals dynamic, marker-specific changes in EVs populations. Preliminary associations with ICANS and treatment response support it as a non-invasive approach for monitoring immune-cell activity after CAR-T infusion. Further studies are needed to validate its clinical utility.

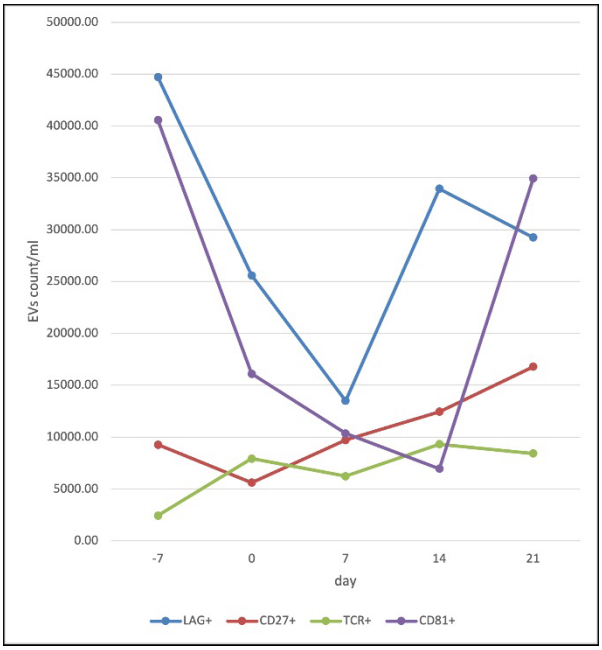


Figure 1. Longitudinal median concentrations (counts/ml) of urinary extracellular vesicles positive for TCR, CD27, LAG, and CD81 following CAR-T cell therapy.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

A NEXT-GENERATION IONIZABLE LIPID LNP PLATFORM FOR EFFICIENT IN VIVO CAR T CELL GENERATION ACROSS SPECIES THROUGH PASSIVE AND ACTIVE IMMUNE CELL TARGETING STRATEGIES

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KEYWORDS: CAR T, LNP, In Vivo.

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Background & Aim

Ex vivo CAR T therapies face complex manufacturing, long timelines, and high cost, limiting access. In vivo approaches may overcome these barriers by enabling repeat dosing without ex vivo manipulation. RNA-LNPs offer a scalable, transient platform, but lymphoid delivery and T cell specificity remain challenges. We present an ionizable LNP platform with spleen/lymph node tropism and T cell-targeted functionalization, evaluated in mice and NHPs.

Methods, Results & Conclusion

Reporter RNA-LNPs were formulated and characterized. Biodistribution after IV administration was assessed in mice via IVIS, and cell-specific delivery in tdTomato mice by flow cytometry. A lead LNP was conjugated to a CD8-nanobody to generate targeted LNPs (tLNPs) and tested in NSG mice with a Nalm6 tumor model. Scalable manufacturing processes and analytics (UHPLC-CAD, HRMS, SEC-MALS) were established. In cynomolgus monkeys, untargeted and targeted LNPs were evaluated for biodistribution, CAR expression, B-cell depletion and tolerability.
Formulation screening identified LNPs with strong splenic tropism, achieving spleen:liver ratios of 3:1 to 30:1 in mice. Untargeted LNPs mainly transfected dendritic cells and macrophages, with ~10% efficiency in T and NK cells and no activity in B cells. A lead formulation was scaled for NHP studies. In cynomolgus monkeys, this LNP showed a biodistribution profile consistent with murine findings, with a spleen:liver ratio >4:1 and lymph node:liver ratio of approximately 1:1, alongside favorable tolerability.
To enhance T cell specificity, an anti-CD8 nanobody was conjugated to the LNP. These tLNPs achieved up to 80% transfection of T cells in blood and spleen in NSG mice. Using CAR-tLNP potent anti-tumor activity in a Nalm6 model, with complete tumor regression at 0.1 mg/kg was shown. In NHPs, tLNPs induced robust and safe CAR expression in >60% of CD8+ T cells at a dose of 0.1 mg/kg, resulting in complete B cell depletion in both blood and spleen, confirming functional CAR activity and efficient in vivo T cell engineering at clinically translatable dose levels.
This work describes a next-generation ionizable LNP platform with intrinsic immune-organ tropism. Combined with a scalable manufacturing and targeting framework, this modular system enables efficient and selective CAR T generation in mice and NHP. The findings support the use of this immune-tropic LNP platform for the delivery of RNAs and other gene-editing payloads, advancing the clinical potential of *in vivo* cell therapies.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

A 7-DAY CAR-T MANUFACTURING PLATFORM DELIVERING THREE-FOLD FASTER VEIN-TO-VEIN TIME THROUGH NEGATIVE SELECTION–DRIVEN CELL PROCESSING AND GMP-COMPLIANT INFRASTRUCTURE

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KEYWORDS: CAR-T, Vein-to-Vein, LMIC.

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2. Vector BioMed, Gaithersburg, MD, United States.
3. Genes2me, Gurugram, Haryana, India.

Background & Aim

Prolonged manufacturing timelines remain a major barrier to CAR-T accessibility, particularly in India and other low- and middle-income countries (LMICs), where patients often require bridging therapy while awaiting product release. We developed an integrated CAR-T platform combining rapid manufacturing, negative-selection–based T-cell enrichment, and GMP-compliant infrastructure to accelerate treatment delivery and expand access.

Methods, Results & Conclusion

Methods

CGT19 is a second-generation anti-CD19 CAR-T product incorporating FMC63 scFv, CD8 hinge/transmembrane, 4-1BB, and CD3ζ signaling domains in-licenced from Vector BioMed, USA. Manufacturing employs a proprietary negative-selection technology that depletes non-T-cell populations while preserving untouched T cells and rare functional subsets without receptor engagement. The process is performed in a functionally closed, semi-automated workflow and completed within 7 days from leukapheresis to cryopreservation.
Manufacturing is supported by a purpose-built GMP-

compliant facility comprising independent ISO Grade 6 manufacturing suites, integrated quality-control laboratories, segregated personnel and material flows, and contamination-control systems aligned with international regulatory expectations.

Results

The platform consistently generated CAR-T products with approximately 70% CAR expression and vector copy numbers of approximately 3 while maintaining potent CD19-specific cytotoxicity. In preclinical studies, complete tumour clearance was achieved by Day 55.
The 7-day manufacturing process enables an estimated three-fold reduction in overall vein-to-vein time compared with conventional CAR-T workflows. This accelerated pathway has the potential to substantially reduce the need for bridging therapy, minimizing treatment delays and improving patient access to infusion. The negative-selection approach eliminates bead-based enrichment steps, preserves less differentiated T-cell populations. The platform supports the production of approximately 800 autologous CAR-T therapies annually from a single site.

Conclusions

This integrated CAR-T platform combines rapid manufacturing, preservation-focused cell processing, and regulatory-compliant infrastructure to address key barriers to CAR-T accessibility. By enabling approximately three-fold faster vein-to-vein time and potentially reducing dependence on bridging therapy, the platform provides a scalable blueprint for deployment of CAR-T and future cell therapies across LMIC.

4

Gene Editing/Gene Therapies

GENE THERAPY FOR MEF2C HAPLOINSUFFICIENCY SYNDROME

J. Ruan[1, 2], Z. Tao[1, 2], H. Zhang[1, 2], K. Zhang[1], X. Yu[1, 2], Y. Zhang[1]

KEYWORDS: Gene Therapy, AAV.

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Background & Aim

MEF2C is a key transcription factor essential for neuronal differentiation, synaptic development, and cortical circuit formation. Heterozygous *MEF2C* mutations or chr5q14.3 microdeletions causing *MEF2C* gene dysfunction result in MEF2C haploinsufficiency syndrome (MCHS), a severe neurodevelopmental disorder characterized by intellectual disability, absent or limited speech, stereotypic movements, seizures, and autistic features. Despite growing clinical recognition, no disease-modifying therapies currently exist. We identified a novel *MEF2C* p.K5X nonsense mutation in a clinical cohort and aimed to establish a faithful mouse model and evaluate the therapeutic potential of AAV-mediated MEF2C gene replacement.

Methods, Results & Conclusion

A *Mef2c* $K5X^{+/-}$ knock-in mouse model was generated via CRISPR/Cas9 and confirmed by Sanger sequencing. Mutant mice showed reduced body weight, smaller brain size, and decreased MEF2C expression in the somatosensory cortex ($p < 0.0001$). $K5X^{+/-}$ mice exhibited impaired novel object recognition, elevated seizure severity scores ($p < 0.01$), and hyperactivity in the open field test ($p < 0.05$). An AAV9 vector carrying a codon-optimized human MEF2C transgene (hMEF2Copt) under the hSyn promoter was developed, yielding significantly higher mRNA and protein expression than the native sequence in HEK293T cells ($p < 0.01$; $p < 0.001$). Stereotaxic AAV delivery into the mPFC showed a trend toward restored mEPSC frequency in layer II/III neurons of treated $K5X^{+/-}$ mice. In the cohort receiving systemic AAV delivery via tail vein injection, treated $K5X^{+/-}$ mice showed rescued novel object recognition ($p < 0.05$) and reduced seizure severity ($p < 0.01$). These findings establish Mef2c $K5X^{+/-}$ mice as a valid preclinical model of MCHS and provide proof-of-concept for AAV-mediated MEF2C replacement as a promising gene therapy strategy.

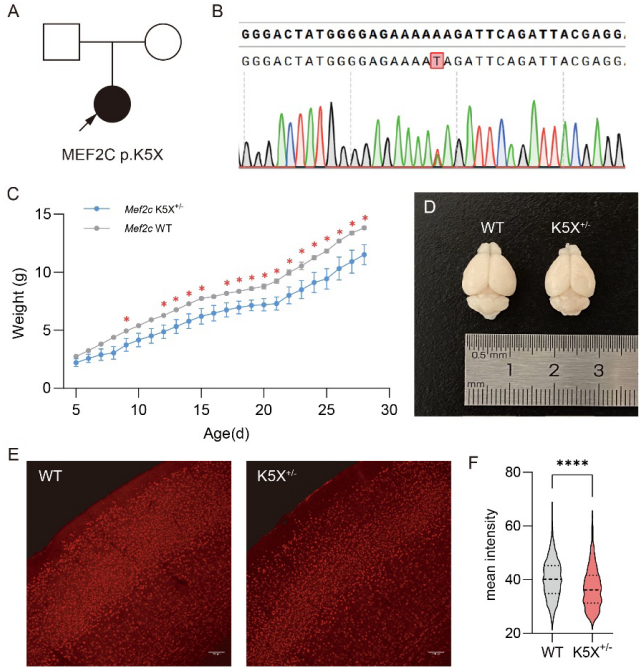


Figure 1. Construction and Basic Physiological Phenotyping of the Mef2c K5X+/− Mouse Model. (A) Pedigree of a family carrying the MEF2C p.K5X nonsense mutation identified in a clinical cohort. The arrow indicates the proband; (B) Sanger sequencing chromatogram alignment of genomic DNA from Mef2c K5X point-mutant mice (F1 generation); (C) Body weight growth curves of WT and Mef2c K5X+/− mice from postnatal day 5 to 28 (P5–P28); (D) Representative gross morphology comparison of brain tissue between WT and Mef2c K5X+/− mice; (E) Representative immunofluorescence staining images of MEF2C protein in the somatosensory cortex of mice; (F) Quantitative statistical analysis of mean MEF2C fluorescence intensity in the somatosensory cortex.

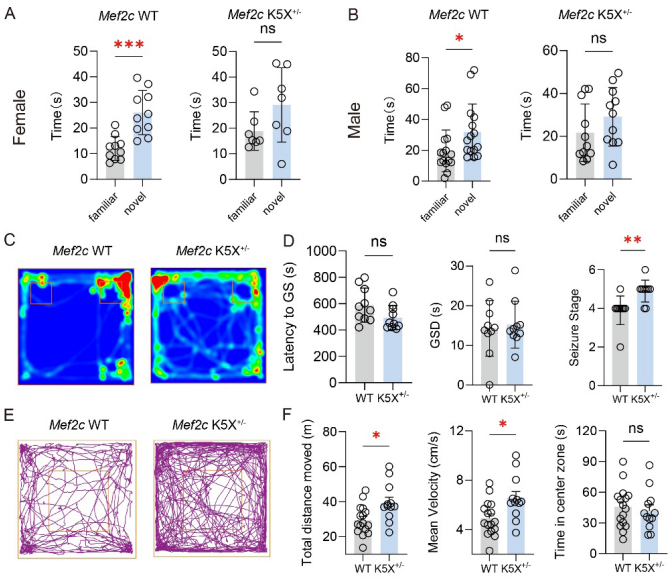


Figure 2. Behavioral Phenotyping of Mef2c K5X+/- Mice. (A–B) Statistical analysis of exploration time toward the familiar object and the novel object during the testing phase of the novel object recognition task in female (A) and male (B) mice; (C) Representative heatmaps of mouse activity during the novel object recognition testing phase, with the familiar object in the upper left and the novel object in the upper right; (D) Results of the heat-induced seizure assay; (E) Representative locomotion trajectory plots of mice in the open field test; (F) Statistical analysis of behavioral parameters in the open field test.

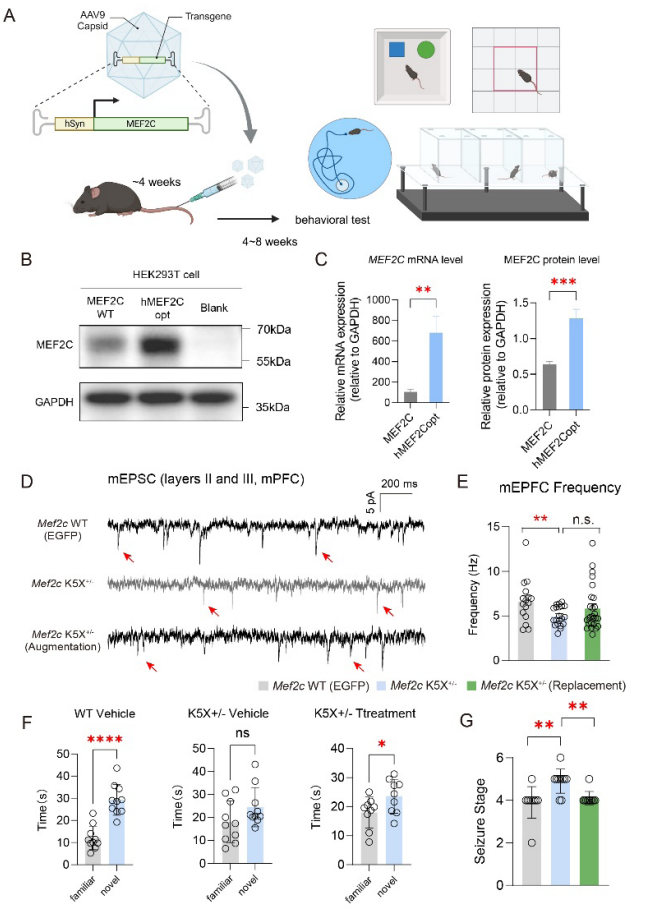


Figure 3. AAV-Mediated MEF2C Augmentation Rescues Behavioral and Electrophysiological Deficits in Mef2c K5X+/- Mice. (A) Schematic diagram of the workflow; (B) Western blot analysis of MEF2C protein expression in HEK293T cells; (C) Quantitative statistical analysis of MEF2C mRNA levels and MEF2C protein levels in HEK293T cells; (D) Representative mEPSC traces recorded from layer II/III neurons of the mPFC; (E) Quantitativ statistical analysis of mEPSC frequency; (F) Statistical analysis of the novel object recognition task; (G) Statistical analysis of seizure severity scores following heat-induced seizure induction across the three groups.

5

Immunotherapy (CAR-T, T Reg, NK Cells etc.)

PHASE-SPECIFIC PD-1 BLOCKADE DURING EARLY CONTRACTION OF IL-7/CCL19–ARMORED CD19 CAR-T CELLS PROMOTES RESPONSE DEEPENING IN HIGH-RISK R/R LBCL: A FIRST-IN-HUMAN PHASE I STUDY

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KEYWORDS: Armored CAR-T cells, PD-1 blockade, Relapsed or refractory large B-cell lymphoma.

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2. Hematology, The Second Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, Zhejiang Province, China.

Background & Aim

CD19 CAR-T therapy has transformed R/R LBCL treatment, yet durable control remains limited in patients with bulky or PD-L1–enriched tumors. IL-7/CCL19–armored CAR-T cells enhance persistence and immune recruitment, but post-expansion functional remodeling may limit efficacy. Whether the early contraction phase represents a targetable window for checkpoint modulation remains undefined.
This phase I study evaluated safety and preliminary efficacy of phase-specific PD-1 blockade during early contraction of IL-7/CCL19–armored CD19 CAR-T cells in high-risk R/R LBCL.

Methods, Results & Conclusion

Methods

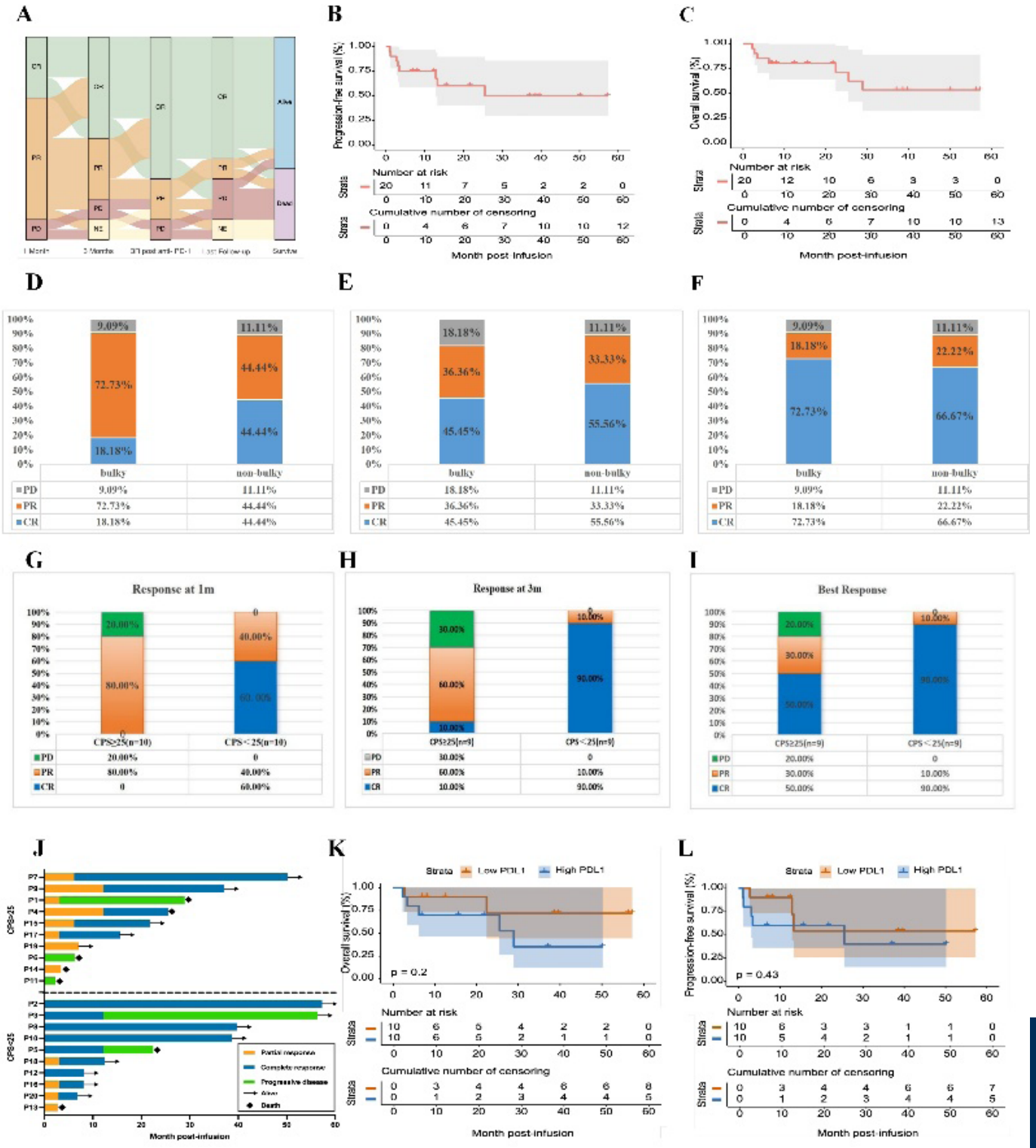
Twenty R/R LBCL patients received lymphodepletion followed by IL-7/CCL19–armored CD19 CAR-T cells (2×10^6/kg). Kinetic monitoring identified peak expansion at days 14–21 and contraction by days 21–30. Tislelizumab 200 mg was initiated on day +30 ± 2. Primary endpoints were safety and 3-month ORR. Secondary endpoints included CR rate, PFS, OS, and DOR. Correlatives included CAR transgene quantification, flow cytometry, scRNA-seq, ex vivo functional assays, and TCR clonotype analysis.

Results

During contraction, CAR-T cells upregulated PD-1, TIGIT, LAG-3, and TOX with reduced memory-like subsets, yet retained functional plasticity. Ex vivo PD-1 blockade enhanced proliferation (Ki-67), IFN-γ production, and degranulation. Sequential PD-1 blockade did not trigger new-onset CRS or ICANS. Pre–PD-1 blockade CR was 30% and PR 60%. After PD-1 blockade, 8/12 PR patients converted to CR, yielding a best CR of 70% and 3-month ORR of 85%. At median follow-up of 21.8 months, 2-year PFS and OS were 60.0% and 71.1%, respectively. PD-L1–high and bulky-disease patients had lower early CR rates but showed response deepening after checkpoint inhibition, with outcomes approaching PD-L1–low and non-bulky subgroups.

Conclusion

Early contraction of IL-7/CCL19–armored CAR-T cells reflects checkpoint-associated functional restraint rather than terminal exhaustion. Phase-specific PD-1 blockade was feasible, safe, and associated with functional restoration and response deepening. Timing is a critical determinant of checkpoint modulation after CAR-T therapy. Results are hypothesis-generating and warrant prospective validation.


A
B
C
Progression-free survival (%)
Overall survival (%)
Number at risk
Cumulative number of censoring
Month post Infusion
Month post-infusion
D
E
F
bulky
non-bulky
PD
PR
CR
G
H
I
Response at 1m
Response at 3m
Best Response
CPS≥25(n=10)
CPS<25(n=10)
CPS≥25(n=9)
CPS<25(n=9)
J
K
L
Low PDL1
High PDL1
p = 0.2
p = 0.43
Partial response
Complete response
Progressive disease
Alive
Death
Month post-infusion

6

Immunotherapy (CAR-T, T Reg, NK Cells etc.)

REAL-WORLD OUTCOMES OF BCMA-TARGETED CAR-T CELL THERAPY IN RELAPSED/REFRACTORY MULTIPLE MYELOMA

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KEYWORDS: CAR-T, CRS.

1. Department of Hematology, Institute of Hematology, West China Hospital, Sichuan University, Chengdu, Sichuan, China.

Background & Aim

BCMA-directed CAR-T therapy is highly effective for relapsed/refractory multiple myeloma (RRMM). However, real-world data comparing the fully human anti-BCMA products Zevorcabtagene autoleucel (zevor-cel) and equecabtagene autoleucel (eque-cel) are limited. This study reports the clinical outcomes of 12 consecutive RRMM patients treated in a single center.

Methods, Results & Conclusion

Methods and results

We conducted a retrospective analysis of 12 consecutive RRMM patients who received BCMA-directed CAR-T therapy at West China Hospital, Sichuan University. Seven patients received zevor-cel and five received eque-cel. All patients received lymphodepleting conditioning with fludarabine and cyclophosphamide (FC) prior to CAR-T infusion. The median age of the whole cohort was 60 years (range 47-80), with 50% female. Patients had a median of 3 prior lines (range 1-5) with 92% daratumumab-refractory. High-risk cytogenetics (1q21, t(4;14), P53) were present in 50% and extramedullary disease was observed in 33% (bone 25%, soft tissue 8%).

A single infusion of CAR-T cells was administered to all patients. Among zevor-cel recipients (n=7), CRS was observed in 6 (85.7%). One patient (14.3%) developed ICANS grade 4. Infections occurred in all 7 patients. Among eque-cel recipients (n=5), CRS occurred in 4 (80%). No ICANS was reported. Infections were observed in 4 patients (80%).

The best overall response rate was 100% (sCR 58%, CR 8%, VGPR 17%, PR 17%). MRD negativity was achieved in 67% of evaluable patients. Median time to the best response was 1.5 months (range 1–10 months). Two deaths were recorded due to HLH and septic shock respectively. Among patients with six-month hematologic recovery data, median Hb increased from 119 to 132 g/L, PLT from 104 to 89×10^9/L, eGFR remained stable >60 mL/min in most.

Conclusions

In this real-world cohort, both zevor-cel and eque-cel demonstrated high response rates and deep remissions in heavily pretreated RRMM patients. CRS and infections remain significant but manageable toxicities. Zevor-cel was associated with one case of grade 4 ICANS, which warrants further monitoring. These findings support the continued use of BCMA-targeted CAR-T therapy in clinical practice and highlight the need for optimized patient selection and proactive toxicity management. Larger comparative studies are warranted to delineate product-specific efficacy and safety profiles.

Patient	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*
Gender	male	female	male	female	male	female	male	female	male	male	male	female
Age	60	80	61	63	54	57	50	67	56	67	62	47
M-protein type	IgG kappa	IgA kappa	IgD lambda	kappa	IgG lambda	IgA kappa	IgA lambda	IgG kappa	IgG lambda	IgG lambda	IgA lambda	lambda
Extramedullary Disease	Bone	Bone	NO	soft tissue	Bone	NO	NO	NO	Bone	Bone	NO	NO
ISS stage	I	III	III	II	II	I	I	I	III	III	I	I
RISS stage	I	III	III	II	II	I	I	I	III	III	I	I
Genetic abnormalities	none	1q21+ , t(4;14)	1q21+	RB1 deletion, P53 deletion, t(11;14), 1q21+	none	1q21+	none	none	P53 deletion	none	none	1q21+
Treatment lines	3	2	2	3	1	5	4	3	3	5	3	2
ASCT	No	No	No	No	Yes	No	Yes	No	No	No	No	No
Renal insufficiency	No	No	No	No	No	No	No	No	No	Yes	No	No
CART type	Zevor-cel	Zevor-cel	Zevor-cel	Zevor-cel	Zevor-cel	Eque-cel	Eque-cel	Eque-cel	Eque-cel	Eque-cel	Eque-cel	Eque-cel
CRS grade	1	3	1	3	0	1	0	2	2	3	1	1
ICANS grade	NO	4	NO	0	0	0	0	0	0	0	0	0
Infection grade	1	3	1	3	0	3	0	3	2	4	2	2
Best response	PR	SCR	SCR	CR	SCR	SCR	SCR	VGPR	SCR	PR	SCR	SCR
MRD	positive	negative	negative	NA	NA	negative	negative	positive	negative	positive	negative	negative
Time to best response	1m	1m	1m	2m	NA	2m	1m	10m	8m	1m	3m	1m
Maintenance therapy	NO	NO	NO	NO	NA	NO	Pomalidomide	NO	Selinexor	NO	NO	NO
Progression	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
Death	NO	NO	NO	YES	NO	NO	NO	NO	NO	YES	NO	NO

7

Hematopoietic Stem/Progenitor Cells and Engineering

AUTOLOGOUS AND ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN NK/T-CELL LYMPHOMA: A LONG-TERM REAL-WORLD ANALYSIS

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KEYWORDS: NKT lymphoma, ASCT, allo-HSCT.

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Background & Aim

The optimal role of autologous hematopoietic stem cell transplantation (ASCT) and allogeneic hematopoietic stem cell transplantation (allo-HSCT) in natural killer/T-cell lymphoma or extranodal NK/T-cell lymphoma (NKT/ENKTCL) remains uncertain. Because allo-HSCT is often selected for higher-risk patients, comparisons based on transplantation modality alone may obscure the effects of disease control, transplant timing, and non-relapse mortality (NRM).

Methods, Results & Conclusion

Methods

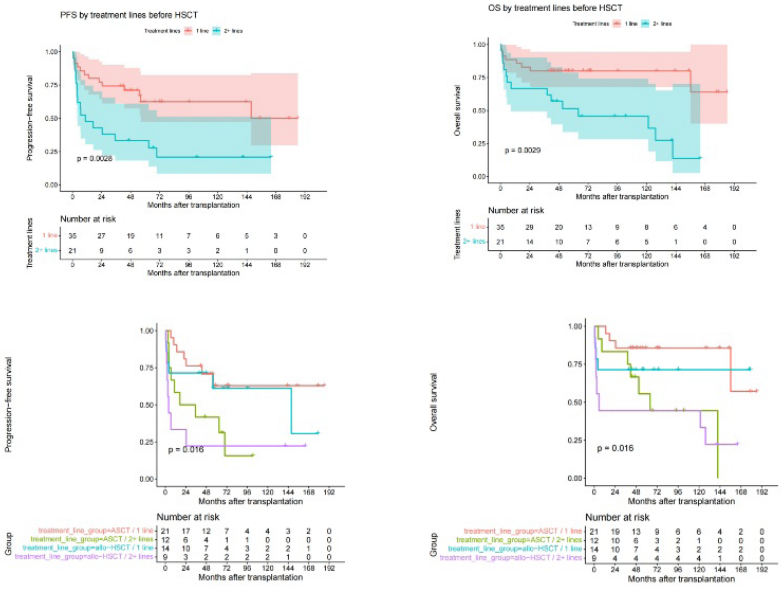
We retrospectively analyzed 56 patients with NKT/ENKTCL who underwent ASCT (n=33) or allo-HSCT (n=23) at the First Affiliated Hospital of Soochow University between 2007 and 2023, with follow-up through May 1, 2026. Endpoints included PFS, OS, relapse/progression, and NRM. Effective pretransplant CR was defined as radiographic CR with negative pretransplant EBV-DNA. Cox regression, competing-risk analyses, IPTW, and 36-month RMST analyses were performed. An exploratory PRRS was constructed using clinically predefined risk domains.

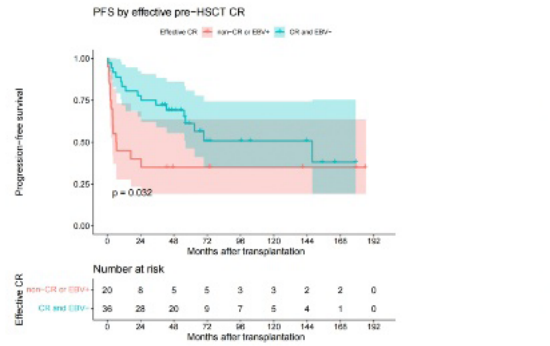
Results

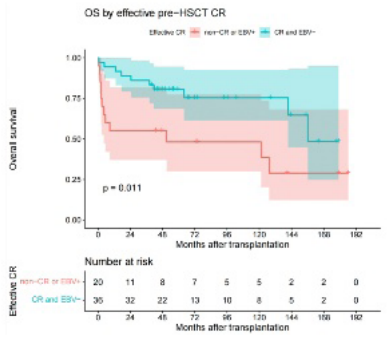
Transplantation modality alone was not significantly associated with outcomes (PFS: HR 1.45, 95% CI 0.70-3.03, P=0.317; OS: HR 1.76, 95% CI 0.76-4.09, P=0.186). Competing-risk analysis showed a trend toward lower relapse/progression with allo-HSCT (Gray's P=0.089) but significantly higher NRM (Gray's P=0.0008), resulting in a 36-month RMST for OS that was 9.80 months shorter after allo-HSCT than after ASCT (P=0.009). Patients transplanted after ≥2 treatment lines had significantly inferior PFS (adjusted HR 2.78, 95% CI 1.30-5.93, P=0.008) and OS (adjusted HR 3.14, 95% CI 1.25-7.85, P=0.015) compared with first-line therapy. Effective pretransplant CR was associated with better PFS (HR 0.45, 95% CI 0.22-0.95, P=0.036) and OS (HR 0.35, 95% CI 0.15-0.82, P=0.015). PRRS per 1-point increase predicted PFS (HR 1.76, 95% CI 1.17-2.64, P=0.006) and OS (HR 1.95, 95% CI 1.26-3.01, P=0.003); PRRS-core showed similar prognostic value (PFS: HR 2.25, 95% CI 1.05-4.79, P=0.036; OS: HR 2.46, 95% CI 1.06-5.72, P=0.037). No PRRS-defined subgroup demonstrated significant differential benefit from allo-HSCT (interaction P > 0.05).

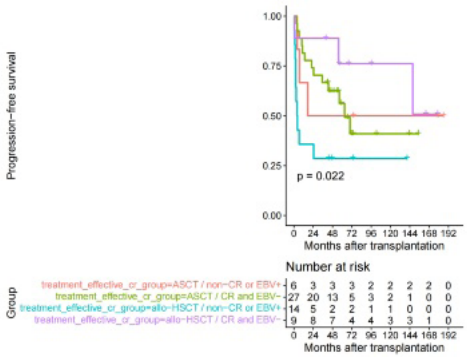
Conclusions

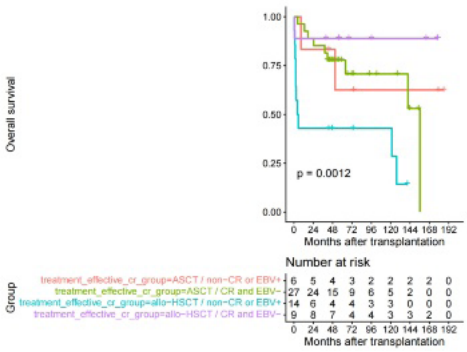
In this real-world NKT/ENKTCL cohort, transplantation modality alone did not determine outcomes. Allo-HSCT may offer relapse control but with increased NRM. Early transplantation (after first-line) and achieving EBV-integrated effective pretransplant CR were key prognostic factors. Residual-risk stratification using PRRS may aid prognosis.

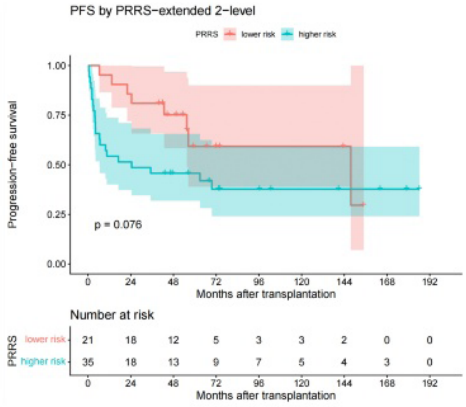


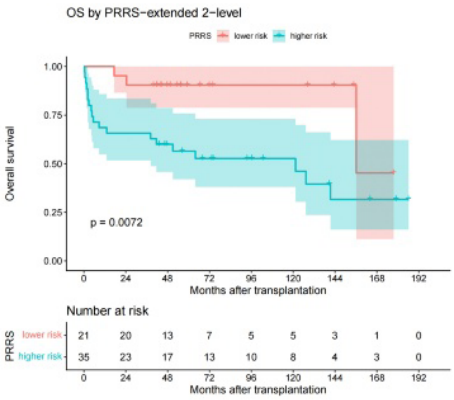

PFS by effective pre−HSCT CR
Progression−free survival
p = 0.032
Months after transplantation
Number at risk
Effective CR
non−CR or EBV+
CR and EBV−


OS by effective pre−HSCT CR
Overall survival
p = 0.011
Months after transplantation
Number at risk
Effective CR
non−CR or EBV+
CR and EBV−


Progression−free survival
p = 0.022
Months after transplantation
Number at risk
Group
treatment_effective_cr_group=ASCT / non−CR or EBV+
treatment_effective_cr_group=ASCT / CR and EBV−
treatment_effective_cr_group=allo−HSCT / non−CR or EBV+
treatment_effective_cr_group=allo−HSCT / CR and EBV−


Overall survival
p = 0.0012
Months after transplantation
Number at risk
Group
treatment_effective_cr_group=ASCT / non−CR or EBV+
treatment_effective_cr_group=ASCT / CR and EBV−
treatment_effective_cr_group=allo−HSCT / non−CR or EBV+
treatment_effective_cr_group=allo−HSCT / CR and EBV−


PFS by PRRS−extended 2−level
PRRS
lower risk
higher risk
Progression−free survival
p = 0.076
Months after transplantation
Number at risk


OS by PRRS−extended 2−level
PRRS
lower risk
higher risk
Overall survival
p = 0.0072
Months after transplantation
Number at risk

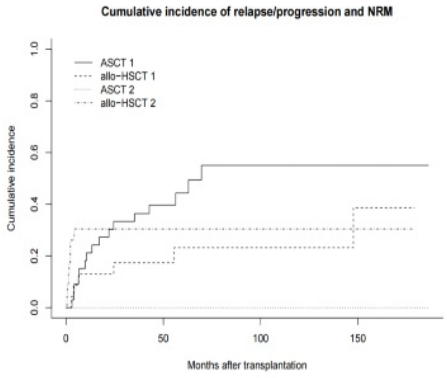

Cumulative incidence of relapse/progression and NRM
ASCT 1
allo−HSCT 1
ASCT 2
allo−HSCT 2
Cumulative incidence
Months after transplantation

Table 1: Overall transplantation modality comparison and sensitivity analyses

Analysis	Endpoint	Effect estimate	P value
Univariable Cox: allo-HSCT vs ASCT	PFS	HR 1.45 (0.70-3.03)	0.317
Univariable Cox: allo-HSCT vs ASCT	OS	HR 1.76 (0.76-4.09)	0.186
Adjusted Cox: allo-HSCT vs ASCT	PFS	HR 1.19 (0.52-2.73)	0.686
Adjusted Cox: allo-HSCT vs ASCT	OS	HR 1.14 (0.44-2.95)	0.787
Competing risk: relapse/ progression	CIF	Lower trend after allo-HSCT	0.089
Competing risk: NRM	CIF	Higher after allo-HSCT	0.0008
IPTW Cox: allo-HSCT vs ASCT	PFS	HR 1.21 (0.51-2.88)	0.669
IPTW Cox: allo-HSCT vs ASCT	OS	HR 1.38 (0.50-3.81)	0.532
36-month RMST: allo-HSCT minus ASCT	PFS	-6.69 months	0.097
36-month RMST: allo-HSCT minus ASCT	OS	-9.80 months	0.009

8

iPSC

HYPOIMMUNE IPSC-DERIVED DOPAMINERGIC PROGENITOR CELL THERAPY FOR PARKINSON'S DISEASE

L. Jiao[1], Y. Zhang[1]

KEYWORDS: iPSC, iDAP, Parkinson's Disease.

1. Nuwacell Biotechnologies Co., Ltd, Hefei, China.

Background & Aim

Cell replacement therapy is a promising strategy for Parkinson's disease (PD), but its clinical application is limited by immune rejection, manufacturing variability, and safety concerns associated with pluripotent stem cell-derived products. This study aimed to develop a standardized hypoimmune human iPSC-derived dopaminergic progenitor cell (iDAP) product (product ID: NCR201) and evaluate its identity, immune-evasive properties, nonclinical efficacy and safety.

Methods, Results & Conclusion

NCR201 cells were generated from wild-type iPSCs through a targeted hypoimmune gene-editing strategy, followed by expansion, banking, and directed differentiation into iDAPs. Product identity and differentiation status were evaluated by phenotypic and lineage marker analyses. Immune-evasive function was assessed using human peripheral blood mononuclear cell (PBMC) co-culture assays. Therapeutic efficacy was examined in a 6-OHDA-induced rat model of PD, while surgical feasibility and long-term graft survival were evaluated in an MPTP-induced non-human primate model. Tumorigenicity was assessed in animal studies.
NCR201 exhibited typical neural morphology and showed a high proportion of cells expressing the neuronal marker β-tubulin III (98.38%), as well as the floor-plate markers FOXA2 (99.13%) and LMX1A (84.03%). After an additional 21-day *in vitro* maturation, NCR201 displayed extensive neurite outgrowth, and released high levels of dopamine. Midbrain dopaminergic neurons (mDAN) identity was further confirmed by $EN1^+$ (84.14%) and TH^+ (89.76%) cells. In a mixed lymphocyte reaction assay, NCR201 showed substantially improved survival and reduced stimulation of allogeneic PBMCs compared with wild-type iDAPs.

In 6-OHDA-lesioned rats, NCR201 grafts reduced apomorphine-induced rotations at 8- and 20-weeks post-transplantation. Histological analysis at 20 weeks confirmed graft survival, with abundant TH^+ mDANs. Safety testing in animal studies showed no significant concerns.

To evaluate surgical feasibility and hypoimmune engineering, NCR201 were transplanted into the putamen of MPTP-induced parkinsonian *Macaca fascicularis*. [^{18}F]-AV133 PET imaging confirmed sustained graft survival for 24 months, including 12 months after complete withdrawal of immunosuppressants.
Together, these findings support the further clinical development of NCR201 as a hypoimmune iPSC-derived cell therapy for Parkinson's disease.

9

Mesenchymal Stem/Stromal Cells

INDUCED PLURIPOTENT STEM CELL-DERIVED MESENCHYMAL STROMAL CELL EXTRACELLULAR VESICLES AMELIORATE MASH-RELATED LIVER FIBROSIS IN MICE

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KEYWORDS: Liver cirrhosis, iPS derived-MSC, Extracellular vesicles.

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Background & Aim

Metabolic dysfunction-associated steatohepatitis (MASH)-related cirrhosis is a major cause of end-stage liver disease with limited therapeutic options. Extracellular vesicles (EVs) from mesenchymal stromal cells (MSCs) have therapeutic potential; however, the limited proliferative capacity of autologous MSCs restricts sustained EV production. To address this limitation, we generated induced pluripotent stem cell-derived MSCs (iMSCs) as a scalable EV source and evaluated the therapeutic efficacy of iMSC-derived EVs (iMSC-EVs) in MASH-related liver fibrosis.

Methods, Results & Conclusion

iMSCs were characterized by EV yield, particle size, and microRNA profiles compared with bone marrow-derived MSCs (BMSCs). Activated human hepatic stellate cells (hHSCs) were treated with iMSC-EVs to assess anti-fibrotic effects in vitro. A murine MASH fibrosis model was induced by a high-fat diet and carbon tetrachloride. Mice received intravenous iMSC-EVs weekly for 4 weeks. Liver function, histology, and hepatic mRNA expression were analyzed. Single-cell RNA sequencing (scRNA-seq) compared iMSCs and BMSCs.
iMSCs produced EVs comparable to BMSCs in yield, size, and microRNA profiles. iMSC-EVs suppressed fibrosis-related genes (*COL1A1*, *COL1A2*, *COL3A1*) in activated hHSCs. In vivo, iMSC-EVs improved liver function and reduced the Sirius Red–positive fibrotic area. These effects were associated with decreased CD11c-positive M1 macrophages and increased CD163-positive M2 macrophages. Transcriptomic analysis showed downregulation of extracellular matrix-related pathways. scRNA-seq revealed that highly proliferative iMSC clusters expressed higher levels of the anti-inflammatory mediator *TNFAIP6* than BMSCs.
iMSC-EVs exert anti-fibrotic effects by inhibiting stellate cell activation and promoting macrophage polarization toward a fibrolytic phenotype. As a renewable and scalable EV source, iMSCs overcome key limitations of MSC therapies and represent a promising cell-free strategy for MASH-related cirrhosis.

10

Process Development, and Manufacturing & Commercialization

ON-DEMAND MICROFLUIDIC AUTOMATED DISSOCIATION OF IPSC AGGREGATES FOR CLOSED BIOREACTOR CULTURE MONITORING

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KEYWORDS: iPSC aggregates, Cell dissociation, Microvortex.

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Background & Aim

Closed bioprocessing is essential for producing clinical-grade cell products under GMP conditions. However, conventional stem cell sampling and dissociation require labor-intensive centrifugation steps that are time-consuming and increase contamination risk. This paper reports a microvortex-induced buffer exchange phenomenon for in-line, membrane-free washing of microcarriers and iPSC aggregates, integrated with direct sampling and automated aggregates dissociation in a closed microfluidic system (Fig 1).

Methods, Results & Conclusion

The microvortex is generated at the junction of two microchannels by introducing a sheath flow at approximately 3–4 times the sample flow rate. When microcarriers/cell aggregates from a bioreactor flow through the vortex region (stage 1), the vortex directs cell debris (2 μm beads) and spent culture media (FITC solution) to the waste outlet (O2), and larger microcarriers/cell aggregates (~50-400 μm) in new sheath buffer (PBS) to the main outlet (O1), achieving on-chip sample washing (Fig 1A). A serpentine-based channel concentrator (stage 2) inertially focuses the particles while removing excess PBS from side channels. Lastly, the enriched microcarriers/cell aggregates are mixed with enzyme in a herringbone mixer (stage 3) and eluted into 37 °C incubation tubing for complete cell dissociation (Fig 1B). Higher sheath flow rate intensifies the vortex,

achieves 96.5% buffer exchange, 100% microcarrier (MC) recovery, and 87.7% cell removal at 2200 µL/min sheath flow and 500 µL/min sample flow rate (Fig 2). The fluorescence imaging validated rapid on-chip mixing of cell aggregates and enzymes solutions (Fig 3A). As a proof-of-concept for closed cell aggregate dissociation, a compact benchtop setup was built to process iPSC aggregates (100-400 µm) from a bioreactor directly (Fig 3B). Brightfield images confirmed efficient aggregates dissociation to single iPSCs (Fig 3C-D). Notably, the on-chip dissociation workflow yielded significantly higher cell viability (> 95%) than manual dissociation while maintaining comparable pluripotency marker expression (Fig 3E-I).

Taken together, these results demonstrate an integrated microfluidic platform for membrane-free continuous-flow sample washing and enzymatic cell dissociation. It can be readily integrated with bioreactors to process a 10 mL sample within 10-20 minutes on-demand for off-line cell monitoring with minimized manual handling and contamination risk in GMP-compatible stem cell manufacturing workflows.

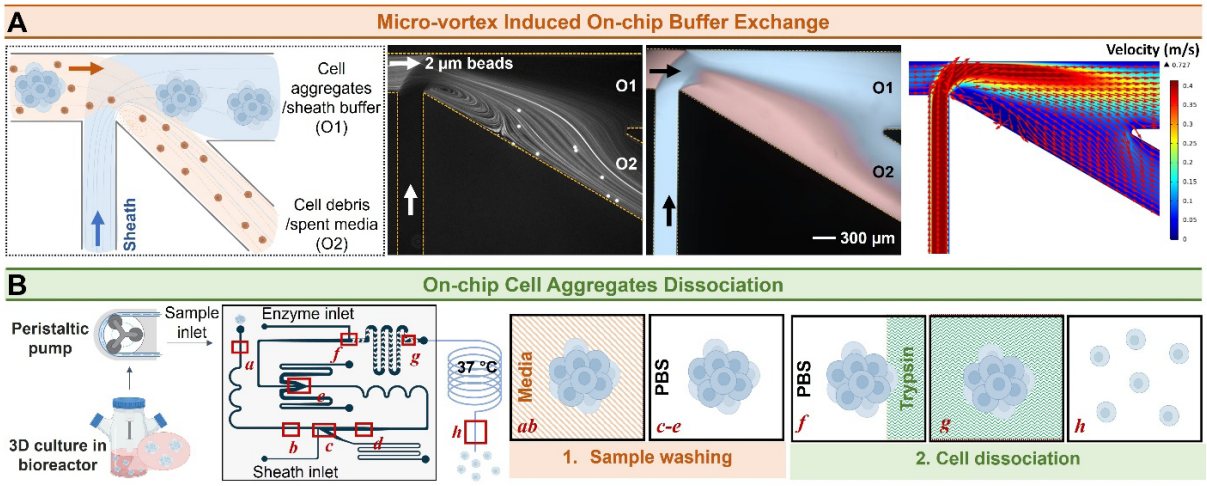


Figure 1. Micro-vortex induced cell aggregates washing (buffer exchange) for automated on-chip cell dissociation. A) Schematics, fluorescent images, and numerical simulation results showing the mechanism of the micro-vortex induced washing of cell aggregates from spent media (orange) to PBS (blue) prior trypsin addition. B) Closed-system workflow of automated in-line microfluidic cell aggregates dissociation from bioreactor directly.

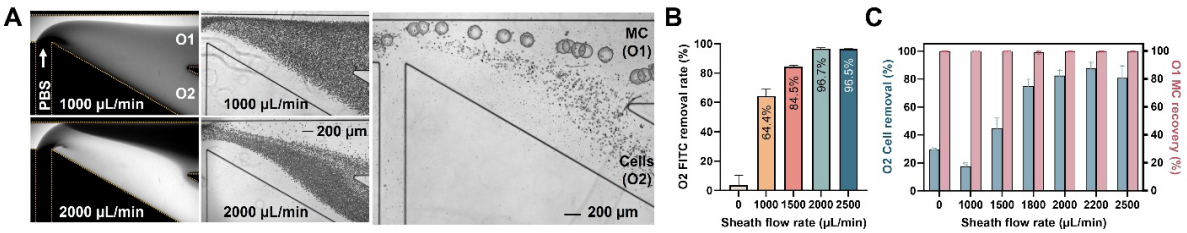


Figure 2. Effect of sheath flow rate on micro-vortex-induced buffer exchange. A) Fluorescent images showing FITC sample flow and PBS sheath flow. High speed images showing flow trajectory of microcarriers (MC) and cell/cell debris. B) FITC removal efficiency at O2, and C) cell removal efficiency from O2 and MC recovery from O1 at different sheath flow rates when sample flow rate is 500 µL/min.

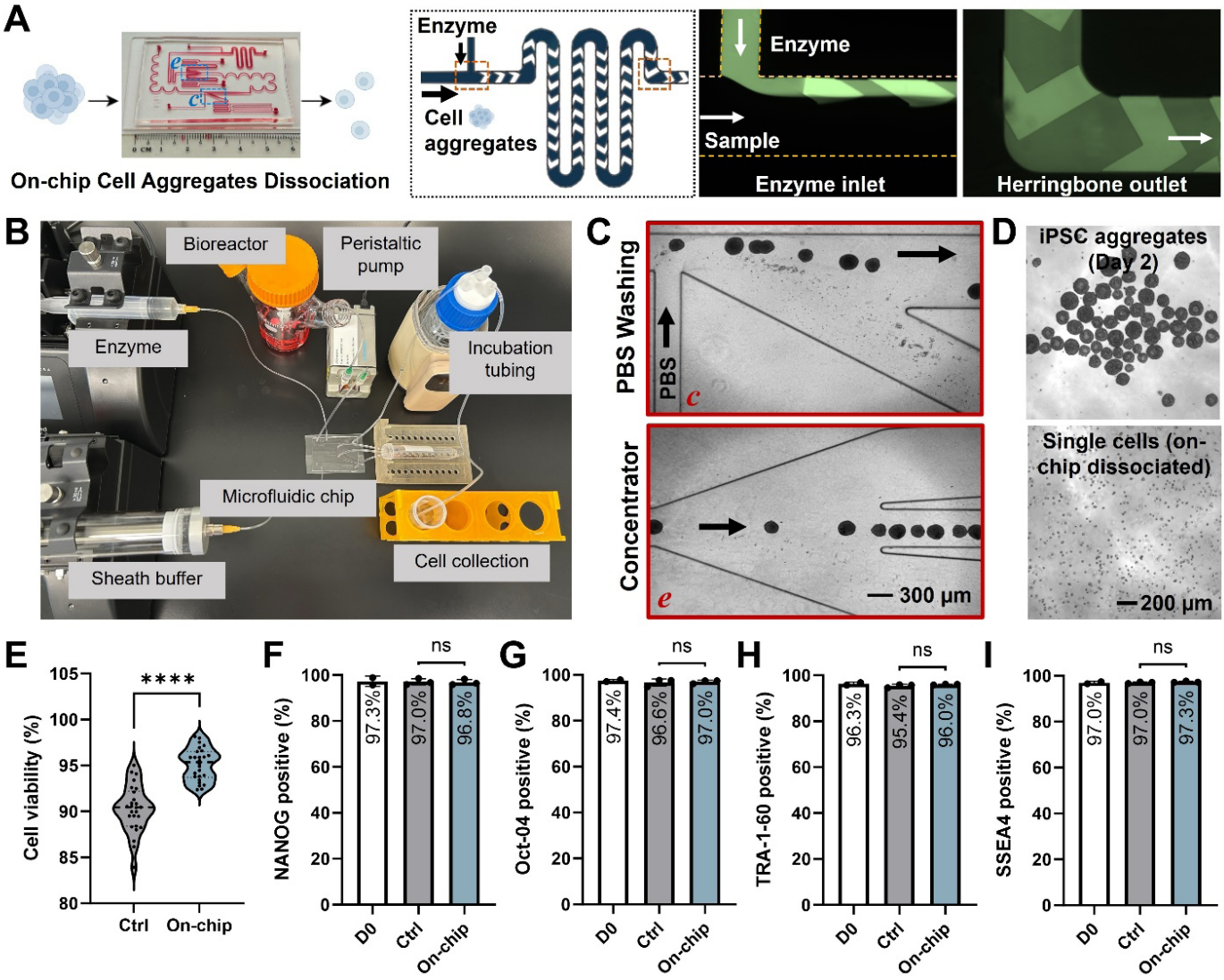


Figure 3. On-chip automated iPSC aggregates dissociation. A) Picture of actual chip and herringbone structure for efficient enzyme mixing. B) Benchtop setup for on-chip cell aggregates dissociation from bioreactor directly. C) Stacked images showing flow trajectory of iPSC aggregates at the vortex and concentrator regions. D) Phase contrast images of iPSC aggregates and on-chip dissociated iPSCs. Comparison of E) viability, and expression of stem cell pluripotency markers F) NANOG, G) Oct-04, H) TRA-1-60, I) SSEA4 between manual dissociated cells (ctrl) and on-chip dissociated cells. D0 are iPSCs pre-aggregation.

11

Regulatory Affairs, Quality Systems, Policy, Ethics, and Patient Access

ADVANCED THERAPY MEDICINAL PRODUCTS IN ICH MEMBER COUNTRIES: A REGULATORY LANDSCAPE ANALYSIS TO ACCELERATE CONVERGENCE, RELIANCE AND PATIENT ACCESS

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KEYWORDS: ATMP , regulatory convergence, ICH.

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Background & Aim

Advanced therapy medicinal products (ATMPs) offer transformative treatments but regulatory frameworks remain non-harmonised. Inconsistent definitions, data requirements and oversight delay patient access. The WHO Considerations (2023) and the IFPMA convergence-and-reliance position paper (2023) set recommendations for risk-based ATMP regulation; this study maps progress across ICH regulatory members.

Methods, Results & Conclusion

Methods

We mapped the ATMP landscape across 17 ICH regulatory members (founding, standing and regulatory) as of December 2024, using agency websites, literature, agency contacts and IFPMA member companies. Five areas were assessed: (1) definitions and reliance; (2) in-country testing; (3) labelling; (4) ATMPs containing genetically modified organisms (GMOs); (5) hospital exemption or equivalents.

Results

Only 8/17 ICH members have clear WHO-aligned ATMP definitions; 7 lack a framework or are in draft. Just 4/17 have established reliance or work-sharing (e.g., ACCESS Consortium, expanded to ATMPs in 2023); the FDA-led CoGenT Global Pilot is underway and 12 have none. For in-country testing, 10/17 apply no requirement/systemic waivers, 5 partial and 2 disallow waivers. GMO regulation is fragmented: timelines range from a US "categorical exclusion" to 15–165 days (EU), 8–10 months (Brazil) and ≥3 months (Japan), with several members lacking any ATMP-GMO pathway. Only 7/17 have ATMP-specific labelling guidelines; 4/17 implement ISBT128; 6/17 mandate patient track-and-trace; 8/17 permit digital labelling (QR/2D codes). About half have a scheme analogous to the EU Hospital Exemption, with wide variation.

Conclusions

Substantial gaps persist across ICH members in ATMP definitions, reliance, testing, GMO assessment, labelling and unlicensed-use frameworks. To accelerate patient access we recommend: harmonised risk-based definitions; broader reliance and work-sharing; waiver of in-country testing using Certificates of Analysis from mature NRAs/WHO Listed Authorities; standardised environmental risk assessment for GMO-ATMPs; labelling convergence (e.g., ISBT128, electronic product information); and aligned Hospital Exemption pathways. Continued regulator–WHO–industry collaboration is essential, with principles applicable to non-ICH and LMIC settings.

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Tissue Engineering

A DUAL EXCITATION-CONTRACTION PLATFORM FOR FUNCTIONAL EVALUATION AND DRUG SAFETY ASSESSMENT OF HUMAN IPSC-DERIVED CARDIAC TISSUES

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KEYWORDS: Human induced pluripotent stem cells , Drug safety assessment , New Approach Methodologies (NAMs)

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Background & Aim

Recent FDA initiatives promoting New Approach Methodologies (NAMs), including organoids and organ-on-chip systems, have accelerated the development of human-relevant alternatives to animal testing. However, most human iPSC-derived cardiac models focus primarily on electrophysiological assessment and do not simultaneously evaluate contractile function. Furthermore, the increasing demand for automated and high-throughput testing platforms in drug discovery and cell therapy development highlights the need for scalable human tissue models compatible with robotic workflows. We developed a scalable hydrogel-free dual excitation-contraction (DEC) platform that enables concurrent measurement of electrical activity and contractile force in engineered human iPSC-derived cardiac tissues for drug testing and disease modeling.

Methods, Results & Conclusion

METHODS

Human iPSC-derived cardiomyocytes were seeded onto an aligned fibrous scaffold to generate three-dimensional cardiac tissues without hydrogels. The DEC platform was designed to be compatible with commercial multi-electrode array systems, enabling simultaneous recording of field potentials and contractile force. The small footprint of the device

supports integration into multi-well plate formats and future automated high-throughput screening workflows. Cardiac responses to compounds with different torsade de pointes (TdP) risks, including isoproterenol, E4031, verapamil, ondansetron, and azimilide, were evaluated. Patient-derived MYBPC3-mutant iPSC lines were further used for disease modeling.

RESULTS & CONCLUSION

The DEC platform enabled rapid formation of anisotropic 3D cardiac tissues and simultaneous assessment of electrophysiological and mechanical function. Drug testing demonstrated concentration-dependent changes in field potential duration, contractile force, and arrhythmogenic events. Importantly, contractility measurements provided additional functional information beyond conventional electrophysiological assessment. MYBPC3-deficient tissues reproduced disease-associated reductions in contractile force and impaired responses to high-frequency pacing. The hydrogel-free design simplifies tissue fabrication while maintaining compatibility with existing cardiac safety testing workflows. These results demonstrate a scalable human iPSC-based platform for drug safety assessment, disease modeling, and future automated high-throughput screening, supporting the transition toward animal-free preclinical testing.

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Gene Editing/Gene Therapies

AAV-MEDIATED DUAL-GENE THERAPY RESTORES METABOLISM AND MITOCHONDRIAL STRUCTURE IN PROPIONIC ACIDEMIA

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KEYWORDS: Propionic Acidemia, AAV, Mitochondrial .

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Background & Aim

Propionic acidemia (PA) arises from PCCA or PCCB deficiency, which destabilizes the mitochondrial propionyl-CoA carboxylase (PCC) holoenzyme and drives toxic-metabolite accumulation, growth failure, and multi-organ injury. Because both subunits are required for holoenzyme stability, we tested whether a single-dose, liver-directed AAV8 vector co-delivering human PCCA and PCCB (AAV8-TBG-hPCCA-hPCCB) achieves durable correction in a Pcca p.R73W knock-in (KI) mouse model.

Methods, Results & Conclusion

Methods

Pcca$^{KI/KI}$ mice received the dual-gene vector, a single-gene PCCA comparator, or vehicle — intravenously at 4 weeks (dose-response, 1E11 to 1E12 vector genomes [vg]) or by facial-vein injection at postnatal day 1 (P1). We assessed growth, plasma biomarkers (UPLC-MS/MS), hepatic transduction and PCC protein restoration (Western blot), liver/heart mitochondrial ultrastructure (TEM), hepatocyte bioenergetics (Seahorse), and safety (histology; serum ALT/AST/urea/CK), including a high-protein-diet (HPD) challenge.

Results

Pcca$^{KI/KI}$ mice recapitulated PA, with elevated C3/C2, 3-HP, and 2-MeCit and disrupted mitochondrial cristae. The dual-gene vector restored both PCCA and PCCB protein and dose-dependently corrected biomarkers, outperforming single-gene PCCA therapy; 5E11 vg was selected as optimal. A single dose sustained correction over 24 weeks (6 months) with no hepatotoxicity or major-organ toxicity. Neonatal (P1) dosing was also effective, normalizing growth toward wild-type through 90 days (P=0.0047), and—critically—maintained biomarker control and growth under sustained HPD stress, a common trigger of clinical decompensation. TEM showed restored cristae in liver and heart; Seahorse confirmed recovered maximal respiration (P=0.0011), corrected proton leak (P=0.0242) and non-mitochondrial oxygen consumption (P=0.0015), and normalized glycolysis (P<0.0001).

Conclusion

Single-dose dual-gene AAV8 delivery of PCCA and PCCB provides durable, safe metabolic and mitochondrial rescue in PA, effective even with neonatal dosing under high-protein dietary stress. Balanced dual-subunit reconstitution — superior to PCCA alone — supports this as a disease-modifying strategy for both type I and type II PA.

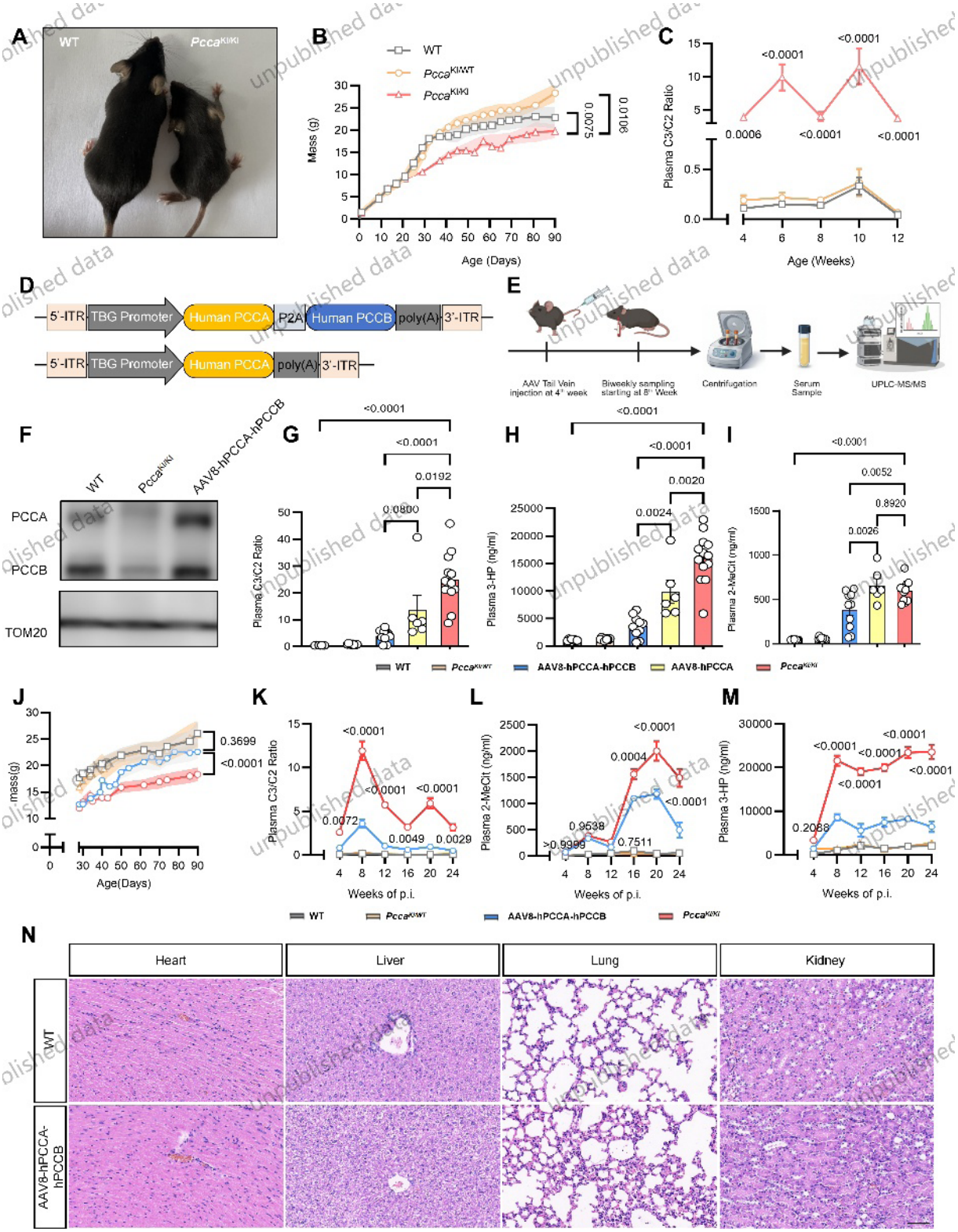


Figure 1. Dual-gene AAV8 therapy restores hepatic PCC and durably corrects PA in PccaKI/KI mice. (A–C) PccaKI/KI mice, carrying the Pcca p.R73W knock-in (modeling human PCCA p.R77W), recapitulate the patient phenotype, with growth retardation and an elevated plasma C3/C2 ratio. (D, E) Design of the dual- and single-gene AAV8 vectors and the experimental scheme. (F–I) After treatment, both PCCA and PCCB proteins are restored, and dual-gene therapy corrects plasma biomarkers more effectively than single-gene therapy. (J–M) A single dose sustains metabolic correction and growth recovery for up to 24 weeks. (N) Treated organs show no overt histological injury. *Mean ± SEM; group sizes and statistical tests as in the corresponding experiments.*

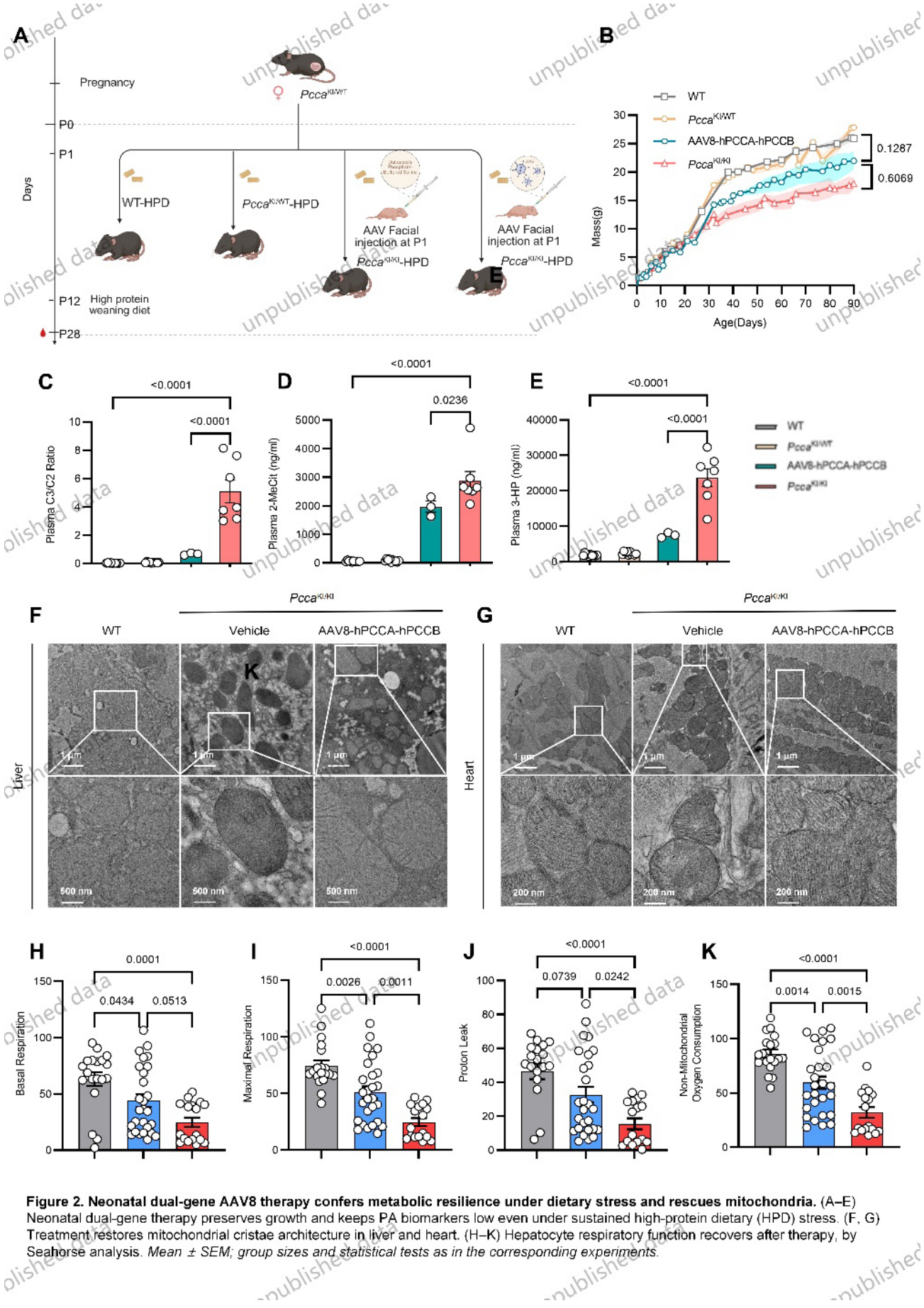


Figure 2. Neonatal dual-gene AAV8 therapy confers metabolic resilience under dietary stress and rescues mitochondria. (A–E) Neonatal dual-gene therapy preserves growth and keeps PA biomarkers low even under sustained high-protein dietary (HPD) stress. (F, G) Treatment restores mitochondrial cristae architecture in liver and heart. (H–K) Hepatocyte respiratory function recovers after therapy, by Seahorse analysis. *Mean ± SEM; group sizes and statistical tests as in the corresponding experiments.*

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Gene Editing/Gene Therapies

PRECISION CORRECTION OF A NONSENSE MUTATION USING BASE EDITING AND PRIME EDITING

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KEYWORDS: Neurofibromatosis type 1, CRISPR.

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Background & Aim

Neurofibromatosis type 1 (NF1) is a common genetic disorder associated with increased tumor formation and multisystem complications. Current disease management is largely limited to surveillance and symptomatic treatment. Recent advances in CRISPR-based gene therapy offer the potential for correction at the genetic level; however, the high heterogeneity of pathogenic NF1 variants necessitates a personalised approach. CRISPR base editors (BEs) and prime editors (PEs) provide a strong theoretical framework for precise correction of such variants, although the technology remains in its early stages. This study evaluates BE- and PE-mediated correction of the *NF1* c.3916C>T (p.Arg1306*) nonsense mutation.

Methods, Results & Conclusion

HEK293T cells and human Schwann cells (ipn02.8) were engineered to carry the *NF1* c.3916C>T mutation using CRISPR–Cas9-mediated homology-directed repair, with constructs delivered via plasmid transfection or electroporation. Multiple adenine base editor (ABE) variants and the *Sp*Cas9 PEmax system were evaluated for gene correction. Editing efficiency and bystander editing were quantified by Sanger sequencing followed by next-generation sequencing. Predicted off-target sites were identified using COSMID for subsequent specificity analyses.
HDR efficiencies were sufficient in both HEK293T and ipn02.8 cells to enable isolation of homozygous mutant (HEK293T) and heterozygous mutant (ipn02.8) clones. Rescue studies in HEK293T NF1 c.3916C>T cells demonstrated that ABE83 achieved the highest editing efficiency (66%) but induced bystander edits, whereas ABE8eWQ exhibited slightly lower efficiency (57%) with minimal bystander activity. PEmax achieved correction efficiencies of 39–51% across pegRNA designs with no detectable bystander edits.
Together, these findings establish a preclinical workflow for the identification and optimisation of CRISPR-based repair strategies for pathogenic NF1 variants. Ongoing studies are validating ABE8eWQ- and PEmax-mediated correction of the NF1 c.3916C>T mutation in ipn02.8 Schwann cells to directly compare editing efficiency, bystander profiles, and platform-specific performance in a disease-relevant context.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

FUNCTIONAL EFFICACY OF EPHA2 CAR T-CELLS GENERATED FROM PAEDIATRIC OSTEOSARCOMA PATIENTS

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KEYWORDS: CAR T, Manufacture, Paediatric.

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Background & Aim

Standard treatment for relapsed paediatric osteosarcoma remains ineffective, with survival rates below 20%. EphA2 (Erythropoietin-producing hepatocellular receptor A2) is highly expressed in paediatric osteosarcoma and Ewing sarcoma with minimal expression on healthy tissue, making it an attractive CAR T-cell target. We have developed an EphA2-directed CAR T and are progressing to Phase I clinical testing. However, autologous T cells collected from patients after intensive chemotherapy may have compromised fitness for CAR T manufacturing. We evaluated the feasibility of generating functional EphA2 CAR T cells from post-treatment paediatric compared to healthy adult donors.

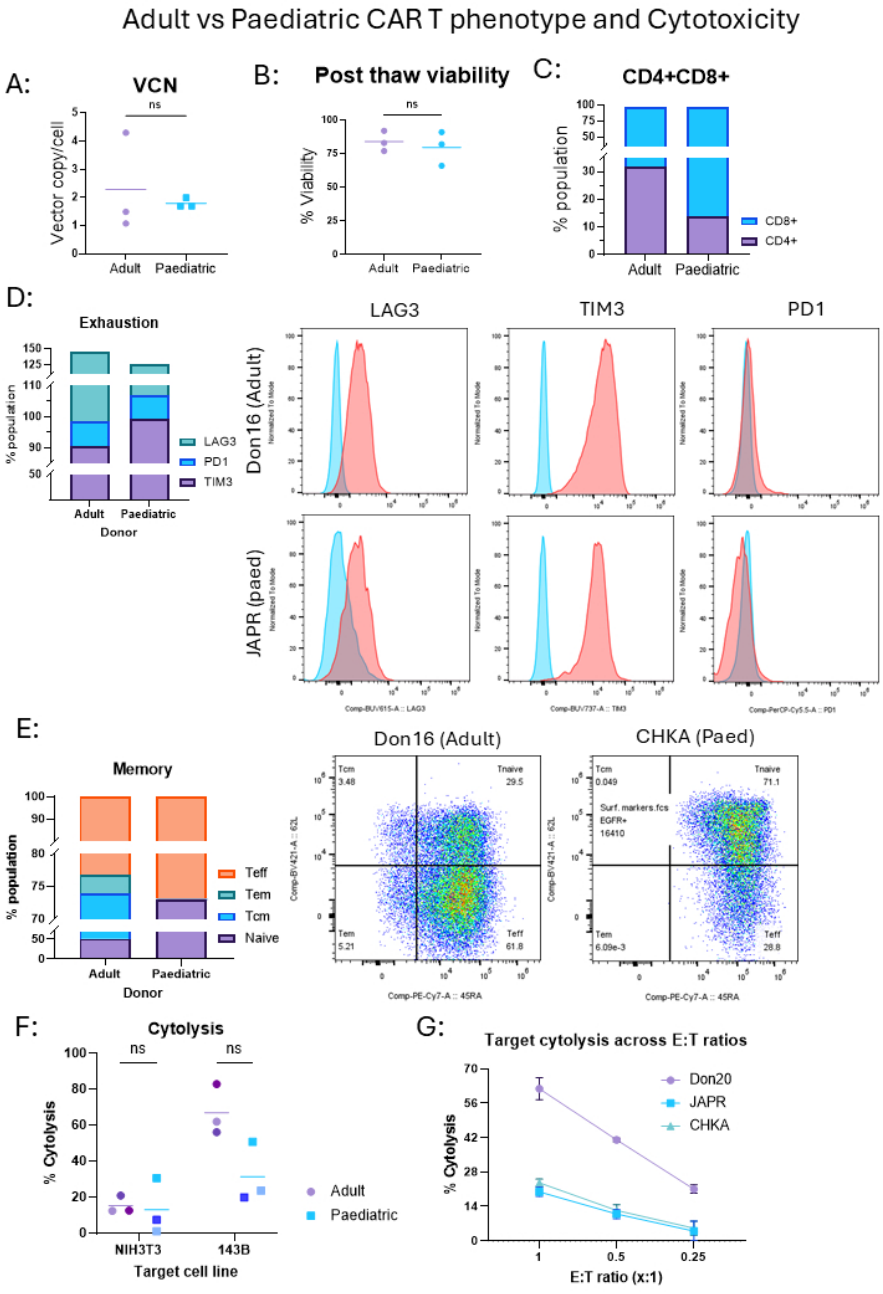
Methods, Results & Conclusion

T cells from adult and paediatric sarcoma donors (n=3) were activated, transduced with a lentiviral EphA2-CAR vector, and expanded using an open G-Rex® system. Transduction efficiency, CD4:CD8 ratio, memory phenotype (Tn, Tcm, Tem, Teff), and exhaustion markers (PD-1, TIM-3, LAG-3) were assessed by flow cytometry. Cytotoxicity against EphA2+ osteosarcoma cell line 143B (1:1 E:T) was measured by xCELLigence or luciferase-based assay. Fold expansion and post-thaw viability were determined by trypan blue exclusion counting. Vector copy number (VCN) was assessed by droplet digital PCR.

Healthy adult and paediatric post-treatment donors showed comparable EphA2 CAR T manufacturing outcomes (mean values, adult vs paediatric). Transduction efficiency (A: 30%-32%), and post-thaw viability (B: ~80%) were similar, however paediatric

donors showed lower CD4/CD8 ratio (C: 0.51), PD1 (D: 7.7%), Tem (D: 0.7%) and Tcm (D: 0.15%). CAR T cells from paediatric donors were overwhelmingly a naïve and effector memory subset (E: 27% Teff, 73% Tnaïve). While cytolysis at 1:1 E:T was lower in paediatric donors (F: 31% vs 66%), there is a dose dependent response to cytolysis (G: 4.5% at 0.25:1 to 21% at 1:1) . All CAR T products met predefined release specifications (CAR expression >10%, VCN <5 copies/cell, post-thaw viability >50%).

Post-chemotherapy treated paediatric T-cells generated functional EphA2 CAR T product and meets predefined release specifications, with comparable transduction, phenotype, and viability to healthy adult donors despite prior intensive chemotherapy. These data were generated as a prelude to our Phase I clinical trial, which will be conducted as an investigator-led trial, with CAR T-cells manufactured at our local place of care site, within an academic and teaching hospital setting.



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iPSC

DEVELOPMENT OF NEXT-GENERATION IPSC-DERIVED NEPHRON PROGENITOR CELLS (INPCS) FOR ADVANCED CKD TOWARD CLINICAL TRANSLATION

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KEYWORDS: CKD, iNPC, Cell therapy.

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Background & Aim

Acute kidney injury (AKI) and chronic kidney disease (CKD) affect millions worldwide. With severe donor shortages in kidney transplantation and the limited efficacy and adverse events associated with mesenchymal stromal cells, human iPS cell-derived nephron progenitor cells (iNPCs) present a promising alternative. However, clinical translation is hindered by the lack of uniform, large-scale production methods due to cell line/batch heterogeneity and by reduced efficacy in advanced CKD. This study aims to establish clinically applicable purification and expansion strategies for uniform, large-scale iNPC production and to generate next-generation iNPCs with enhanced therapeutic efficacy for advanced CKD.

Methods, Results & Conclusion

Methods

We screened low-molecular-weight compounds and growth factors on iNPC aggregates to establish efficient expansion. RNA-sequencing was examined to identify iNPC-specific surface markers. Purified and expanded iNPCs were transplanted into the renal subcapsules of cisplatin-induced AKI (cis-AKI) and aristolochic acid-induced CKD (AA-CKD) mice to evaluate kidney function and histology. To assess paracrine effects, iNPC-conditioned medium (CM) was administered intraperitoneally to cis-AKI mice and analyzed via mass spectrometry. Additionally, we explored factors downregulated in AA-CKD kidneys.

Results

We developed CFY medium (CHIR99021, FGF9, and Y-27632), enabling >100-fold iNPC expansion within two passages while maintaining NPC marker expression and differentiation potential across multiple iPS cell lines. Expanded iNPCs attenuated kidney injury and improved survival in cis-AKI mice and prevented renal dysfunction, fibrosis, and senescence in AA-CKD mice. c-MET was identified as a specific surface marker, and purified c-MET+ iNPCs exhibited therapeutic efficacy in both models. Improvements in contralateral kidneys and the efficacy of intraperitoneal CM administration, which contained secreted factors including VEGF-A, highlighted robust reno-protective paracrine effects. Furthermore, genetic engineering enabled iNPCs to express factors downregulated in diseased kidneys, yielding "next-generation iNPCs" with enhanced reno-protective functions.

Conclusion

Purified and expanded iNPCs, alongside genetically engineered next-generation iNPCs, demonstrate significant potential to overcome current manufacturing and efficacy barriers. These advanced cell therapies open new avenues for treating severe kidney diseases.

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Mesenchymal Stem/Stromal Cells

UMBILICAL CORD MESENCHYMAL STEM CELL-DERIVED SECRETOME AS A POTENTIAL TREATMENT FOR SYSTEMIC LUPUS ERYTHEMATOSUS: A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL

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KEYWORDS: Systemic lupus erythematosus, secretome, mesenchymal stem cell.

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Background & Aim

Background

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by immune dysregulation and multi-organ involvement. Conventional therapies often present limitations, including significant side effects and low remission rates. Umbilical cord mesenchymal stem cell-derived (UCMSC-derived) secretome, containing bioactive molecules with immunomodulatory and anti-inflammatory properties, emerges as a promising adjunct therapy.

Objective

This study aimed to evaluate the efficacy and safety of UCMSC-derived secretome in reducing disease activity and modulating key biomarkers in SLE patients.

Methods, Results & Conclusion

Methods

A double-blind, randomized, placebo-controlled trial was conducted involving 29 female SLE patients with moderate disease activity. Participants were randomized to receive weekly 1.5 cc intramuscular injections of either UCMSC-derived secretome (n=15) or a 0.9% NaCl placebo (n=14) for six weeks. Efficacy was assessed using the Mexican Systemic Lupus

Erythematosus Disease Activity Index (MEX-SLEDAI) score, complement levels (C3, C4), pro-inflammatory cytokines (IL-6, TNF-α), and anti-dsDNA antibodies at baseline, Day 22, and Day 43.

Results

The secretome group demonstrated a significant reduction in MEX-SLEDAI scores compared to the placebo group at Day 22 (p=0.010) and Day 43 (p=0.012). Complement C3 levels in the secretome group were significantly higher than the placebo group by Day 43 (p=0.044), suggesting improved immune homeostasis. Although not statistically significant, decreasing trends were observed in IL-6, TNF-α, and anti-dsDNA levels within the secretome group. No severe adverse events were reported, confirming the intervention's safety profile.

Conclusion

UCMSC-derived secretome is a safe and effective adjunct therapy that significantly reduces disease activity in patients with moderate SLE. These findings highlight its potential for clinical application in autoimmune management.

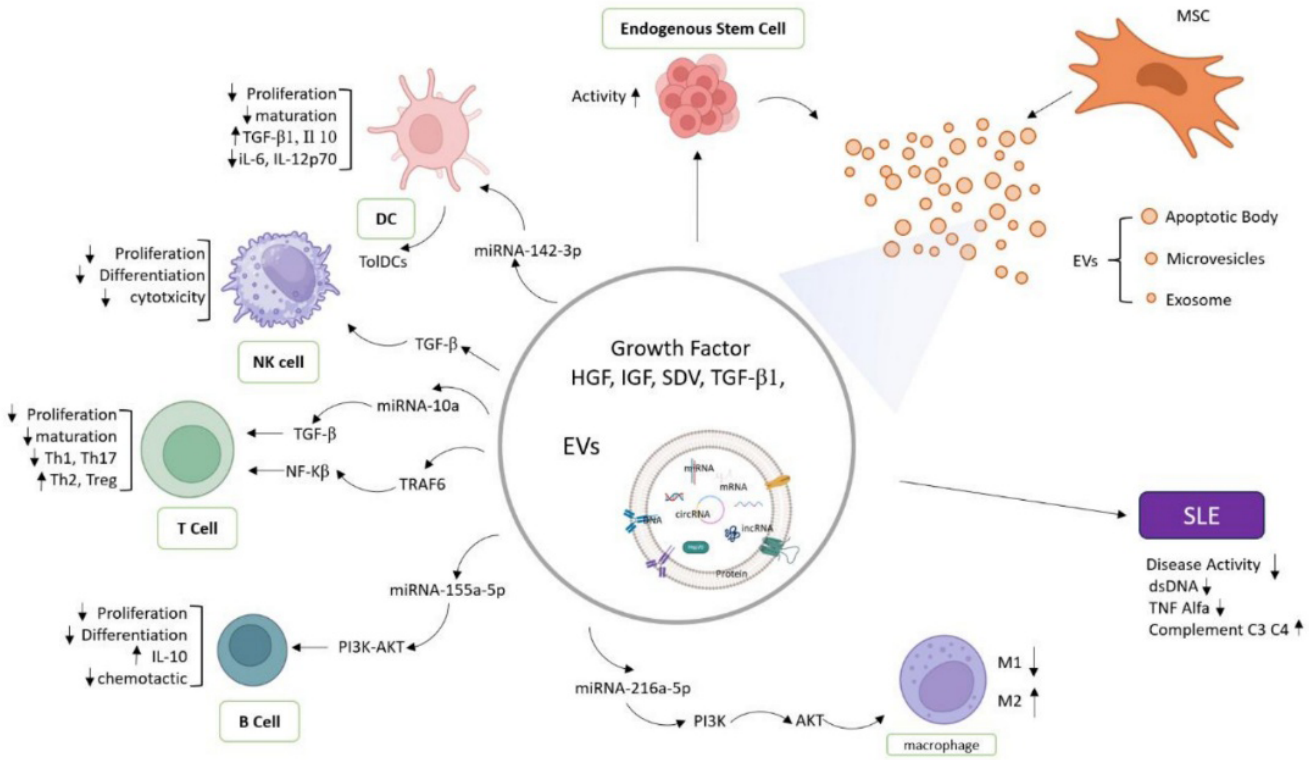


Figure 1. MSC-derived secretome, containing growth factors (TGF-β1, HGF, SGF, IGF), cytokines, and extracellular vesicles (EVs), plays a vital role in modulating SLE immune responses. EVs facilitate genetic exchange and cell reprogramming via multiple signaling pathways. This secretome inhibits B cell differentiation and reduces IL-10 production through the PI3K-AKT pathway. T cell modulation occurs by decreasing Th17/Th1 differentiation while enhancing Treg/Th2 functions via TGF-β/NF-κB signaling. Furthermore, EVs promote tolerogenic dendritic cells and induce the M2 anti-inflammatory macrophage phenotype through PI3K/AKT. NK cell pathogenicity is suppressed via TGF-β signaling. Additionally, the secretome activates endogenous stem cells, further enhancing immunological tolerance in SLE. This multifaceted approach addresses the core immune dysregulations of the disease.

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Tissue Engineering

MULTIFUNCTIONAL CHITOSAN/TANNIC ACID CRYOGELS AS A CHARGE-SELECTIVE BMP-4 DELIVERY PLATFORM FOR BONE REGENERATION

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KEYWORDS: Bone Regeneration, Biomaterial, Stem Cell.

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Background & Aim

Bone defects complicated by infection and oxidative stress remain a challenge, as bacterial colonization and reactive oxygen species suppress osteogenic signaling and impair repair. Thus, an ideal scaffold should support bone regeneration while providing antibacterial and antioxidant activity with sustained osteoinductive delivery. Here, we engineered chitosan/polyphenolic tannic acid (CT) cryogel with varying tannic acid (TA) concentrations, reinforced by glutaraldehyde, as a charge-selective BMP-4 delivery platform.

Methods, Results & Conclusion

CT cryogel were fabricated by freeze-templated crosslinking of chitosan and TA with glutaraldehyde reinforcement. Pore structure, porosity, swelling, modulus, and enzymatic degradation were characterized. Apatite formation was assessed in simulated body fluid (SBF), and antioxidant and antibacterial activities were evaluated by ABTS scavenging and assays against Escherichia coli and Staphylococcus aureus. In vitro hMSC responses were analyzed by viability, ALP activity, Alizarin Red S staining, and RT-qPCR. FITC-BSA and BMP-4 release were monitored for 28 days, and in vivo regeneration was evaluated in a mouse 6 mm calvarial defect model at 8 weeks using micro-CT and histology. Increasing TA densified the cryogel network, increasing modulus threefold while reducing porosity and swelling. Nevertheless, all CT cryogel recovered their shape after compression and resisted lysozyme degradation for 49 days. CT cryogel formed dense surface apatite in SBF, scavenged up to 85% of ABTS radicals, reduced E. coli growth by over 90%, and inhibited S. aureus. hMSC viability exceeded 90%, with hemolysis below 5%. Critically, release behavior was charge-selective: anionic FITC-BSA was released faster with increasing TA, whereas cationic BMP-4 was progressively retained, indicating electrostatic sequestration within the polyanionic TA-rich network. Consequently, sustained BMP-4 presentation promoted TA-dependent increases in ALP activity, calcium deposition, and osteogenic genes, including RUNX2, ALP, OSX, and OCN. In vivo, BMP-4-loaded CT cryogel improved micro-CT indices in a TA-dependent manner, increasing bone volume fraction (BV/TV) and trabecular number (Tb.N) while decreasing trabecular separation (Tb.Sp). Collectively, CT cryogel integrate antibacterial, antioxidant, and osteoinductive functions into a mechanically reinforced natural polymer-based platform for infected bone defect regeneration.

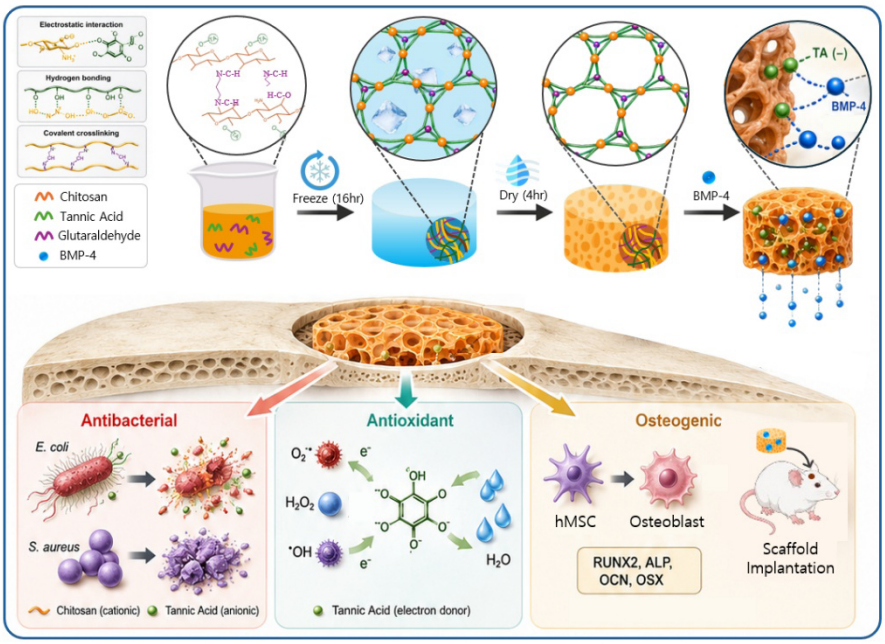


Figure1. Schematic illustration of the multifunctional CT cryogel platform

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Education & Workforce Development

DATA-DRIVEN APPROACH TO GROWING A CELL AND GENE THERAPY (CGT) LABORATORY: MEMORIAL SLOAN KETTERING CANCER CENTER (MSKCC) CELL THERAPY LABORATORY (CTL) EXPERIENCE

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KEYWORDS: Sustainable growth of CGT lab, Data-driven growth of CGT lab, Dedicated training program.

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Background & Aim

The rapid expansion of the CGT field is placing increasing demands on cell therapy laboratories. Reactive growth in response to bottlenecks is suboptimal because it relies on deficits affecting patient care to drive change. However, maintaining excess staffing capacity is not feasible given current healthcare constrains. Data-driven proactive planning is necessary to strike a balance between judicious use of resources and meeting patient care needs.

Methods, Results & Conclusion

In response to the rapid growth of the MSKCC CGT program, the CTL developed a quantitative model to define staffing requirements. We analyzed procedure volume, complexity, technologist time and expertise level. Non-processing functions, including equipment maintenance, documentation and compliance, were incorporated along with supervisory, regulatory and quality assurance (QA) activities. From these data, full-time equivalent (FTE) needs were calculated for each role. Growth projections, generated by working with clinical teams to assess recent trends, as well as by ensuring earlier CTL involvement in the planning of upcoming clinical trials, were integrated into the model. The model was presented to the MSKCC resource planning committee as a dynamic algorithm for ongoing calculation of CTL staffing needs.

Training newly hired personnel presented an additional challenge. In a traditional model, new technologists were trained one-on-one by preceptors, and a new trainee was not added until a previous one was trained. Training several technologists at once could expedite throughput but would require a dedicated trainer. We compared the time and cost of a traditional model vs a dedicated trainer and calculated a break-even point where improvement in laboratory operational efficiency would pay for a dedicated trainer (Figure 1).

Data-driven algorithm for the estimation of CTL staffing and training needs was well received by MSKCC resource planning committee and resulted in an institutional approval to increase CTL staff by 43% (37% processing technologists, 150% supervisory/ QA FTE) and an approval for a dedicated trainer. Implementation of dedicated training allowed CTL to reach the optimal processing capacity at least twice faster than a traditional method.

A data-driven approach to staffing and training establishes a proactive resource management system designed to meet patient care needs in a financially sustainable manner.

$$Net\ Improvement\ (\$) = \sum_1^m (\sum_1^n (E_n * R - C_n)_{dedicated} - \sum_1^n (E_n * R - C_n)_{traditional})_m$$

Net Improvement = difference in revenue generated by a laboratory with a dedicated vs a traditional training program over the period of m months ($)
m = months necessary to train ALL trainees sequentially in a traditional training program
n = total number of trainees needed train to reach full laboratory operational capacity
E = relative efficiency of a trainee comparing to a fully trained technologist (in a given month for a given program, expressed as a decimal)
R = revenue expected to be generated by a fully trained technologist per month ($)
C = cost of trainee per month (salary + benefits + institutional overhead, $)

Figure 1. Calculating the net improvement in laboratory productivity with a dedicated trainer vs a traditional training program.

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Embryonic, Organ and Other Tissue Specific Stem Cells

DETERMINING REGION-SPECIFIC DIFFERENCES IN OLFACTORY MESENCHYMAL STEM CELL PROPERTIES USING LIVE CELL PTYCHOGRAPHIC IMAGING

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KEYWORDS: olfactory mucosa, mesenchymal stem cell, neural repair.

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Background & Aim

Human olfactory mesenchymal stem cells (hOMSCs) are a unique source of cells obtained by an intranasal biopsy with the potential for neural repair in traumatic injuries for the nervous system. We have commenced a phase I clinical trial autologous using the olfactory cells to form three-dimensional cellular

constructs. However, current process analytical technologies for cells are limited and require a large number of cells. Further, there is a need to better understand variation in the cells obtained from different anatomical regions of the olfactory mucosa to understand whether there are region-specific differences.

Aim

To utilise label-free live-cell imaging to quantify the intrinsic phenotypic properties of primary hOMCs from different anatomical regions of the olfactory mucosa under routine culture conditions.

Methods, Results & Conclusion

Methods

Biopsies were obtained from anterior and posterior middle turbinates and septum regions. Primary hOMSCs were isolated and cultured using our previously established methods. Live cell imaging was performed for 5 days using a Phasefocus Livecyte microscope to generate high-contrast ptychographic images of unstained cells. Quantitative analyses of cell proliferation, morphology and migration was performed using automated image segmentation and analysis software.

Results

Label-free imaging enabled longitudinal imaging of live olfactory cells while preserving their native state. Continuous monitoring of cellular behaviour did not affect cell viability or growth. Cells derived from turbinates and septum displayed active migration and proliferation. Quantitative analysis demonstrated no significant heterogeneity in cellular morphology and motility that were region-specific.

Conclusion

This systematic quantitative profiling approach enables detailed analysis of intrinsic properties of primary hOMSCs and may facilitate the development of standardised and translationally relevant assays for patient-derived olfactory cells.

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Exosomes/EVs

MESENCHYMAL STROMAL CELL-DERIVED EXTRACELLULAR VESICLES ATTENUATE HUMAN DERMAL FIBROBLAST SENESCENCE IN VITRO

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KEYWORDS: Extracellular vesicles (EVs), Mesenchymal stromal cells (MSCs), Skin aging.

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Background & Aim

Skin aging involves intrinsic and extrinsic factors that promote dermal fibroblast senescence, leading to increased inflammation, impaired matrix regulation, and reduced cellular function. Mesenchymal stromal cells (MSCs) exert therapeutic effects through paracrine signaling, particularly via extracellular vesicles (EVs). MSC-derived EV-enriched fractions may provide a cell-free approach to restore cellular function. This study aimed to evaluate the effects of MSC-derived EVs on senescence-associated changes in human dermal fibroblasts *in vitro*.

Methods, Results & Conclusion

MSCs were cultured in xeno-free medium, and EV-enriched fractions were isolated using ultrafiltration. The fractions were characterized by nanoparticle tracking analysis (NTA), bicinchoninic acid (BCA) protein assay, and protein profiling. Serially passaged human dermal fibroblasts were used as a replicative senescence-associated model and treated with MSC-derived EV-enriched fractions. EV internalization was confirmed using fluorescently labeled EVs. Senescence-associated responses were assessed using morphological assessment, senescence-associated β-galactosidase (SA-β-gal) staining, Cell Counting Kit-8 (CCK-8), scratch wound, mitochondrial activity, and quantitative polymerase chain reaction (qPCR) assays. The results showed that these EV-enriched fractions exhibited nanosized particles with EV-associated markers. By *In Vitro* experiments, compared with young fibroblasts, senescent fibroblasts showed hypertrophic and flattened morphology. Fluorescence microscopy confirmed the uptake of fluorescently labeled EVs into human dermal fibroblasts. EV-enriched fraction treatment shifted senescent fibroblasts toward a less senescent phenotype, as indicated by a more spindle-like morphology, reduced SA-β-gal positivity, enhanced proliferation and migration, improved mitochondrial activity, and suppression of

senescence-associated secretory phenotype (SASP)-related gene expression. Therefore, MSC-derived EV-enriched fractions attenuated senescence-associated changes in senescent fibroblasts, supporting their potential as a cell-free strategy for reducing dermal fibroblast senescence.

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Exosomes/EVs

THERAPEUTIC POTENTIAL OF PLACENTA-DERIVED MESENCHYMAL STROMAL CELL-DERIVED SMALL EXTRACELLULAR VESICLES AND CHIMERIC ANTIGEN RECEPTOR-MODIFIED SMALL EXTRACELLULAR VESICLES (CAR-SEVS) FOR LIVER FIBROSIS.

T. Ling[1]

KEYWORDS: Liver Fibrosis, Small Extracellular Vesicles, Mesenchymal Stromal Cell.

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Background & Aim

Liver fibrosis is a progressive pathological process characterized by chronic hepatic injury and persistent activation of hepatic stellate cells (HSCs), culminating in cirrhosis and liver failure. Small extracellular vesicles (sEVs) derived from mesenchymal stromal cells (MSCs) have garnered considerable attention as a promising cell-free therapeutic modality owing to their immunomodulatory and anti-fibrotic properties. Nevertheless, their therapeutic translation remains significantly hindered by the lack of tissue-specific targeting following systemic administration.

Methods, Results & Conclusion

Materials and Methods

To overcome this limitation, we developed a bioorthogonal engineering platform to generate chimeric antigen receptor–modified small extracellular vesicles (CAR-sEVs) from human placenta choriodecidual membrane–derived mesenchymal stromal cells (pcMSCs). Azide groups were introduced onto pcMSCs and their secreted sEVs via metabolic glycan engineering with Ac4ManNAz, followed by copper-free click chemistry to conjugate DBCO-functionalized single-chain variable fragments (scFvs) against hepatocyte-associated antigens.

Results

CAR-sEVs exhibited a size distribution and physicochemical properties comparable to those of unmodified pcMSC-sEVs, while demonstrating significantly enhanced uptake by human hepatic cells in vitro. In a bile duct ligation (BDL)-induced mouse model of cholestatic liver fibrosis, systemic administration of CAR-sEVs markedly alleviated liver injury and fibrosis, as evidenced by reductions in necrotic area, collagen deposition, α-smooth muscle actin (α-SMA) expression, and extracellular matrix accumulation, along with improvements in liver function parameters.

Conclusions

Collectively, these findings demonstrate that bioorthogonally engineered chimeric antigen receptor–modified small extracellular vesicles (CAR-sEVs) exert dual anti-fibrotic effects through enhanced liver targeting while preserving the intrinsic anti-fibrotic activity of pcMSC-sEVs in transforming growth factor-β (TGF-β)-activated hepatic stellate cells (HSCs). Mechanistically, hepatocyte injury altered hepatocyte-derived sEV signaling, thereby promoting pro-fibrotic activation of HSCs, whereas treatment with pcMSC-sEVs or CAR-sEVs partially reprogrammed injured hepatocytes and attenuated downstream pro-fibrotic hepatocyte–stellate cell crosstalk. Together, these results highlight a versatile, non-genetic platform for precision extracellular vesicle–based therapy in liver fibrosis.

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Exosomes/EVs

NATURAL PRODUCT-ENRICHED NEURAL STEM CELL-DERIVED SMALL EXTRACELLULAR VESICLES AS A NOVEL CELL-FREE PLATFORM FOR ENHANCING NEUROGENIC ACTIVITY

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KEYWORDS: Small Extracellular Vesicles , Stem Cells , Natural Product.

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3. Department of Human Anatomy, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang, Malaysia.
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5. Simons Initiative for the Developing Brain and Centre for Discovery Brain Sciences, University of Edinburgh, Edinburgh, United Kingdom.

Background & Aim

Neurodegenerative diseases (NDs) are characterised by progressive neuronal loss and limited regenerative capacity of the central nervous system. Small extracellular vesicles (sEVs) derived from neural stem cells (NSCs) have emerged as promising cell-free

mediators capable of delivering bioactive cargo that regulates neurogenesis and neuronal survival. However, the effects of natural product-enriched NSC-derived sEVs and their underlying mechanisms remain poorly understood. This study evaluated the ability of natural product-enriched sEVs derived from rat full-term amniotic fluid stem cell (FT-AFSC)-generated NSCs to enhance neural stem cell activity and neurogenic responses in homologous and heterologous systems, and investigated the associated molecular pathways through transcriptomic profiling.

Methods, Results & Conclusion

FT-AFSCs undergoing NSC induction were treated with a natural product extract for 2 days, followed by 2 days in serum-free medium. Enriched sEVs were isolated by sequential ultracentrifugation and characterised by NTA, TEM, and ELISA. Their biological effects were assessed in homologous FT-AFSC-derived NSCs and heterologous mouse embryonic stem cell (ESC)-derived neural cultures. Neural induction, neurosphere formation, neuronal differentiation, and maturation were analysed using RT-qPCR and immunocytochemistry. Transcriptomic profiling (RNA Seq) was performed on recipient FT-AFSC-derived NSCs. Natural product-enriched sEVs significantly enhanced neural induction in the homologous system, evidenced by increased expression of Nestin and Sox1, and promoted neurosphere formation, indicating enhanced viability and self-renewal. Transcriptomic analysis revealed enrichment of antioxidant, anti-inflammatory, and cellular homeostasis pathways, suggesting that modulation of oxidative stress and inflammatory signalling contributes to enhanced neurogenic responses. In the heterologous system, enriched sEVs promoted neuronal differentiation and maturation in mouse ESC-derived neural cultures, as shown by increased expression of TUJ1, MAP2, SYP, and ChAT, demonstrating cross-species bioactivity. Natural product-enriched NSC-derived sEVs enhance neural stem cell activity, neurogenic responses, and neuronal maturation in homologous and heterologous systems. Their effects are linked to antioxidant and anti-inflammatory pathways, supporting their potential as an acellular therapeutic platform.

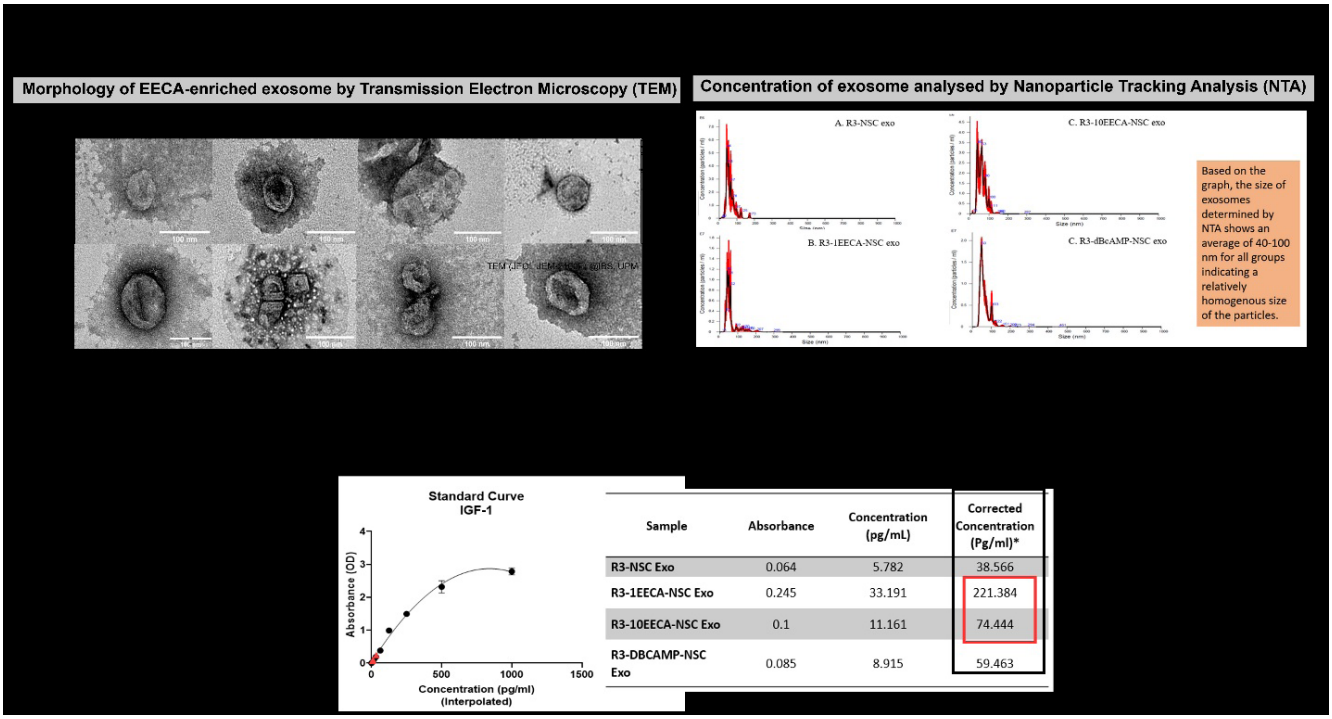


Figure 1. Characterisation of sEVs (exosomes) derived from NSCs generated from FT-AFSCs.

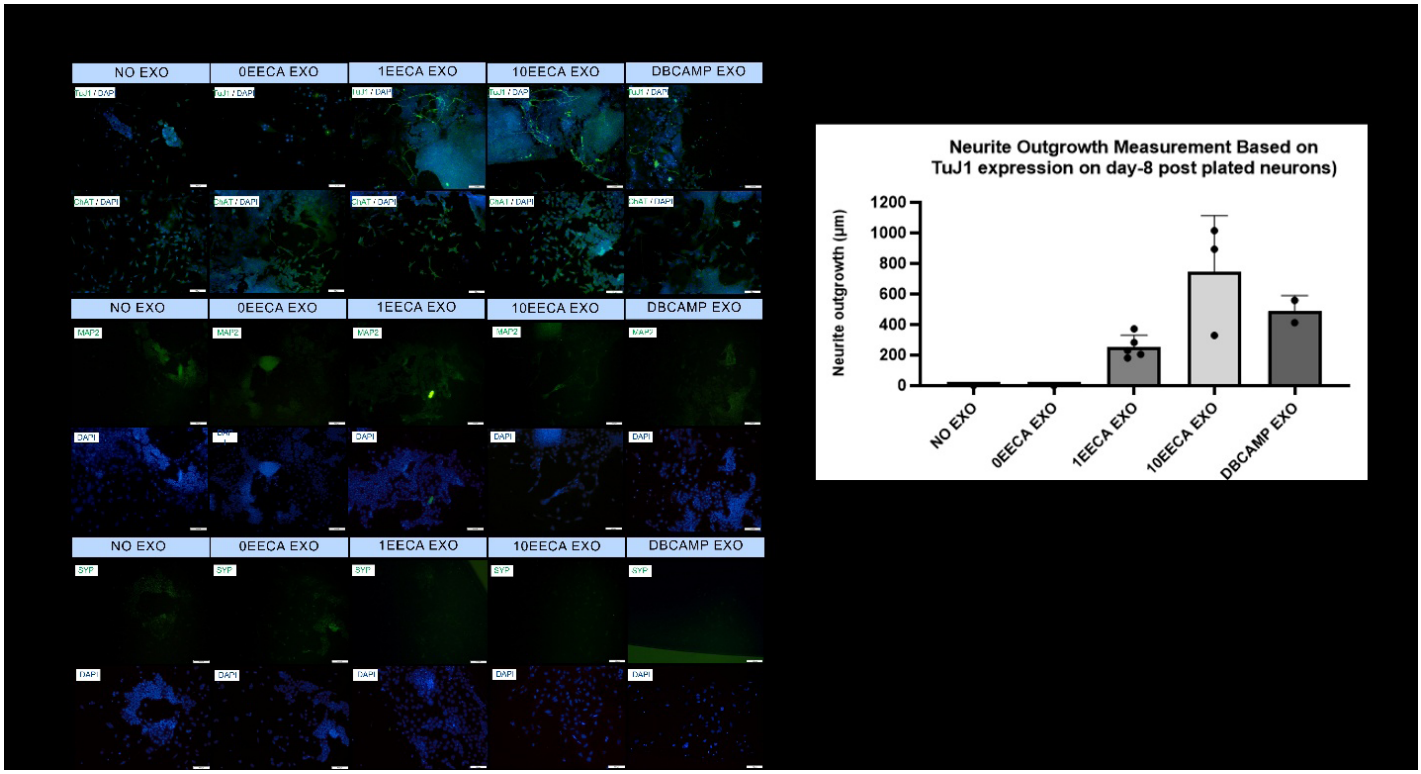


Figure 2. Neuronal protein marker analysis via immunocytochemistry (ICC) and neurite outgrowth on day-8 of post-plated neurons derived from mouse embryonic stem cells (heterologous system).

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Exosomes/EVs

DENTAL PULP STEM CELL-DERIVED EXOSOMES ATTENUATE OVARIECTOMY-INDUCED BONE LOSS THROUGH RESTORATION OF BONE REMODELING BALANCE

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KEYWORDS: Dental pulp stem cell, Exosome, Osteoporosis.

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Background & Aim

Osteoporosis is a metabolic bone disorder characterized by an imbalance between bone formation and bone resorption. Mesenchymal stem cell-derived exosomes have emerged as promising cell-free therapeutic agents; however, the therapeutic potential of dental pulp stem cell (DPSC)-derived exosomes in osteoporosis remains incompletely understood. This study aimed to evaluate the therapeutic efficacy of DPSC-derived exosomes and their role in regulating bone remodeling in an ovariectomy (OVX)-induced osteoporosis model.

Methods, Results & Conclusion

Exosomes were isolated from human DPSCs and characterized by nanoparticle tracking analysis (NTA), transmission electron microscopy (TEM), and western blotting. Osteoporosis was induced in mice by ovariectomy, followed by administration of DPSC-derived exosomes. Therapeutic efficacy was assessed using micro-computed tomography (μCT), hematoxylin and eosin (H&E) staining, and tartrate-resistant acid phosphatase (TRAP) staining.
DPSC-derived exosomes exhibited characteristic exosomal morphology and expression of exosomal markers, including CD9 and CD81. In OVX mice, exosome treatment attenuated bone loss and improved bone microarchitecture compared with untreated controls. Histological analyses demonstrated increased osteoblast activity and reduced osteoclast numbers following exosome administration. In addition, DPSC-derived exosomes promoted osteogenic differentiation and enhanced the expression of osteogenesis-related markers. Collectively, these findings suggest that DPSC-derived exosomes restore bone homeostasis by simultaneously promoting bone formation and suppressing bone resorption.
In conclusion, DPSC-derived exosomes demonstrated therapeutic potential for osteoporosis and may serve as a promising cell-free regenerative strategy for restoring bone remodeling balance. These findings further suggest that regulation of bone remodeling may represent a key mechanism underlying the therapeutic effects of DPSC-derived exosomes.

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Exosomes/EVs

THE ANTI-FIBROTIC PROPERTIES OF HTERT-OVEREXPRESSED MESENCHYMAL STEM CELL-DERIVED EXTRACELLULAR VESICLES

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KEYWORDS: Mesenchymal stem cell, Extracellular vesicle, Pulmonary fibrosis.

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Background & Aim

Pulmonary fibrosis (PF) is chronic and progressive lung disease which is a form of interstitial lung disease, characterized by the irreversible of lung architecture and functions. Globally, the number of PF patient are rising which may attribute to an aging population worldwide. At present, there is no therapeutic approach that promote lung recovery and prevent disease progression, making lung transplantation is the most effective strategy to improve a patient's quality of life. Currently, novel therapeutic agents that substantially prevent PF disease progression urgently needed. For many years, safe and effective interventions for PF treatment have been explored, especially mesenchymal stem cells-based therapy due to its properties and roles in tissue regeneration. The therapeutic potential of MSCs is mainly demonstrated by the production of crucial paracrine factors, particularly extracellular vesicle (EV) that making MSC- EVs are viable candidate for PF treatment. However, previous studies indicate that one of the most difficult challenges of MSCs and MSC-EVs therapies are cellular senescence during long-term expansion, which leads to a reduced proliferation rate and decreased extracellular vesicles production. As aforementioned, this study aims to improve the properties of MSCs via overexpression *hTERT* gene and investigate the anti-fibrotic properties of *hTERT*-MSC EVs.

Methods, Results & Conclusion

The effects and properties of *hTERT*-MSCs and native-MSCs were investigated. Subsequently, lung fibroblast cells were induced to differentiate into

myofibroblasts using TGF- β1 and the anti-fibrotic effects of hTERT-MSC EVs and MSC-EVs were investigated. Our findings indicate that *hTERT*-MSCs significantly exhibit the *hTERT* gene expression and telomerase activity, while effectively prevent the cellular senescence. In addition, the *hTERT*-MSC EVs maintains the anti-fibrotic properties via reduced the expression of α-SMA and ColIAI during myofibroblast differentiation. Subsequently, some bioactive molecules of hTERT-MSC EVs and MSC-EVs will be investigated as potency markers for anti-fibrotic signaling pathways. These results suggest that *hTERT*-overexpressing MSCs effectively prevent cellular senescence during long-term expansion and exhibit anti-fibrotic effects by reducing myofibroblast differentiation.

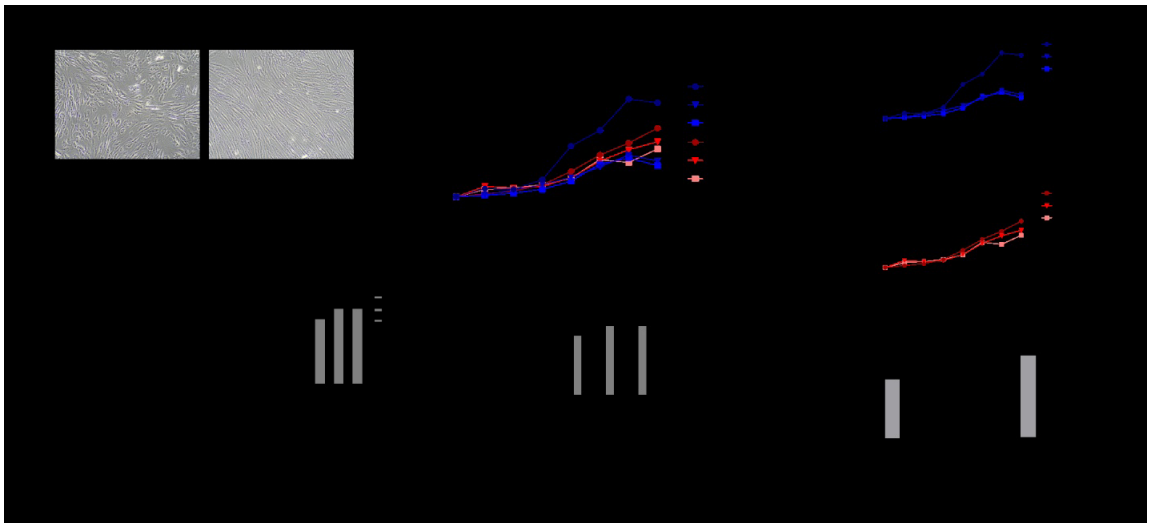


Figure 1. Investigation of the effect of hTERT-MSCs. (A) Cellular morphology of native MSCs and hTERT-MSCs. (B) Cell growth kinetic of native MSCs and hTERT-MSCs during passage 5 to 7. (C) Population doubling time (PDT) of native MSCs and hTERT-MSCs during passage 5 to 7. (D) Gene expression and telomerase activity of native MSCs and hTERT-MSCs. (E) Effect of hTERT overexpression on cellular senescence during passage 5 to 7.

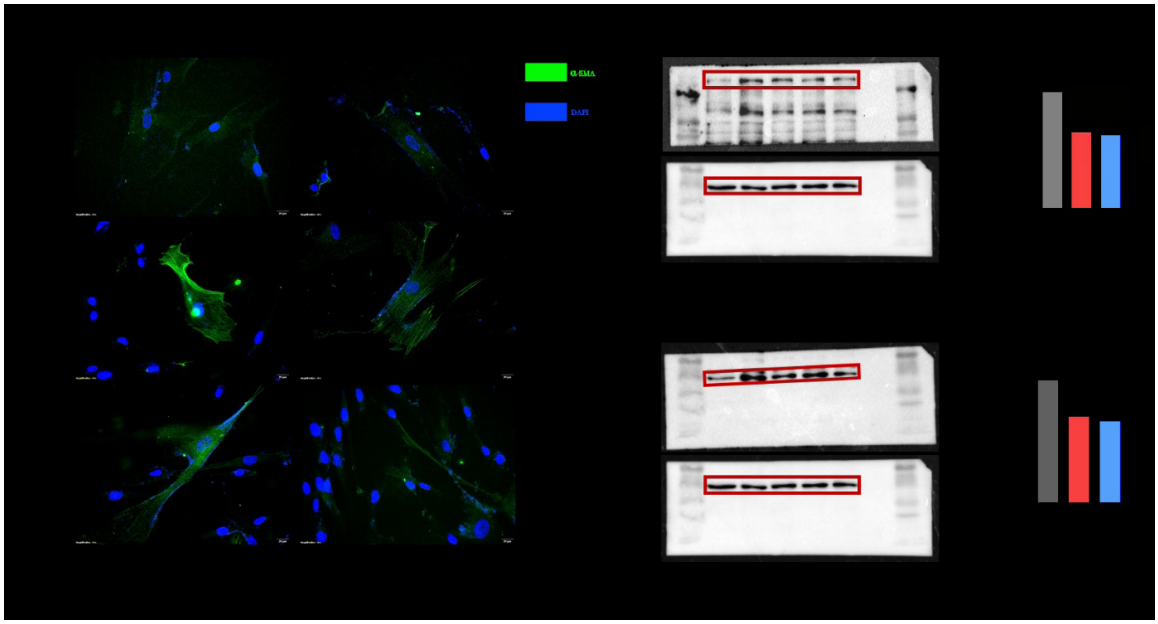


Figure 2. Investigation of the anti-fibrotic properties of MSC-EVs and hTERT-MSC EVs on myofibroblast differentiation. (A) Immunofluorescence staining of □-SMA expression after incubation with hTERT-EVs for 24h. Western blot analysis of ColIAI expression (B) and □-SMA expression (C) after incubation with MSC-EVs and hTERT-EVs for 24h.

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Gene Editing/Gene Therapies

EVALUATION OF BIOPROCESS CONSIDERATIONS FOR THE DEVELOPMENT OF INTERNAL GUIDELINES FOR REGISTRATION AND SANITARY AUTHORIZATIONS OF ADVANCED THERAPY PRODUCTS IN CHILE

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KEYWORDS: Cell and Gene Therapy, Manufacturing Process, Quality Control.

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Background & Aim

The advancement of Advanced Therapy Medicinal Products (ATMPs), which include gene therapy, cell therapy, and tissue engineering, presents unique regulatory challenges due to their biological complexity and inherent variability. In Chile, the Public Health Institute (ISP) faces the need to implement technical tools to standardize and streamline the evaluation processes and expedite the application of recent national regulations. This study aims to establish a technical basis for developing internal guidelines for the registration and marketing authorization of ATMPs in the country

Methods, Results & Conclusion

Methodology

A technological surveillance methodology and systematic analysis of the regulatory and technical framework of international reference agencies (FDA, EMA, PMDA, and ANVISA) were employed. Trends and statistics for 105 approved therapies corresponding to 69 different formulations were analyzed. A detailed mapping of upstream and downstream manufacturing processes was performed to identify critical control points.

Results

The analysis reveals a predominance of cell therapy products, particularly mesenchymal stem cells and HPC, followed by gene therapies, mainly using AAV, LVV, and retrovirus vectors as the active ingredient. It was identified that 45% of the products are of autologous origin, which implies significant challenges for process standardization. Identity, purity, safety, potency, dosage, and viability were defined as fundamental Critical Quality Attributes, and suitable analytical methods for their evaluation were selected, such as flow cytometry, NGS sequencing, PCR, etc. This allows for the development of a comprehensive control strategy in conjunction with the ISP (Chilean Public Health Institute), establishing a flexible baseline for evaluating manufacturing and finished product specifications for each biological platform.

Conclusions

This research lays the foundation for the technical and regulatory framework to expedite the sanitary registration of MTAs (Medical Treatment Approaches) in Chile. Standardizing bioprocess evaluation criteria optimizes response times for health authorities and facilitates the integration of these therapies into public policy. This work directly contributes to ensuring safe and efficient access to cutting-edge biotechnological treatments under the highest quality standards.

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Gene Editing/Gene Therapies

DEVELOPMENT OF A SEROTYPE-AGNOSTIC CELL LYSIS BUFFER FOR EFFICIENT AAV MANUFACTURING

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KEYWORDS: AAV manufacture, cell lysis buffer, AAV2 clarification.

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Background & Aim

Adeno-associated virus (AAV) vector manufacturing is constrained by high costs and variability in early downstream processing, particularly during cell lysis for predominantly cell-associated serotypes. We developed a serotype-agnostic, GMP-compliant, biohazard-free cell lysis buffer and evaluated its performance across five AAV serotypes (AAV1, AAV2, AAV5, AAV8 and AAV9) produced transiently in HEK293 cells.

Methods, Results & Conclusion

Lysis efficiency, particle stability and downstream compatibility were assessed with advanced semi-automated analytical tools for genomic titers, capsid titers, and functional infectivity titers.
The buffer achieved rapid and robust lysis, reducing cell viability to below 5% across all tested serotypes within the target process window, while maintaining AAV particle integrity. It showed broad compatibility with multiple commercially available nucleases. In addition, the solution is scalable, GMP-compliant, biohazard-free, and safe for use in single-use

equipment, without causing leachable or extractables from process-contact materials. Compared with published or established lysis formulations, the novel buffer delivered comparable or superior AAV2 functional titers. Furthermore, it can be applied directly in the production vessel.
Scalability was demonstrated in a 10 L HEK293 AAV2 process using depth and sterile filtration. 11.2L clarified filtrate was obtained without filter blockage and achieved 120 L/sqm throughput without filter blockage. We achieved 96% capsid recovery and 90% functional recovery, with approximately 22% DNA and 16% host cell protein reduction after clarification. Overall, this serotype-agnostic lysis buffer enhances lysis robustness, nuclease flexibility, clarification performance and assay compatibility, supporting more efficient, scalable and cost-effective AAV manufacturing.

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Gene Editing/Gene Therapies

IDENTIFICATION OF A RECURRENT SPTAN1 P.ARG19TRP VARIANT IN A KOREAN FAMILY WITH SPG91: EXPANDING EVIDENCE FOR A POTENTIAL THERAPEUTIC HOT SPOT

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KEYWORDS: Hereditary Spastic Paraplegia (SPG91), SPTAN1 gene, Genomic Hot Spot.

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Background & Aim

Hereditary spastic paraplegia (HSP) is a genetically heterogeneous group of neurodegenerative disorders characterized by progressive lower-extremity spasticity and weakness. Recently, heterozygous *SPTAN1* variants have been recognized as a cause of autosomal dominant HSP (SPG91). Although only a small number of SPG91 patients have been reported worldwide, most reported cases have carried the same *SPTAN1* p.Arg19Trp variant, suggesting a possible recurrent disease-associated allele. Confirmation of this observation across diverse populations may have implications for future mutation-directed therapeutic strategies. We report the first Korean family with SPG91 associated with the recurrent *SPTAN1* p.Arg19Trp variant.

Methods, Results & Conclusion

Methods

Clinical and genetic evaluations were performed in a Korean family with autosomal dominant pure HSP. Targeted next-generation sequencing was conducted in the proband and her affected father. Clinical phenotyping included neurological examination, cognitive assessment, and brain magnetic resonance imaging.

Results

A 10-year-old girl and her 45-year-old father presented with slowly progressive gait disturbance beginning in late childhood. Neurological examination demonstrated bilateral lower-extremity spasticity, mild weakness, and hyperreflexia. Cognitive function and brain MRI findings were normal, consistent with a pure HSP phenotype.
Genetic analysis identified a heterozygous *SPTAN1* variant, NM_001130438.3:c.55C>T (p.Arg19Trp), in both affected individuals. This variant is extremely rare in population databases and has been reported previously in a small number of unrelated SPG91 families. Its recurrence across different populations may suggest a non-random distribution of pathogenic alleles within *SPTAN1*, although currently available evidence remains limited.

Conclusion

To our knowledge, we report the first Korean family with genetically confirmed SPG91 associated with the *SPTAN1* p.Arg19Trp variant. Although the total number of reported SPG91 cases remains limited, the repeated identification of the same variant across unrelated families from different ethnic backgrounds strengthens the evidence for its pathogenic role and supports the possibility that p.Arg19Trp represents a recurrent disease-associated allele in SPG91. Continued accumulation of clinical and genetic data will be necessary to clarify its prevalence, phenotypic spectrum, and potential suitability as a target for future precision therapeutic approaches.

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Gene Editing/Gene Therapies

DEVELOPMENT OF INDIA'S FIRST INDIGENOUS HSV-1-BASED ONCOLYTIC IMMUNOVIROTHERAPY PLATFORM FOR SOLID TUMOURS

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KEYWORDS: Oncolytic Virotherapy, India, Solid tumours.

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Background & Aim

Oncolytic immunovirotherapy (OIVT) integrates direct tumour lysis with immune microenvironment reprogramming to generate durable antitumour responses in solid tumours. We report the ongoing development of India's first indigenous HSV-1-based OIVT platform, integrating viral genomics, systems virology, and genome engineering to enable rational design and translational development of next-generation oncolytic therapies for solid tumour applications.

Methods, Results & Conclusion

An indigenous HSV-1 isolate was propagated in BHK-21 cells under optimized adsorption kinetics & serum-restricted culture conditions to establish a scalable viral production system. Downstream processing, including sucrose gradient density ultracentrifugation & plaque purification assays, was standardized for clonal isolation, viral titration, & batch-to-batch consistency. Whole-genome characterization was performed using ONT long-read sequencing, followed by hybrid de novo assembly, structural variant analysis, & genome annotation. Comparative genomics against reference HSV-1 strains identified strain-specific polymorphisms, indels, & putative adaptive mutations associated with host tropism & immune evasion. CRISPR/Cas9-based editing is being established for sequential gene knockouts, including RL1, US12, UL39, & UL30, enabling rational attenuation strategies, promoter rewiring, & therapeutic transgene insertion (IL-12, GM-CSF, & checkpoint-modulatory fusion constructs), designed to enhance antigen presentation, reprogram tumour-associated macrophages and promote CD8 T-cell infiltration. Preclinical systems biology pipelines integrating transcriptomic profiling & tumour microenvironment modelling are being deployed across glioblastoma, melanoma, & PDAC platforms. Three-dimensional organoid systems & syngeneic murine models are being developed to evaluate biodistribution, oncolytic efficacy, & immune infiltration dynamics. Early studies demonstrate robust cytopathic activity, productive viral replication in tumour-selective contexts, & differential tumour lineage susceptibility. Ongoing in vivo studies aim to validate immune conversion of "cold" tumours into immunologically "hot" phenotypes, particularly in combination with immune checkpoint blockade. This integrated platform establishes a first-in-India, cost-effective translational framework for FIH oncolytic immunovirotherapeutics, enabling standalone and combinatorial application of OIVT with other cellular therapy modalities for solid tumours.

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Gene Editing/Gene Therapies

MULTITAP-CRISPRA: A TANDEM GRNA CRISPR ACTIVATION PLATFORM FOR SYNCHRONIZED MULTIPLEX ENDOGENOUS GENE ACTIVATION IN MAMMALIAN CELLS

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KEYWORDS: CRISPR activation, epigenome editing, multiplex gene activation.

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Background & Aim

Multiplex gene manipulation is essential for dissecting complex gene networks and precisely controlling cell fate. However, current CRISPR activation systems frequently generate unbalanced gene expression and exhibit low stability when expressing long tandem gRNA transcripts, limiting their capacity for synchronized multi-gene activation. To overcome these technical bottlenecks, this study aimed to establish a robust, modular, and generalizable tandem gRNA-based CRISPRa platform (MultiTap-CRISPRa; Multiplex Tandem gRNA-Mediated Activation Platform for CRISPR Activation) for synchronized and balanced activation of multiple endogenous genes in mammalian cells. By optimizing assembly workflows for tRNA-gRNA arrays and multi-U6 cassettes, we aim to achieve potent and consistent multiplex activation of core reprogramming genes under both normal and stress-induced senescent cellular conditions.

Methods, Results & Conclusion

Methods

We established an efficient dual-assembly workflow based on Golden Gate and Gibson cloning, allowing seamless insertion of multiple discrete tandem tRNA-gRNA arrays. Each array unit is regulated

by an individual U6 promoter, yielding a stable modular multi-U6 expression vector for synchronized activation of multiple target genes. Specific gRNAs targeting the promoter regions of core reprogramming genes *OCT4*, *SOX2*, and *KLF4* (OSK) were designed and systematically screened. The constructed MultiTap-CRISPRa platform was transfected into HEK293T cells, and its multiplex gene activation performance was tested in both normal and stress-induced senescent cell models.

Results

The established MultiTap-CRISPRa platform realized potent, balanced and synchronized multiplex endogenous gene activation. In tested mammalian cells, it achieved significant upregulation of core reprogramming genes, with 10.5-fold activation for *OCT4*, 5.7-fold for *SOX2*, and 8.7-fold for *KLF4*. Notably, the platform maintained stable and efficient activation performance in both normal and stress-induced senescent HEK293T cells.

Conclusion

MultiTap-CRISPRa utilizes engineered tandem gRNA arrays and multi-U6 cassettes to overcome the unbalanced activation and transcript instability observed in current CRISPRa systems. As a modular, robust and universal multiplex gene activation tool, it enables synchronized and precise modulation of multiple endogenous genes. This platform provides a reliable technical support for epigenetic manipulation, cell fate regulation and cellular reprogramming studies.

Special acknowledgement: This work is supported by the Basic Research Program of Jiangsu Province – Fundamental Research Plan Funding (Grant No. BK20240455)

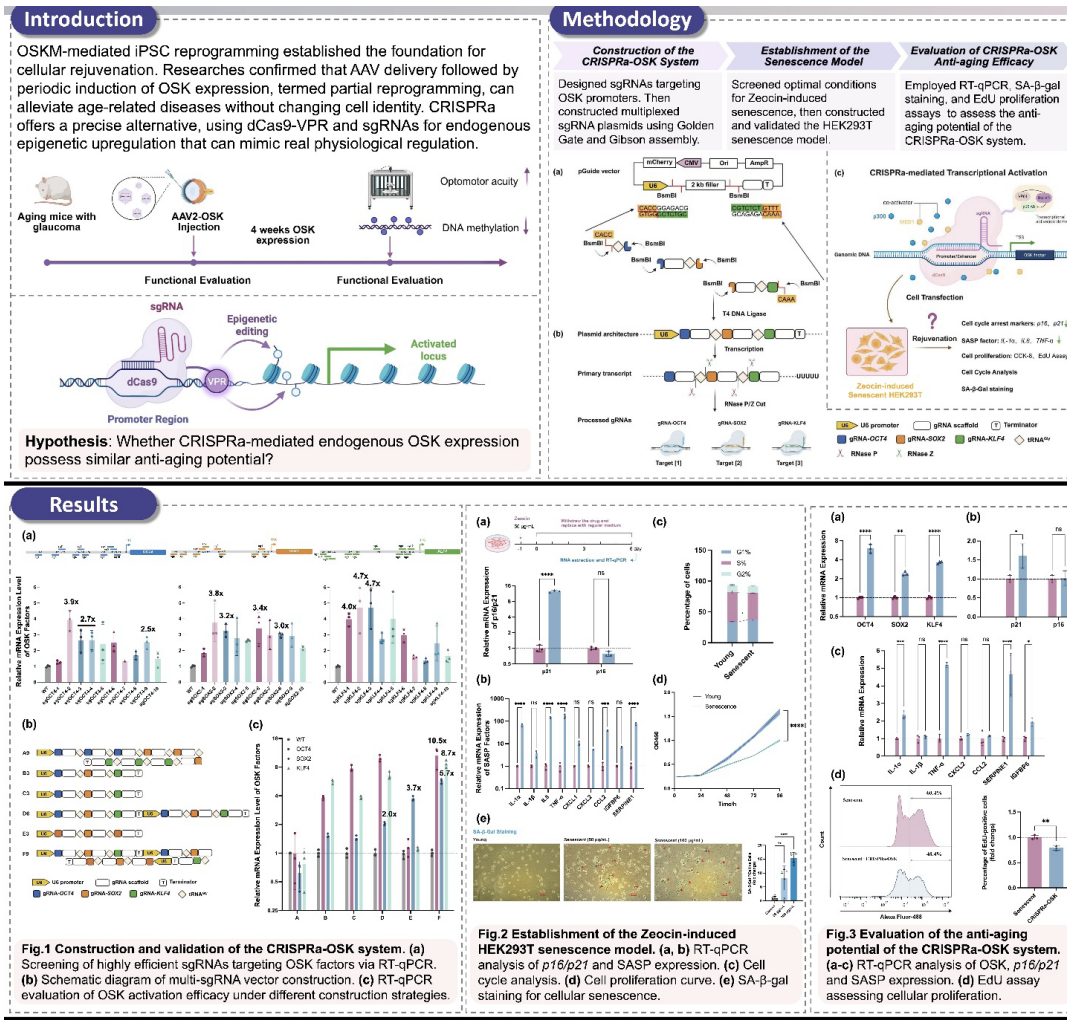


Fig.1 Construction and validation of the CRISPRa-OSK system. (a) Screening of highly efficient sgRNAs targeting OSK factors via RT-qPCR. **(b)** Schematic diagram of multi-sgRNA vector construction. **(c)** RT-qPCR evaluation of OSK activation efficacy under different construction strategies.

Fig.2 Establishment of the Zeocin-induced HEK293T senescence model. (a, b) RT-qPCR analysis of *p16/p21* and SASP expression. **(c)** Cell cycle analysis. **(d)** Cell proliferation curve. **(e)** SA-β-gal staining for cellular senescence.

Fig.3 Evaluation of the anti-aging potential of the CRISPRa-OSK system. (a-c) RT-qPCR analysis of OSK, *p16/p21* and SASP expression. **(d)** EdU assay assessing cellular proliferation.

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Gene Editing/Gene Therapies

ENGINEERING CRISPR/CAS12J8 SYSTEM FOR EFFICIENT GENOME EDITING THROUGH A NOVEL PROTEIN ENGINEERING STRATEGY

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KEYWORDS: Protein engineering, CRISPR\Cas12j, Efe1-Retron.

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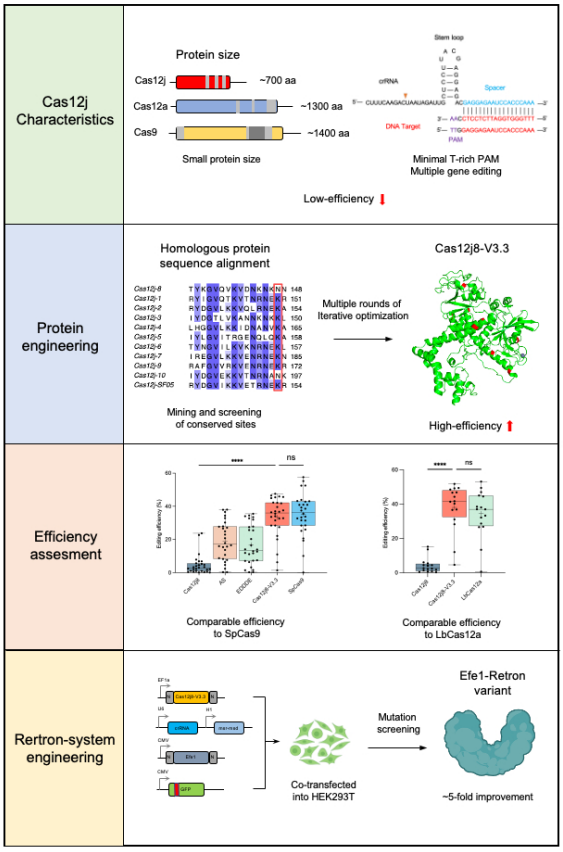
Background & Aim

The CRISPR gene-editing technology presents notable challenges, including the large size, high immunogenicity, and complex delivery mechanisms associated with the SpCas9 protein. In contrast, Cas12j (CasΦ) is an ultra-compact RNA-guided endonuclease derived from large bacteriophages, with a protein size of approximately 700~800 amino acids, making it significantly smaller than SpCas9 and LbCas12a. However, the native editing efficiency of Cas12j is lower than that of SpCas9, highlighting the need to enhance its editing capabilities for broader applications. Current strategies for modifying Cas proteins include phage-assisted directed evolution, structure-guided protein engineering, AI-assisted protein engineering, and the introduction of alkaline amino acid mutations. While these methods have effectively enhanced the editing efficiency of multiple Cas proteins, they face challenges such as being time-consuming and labor-intensive, high technical barriers, and limited efficiency improvements. To overcome these issues, we aim to develop a straightforward and rapid protein engineering strategy to engineer hypercompact CRISPR\Cas12j system with enhanced genome editing activity.

Methods, Results & Conclusion

Conserved sites in the evolutionary development of proteins typically play crucial roles in their structure and function. Therefore, we hypothesize that modifying these conserved sites can effectively enhance the editing efficiency of Cas proteins. We focused on the CRISPR\Cas12j8 system as our target protein, which has the highest editing efficiency among all the Cas12j homologues. Through sequence alignment of 10 homologs of Cas12j8, we identified 39 conserved amino acid sites and assessed their editing efficiency in HEK293T cells. After conducting multiple rounds of combinatorial screening, we successfully obtained a Cas12j8 variant that exhibited an approximately 18-fold increase in editing efficiency. Furthermore, in the whole-genome assessment of editing efficiency, it demonstrated comparable editing capabilities to SpCas9 and slightly higher efficiency than LbCas12a.

Next, we further applied this method to a retron protein, Efe1. Fortunately, we discovered that the editing efficiency of Efe1 variants increased by 5-fold. In summary, our findings underscore the potential of targeted protein engineering strategies to enhance the efficiency of CRISPR systems, paving the way for improved genome editing applications.



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Hematopoietic Stem/Progenitor Cells and Engineering

DIRECT BACTERIAL STIMULATION ALTERS HEMATOPOIETIC STEM CELL TRANSCRIPTIONAL IDENTITY AND ACTIVATE INNATE IMMUNE SIGNALLING

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KEYWORDS: Hematopoietic stem cells, Bone marrow failure, pattern recognition receptors.

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Background & Aim

Hematopoietic stem cells (HSCs) serve as the lifelong source of all blood lineages and are now known to directly sense microbial signals. Bacterial infections pose a significant challenge in clinical hematopoietic cell therapy, often leading to engraftment failure and bone marrow stress. Despite this, how bacteria directly alter HSC gene expression and stemness remains poorly understood. Defining these molecular events is essential to better protect HSCs during infection and to improve outcomes in transplantation settings.

Methods, Results & Conclusion

Methods

Mouse bone marrow HSCs (LSK CD150+ CD48-) were stimulated *in vitro* with heat-killed *Pseudomonas aeruginosa*(HKPA) or heat-killed *Staphylococcus aureus* (HKSA) at MOI 50. Cells were harvested at 12 hours post-infection (hpi) for bulk RNA sequencing. Western blotting for phosphorylated NF-κB, ERK, and c-Jun was carried out at 1 to 6 hpi to assess downstream signalling. Studies using pharmacological inhibitors of the discovered pathways are currently underway.

Results

Following HKPA stimulation, we identified 317 upregulated and 83 downregulated genes in HSCs. Among the downregulated genes were *Erg* and key stemness-associated transcripts, suggesting a loss of HSC self-renewal capacity. Upregulated genes included lymphoid progenitor markers (*Ebf1, Cd79a*), innate immune receptors (*Tlr2, Tlr6, Nod2*), signalling components (*Jun, NF-κB*), transcription factors (*Gata2, Gata3*), early activation marker *Cd69*, and cytokines*Il1ß and Ccl3*, pointing toward inflammatory activation and lineage bias. Western blot analysis showed a progressive increase in p-NF-κB, p-ERK, and p-c-Jun levels from 1 to 6 hpi in both HKPA and HKSA stimulated HSCs, validating the transcriptomic findings at protein level for both stimuli.

Conclusion

Direct bacterial stimuli rapidly reshapes HSC transcriptional programs reducing stemness-associated genes while activating innate immune and progenitor associated networks. These findings provide insight into how bacterial exposure may compromise HSC function and suggest that TLR and NOD signalling could be relevant pathways to explore further in context of HSC protection during infection.

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Hematopoietic Stem/Progenitor Cells and Engineering

ORAL MUCOSITIS OUTCOMES WITH METHOTREXATE-BASED GRAFT-VERSUS-HOST DISEASE PROPHYLAXIS IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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KEYWORDS: Methotrexate , Oral mucositis, Hematopoietic stem cell transplantation.

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Background & Aim

Methotrexate (MTX) is widely used for graft-versus-host disease (GVHD) prophylaxis following hematopoietic stem cell transplantation (HSCT). MTX use was found to be associated with epithelial toxicity and increased risk of oral mucositis (OM) in adult patients who underwent HSCT. However, evidence in pediatric patients is limited, with no published studies specifically examining this association in such population. This study evaluated the association between MTX-containing GVHD prophylaxis regimens and OM among pediatric patients who underwent allogeneic HSCT.

Methods, Results & Conclusion

Methods

A retrospective cohort study was conducted at a tertiary hospital in Saudi Arabia, including pediatric patients aged ≤14 years who underwent allogeneic HSCT between May 1, 2020 and December 31, 2023. Patients were categorized into MTX-containing GVHD prophylaxis recipient group, and non-MTX recipient group. Outcomes included OM incidence and grades, total parenteral nutrition (TPN) initiation, GVHD incidence, 100-day survival, and overall non-relapse mortality were collected.

Results

Among 204 included patients, 136 received MTX-containing GVHD prophylaxis regimens, and 68

received non-MTX-containing regimens. Median age at transplant was 6.7 (3.8-10.1) years, with (n=118, 57%) males. The common underlying diseases were sickle cell anemia (n=81, 39.7%), beta-thalassemia major (n=20, 9.8%), and acute myeloid leukemia (n=17, 8.3%). MTX-containing GVHD prophylaxis group had higher OM incidence (85.29% vs. 63.23%, p < 0.001), moderate-to-severe (grade 2-3) OM (52.94% vs. 25%, p=0.039), TPN initiation (78.67% vs. 60.29%, p=0.006), and earlier onset of MTX prophylaxis as demonstrated in the Kaplan-Meier curve. Conversely, acute GVHD incidence was lower in the MTX recipients (9.55% vs. 25%, p=0.003), and no difference was observed in chronic GVHD, 100-day survival, and overall non-relapse mortality. Also, acute and chronic GVHD outcomes remained unchanged even after subgroup analysis of patients who underwent HSCT from a matched related donor.

Conclusion

MTX-containing GVHD prophylaxis was associated with increased incidence, earlier onset, and greater severity of OM, with higher rate of TPN initiation, while demonstrating a protective effect against GVHD in pediatric patients underwent allogeneic HSCT. Oral mucositis preventive strategies are recommended when using MTX in the pediatric population.

Figure1. Kaplan-Maier curve of time from HSCT until developing oral mucositis.

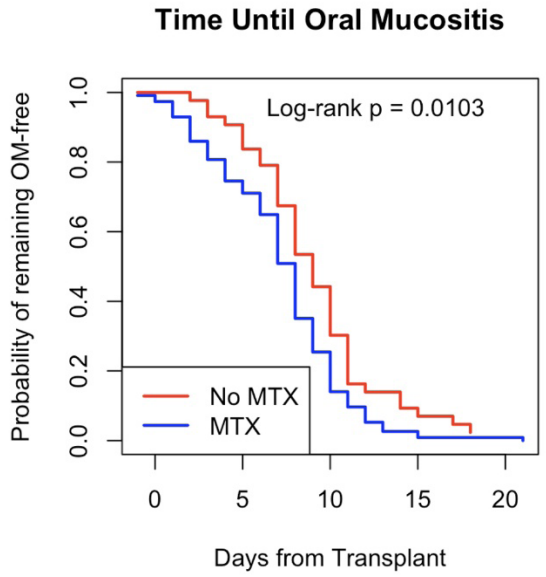


Table 1: Outcomes in methotrexate-containing GVHD prophylaxis regimens users versus non-methotrexate users among pedantic patients underwent allogenic HSCT

Outcomes	Methotrexate Users, n= 136	Non-Methotrexate Users, n= 68	P-value
Oral mucositis, n (%)	116 (85.29)	43 (63.23)	<0.001
Oral mucositis grade 2-3*, n (%)	72 (52.94)	17 (25.00)	0.039
TPN initiation, n (%)	107 (78.67)	41 (60.29)	0.006
Acute GVHD, n (%)	13 (9.55)	17 (25.00)	0.003
Chronic GVHD, n (%)	29 (21.32)	13 (19.11)	0.713
100-day survival, n (%)	133 (97.79)	66 (97.05)	0.731
Overall non-relapse mortality, n (%)	3 (2.20)	2 (2.94)	0.742

Abbreviation: GVHD: graft-versus-host disease; HSCT: hematopoietic stem cell transplantation; TPN: total parenteral nutrition.
*Oral mucositis grading was according to the National Cancer Institute (NCI) scale for oral mucositis

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Hematopoietic Stem/Progenitor Cells and Engineering

CLINICAL EFFICACY AND SAFETY ANALYSIS OF TANDEM AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN THE TREATMENT OF HIGH-RISK MULTIPLE MYELOMA

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KEYWORDS: Tandem autologous hematopoietic stem cell transplantation.

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Background & Aim

Autologous hematopoietic stem cell transplantation (ASCT) is a core therapeutic approach for multiple myeloma (MM). Patients with high-risk multiple myeloma are confronted with a high risk of early relapse and poor prognosis after single ASCT. Domestic and international guidelines recommend tandem second transplantation to improve remission depth and reduce relapse risk, while relevant clinical studies and data remain insufficient in China.

Methods, Results & Conclusion

Methods

A retrospective analysis was conducted on the clinical data of 19 patients with high-risk multiple myeloma who received tandem autologous hematopoietic stem cell transplantation. The clinical efficacy, safety and long-term survival outcomes of this regimen were systematically evaluated.

Results

The enrolled patients had a high proportion of high-risk cytogenetic abnormalities and extramedullary lesions with high malignancy. The remission level

was gradually improved after induction therapy, the first transplantation and the second tandem transplantation. The complete remission rate and negative rate of minimal residual disease both reached 78.9% after the second transplantation. With a median follow-up of 52 months, the 5-year progression-free survival rate was 56% and the 5-year overall survival rate was 79%, which were superior to those of conventional pharmacotherapy. All patients successfully completed two sessions of transplantation without transplantation-related mortality, and hematopoietic reconstitution was achieved smoothly. Adverse reactions were mainly mild hematological and non-hematological toxicities. The second transplantation did not increase the risk of severe adverse reactions, and all patients showed favorable tolerance.

Conclusion

Tandem autologous hematopoietic stem cell transplantation can effectively deepen disease remission, optimize long-term survival and possess satisfactory safety profile, which provides reference for clinical treatment selection. Nevertheless, this study is a single-center retrospective research with limited sample size. Further multicenter, large-sample prospective studies are required for subsequent verification.

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Hematopoietic Stem/Progenitor Cells and Engineering

IMPACT OF BASAL MEDIUM ON THE CELL FATE DECISIONS OF HIPSC DERIVED HEMATOPOIESIS

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KEYWORDS: Hematopoiesis, erythro-myeloid progenitor , basal medium.

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Background & Aim

Hematopoiesis proceeds through two distinct embryonic waves: a rapid first wave that predominantly generates primitive macrophages, and a second wave that gives rise to bone marrow-residing definitive hematopoietic stem cells (HSCs) responsible for lifelong blood cell generation. Recapitulating these complex waves in vitro using human induced pluripotent stem cells (hiPSCs) remains challenging due to poorly defined microenvironmental cues. While exogenous factors, such as growth factors and small molecules, are widely investigated as the principal determinants of hiPSC hematopoietic fate, the contribution of the basal medium itself remains largely unexplored. Here, we aimed to interrogate how basal medium composition, independent of the exogenous growth-factor program, directs hiPSC lineage specification.

Methods, Results & Conclusion

Using an identical growth-factor and small-molecule cocktail, we differentiated hiPSCs in either a defined serum-free medium or a medium supplemented with 5% or 20% KnockOut Serum Replacement (KSR; denoted KSR5 and KSR20, respectively). The serum-free medium efficiently induced definitive CD34+/CD45+ HSCs, whereas KSR5 failed to support robust hematopoietic differentiation and KSR20 redirected cell fate toward a CD45-/CD11b+/CD33+ myeloid program. This KSR20-driven myeloid output emerged through a transient erythro-myeloid progenitor (EMP)-like intermediate, characterized by a temporary wave of c-KIT+ cells at day 5 and progressive downregulation of MYB, consistent with an MYB-independent primitive/EMP program. Collectively, our results demonstrate that basal medium composition critically impacts cell fate decisions, capable of rerouting differentiation between definitive HSC and primitive/EMP-derived myeloid lineages.

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Hematopoietic Stem/Progenitor Cells and Engineering

FROM CORD BLOOD TO SCALABLE NK THERAPIES: A COST-EFFICIENT, AUTOMATED BIOREACTOR PLATFORM FOR HSC EXPANSION

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KEYWORDS: Cord Blood-Derived HSCs (CBU-HSCs), Stirred-Tank Bioreactors, Allogeneic Immune Therapies.

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Background & Aim

Hematopoietic stem cells (HSCs) are pivotal for off-the-shelf allogeneic immune cell therapies, including natural killer (NK) cells. While HSC expansion molecules like IBR403 enable CD34+ cell growth, conventional 2D cell culture methods are inefficient, costly, labor-intensive, and lack scalability, limiting large-scale clinical and commercial production. To address these challenges, we developed a robust, scalable, and high-throughput platform using

automated stirred-tank bioreactors to expand cord blood-derived HSCs(CBUs) and differentiate them into NK cells.

Methods, Results & Conclusion

Methodology

Using a Design of Experiments (DoE) approach with MODDE® software and multivariate data analysis, we optimized culture conditions by comparing GMP-grade media with RUO media, supplemented with IBR403 and key cytokines (SCF, Flt-3 ligand, TPO, IL-6). Over 50 bioreactor conditions were tested, evaluating critical parameters such as perfusion rates (0.5-2 VVD) and cytokine concentrations (0-100 ng/mL) across multiple donors over 28 days. CD34+ cell expansion and differentiation were performed in the Ambr® 15 bioreactor system, with functionality and purity assessed to ensure clinical relevance.

Results

HSCs cultured at 2 VVD perfusion rate produced an average of 50 million CD34+ cells per mL of input cord blood in GMP-grade media, compared to 1.4 million in RUO media. The DoE identified an optimal cytokine strategy (R10) that reduced costs by 50% while achieving >60 million CD34+ cells/mL of input cord blood. Both media formulation and a higher perfusion rate (2 VVD) were critical for maximizing CD34+ yields per mL of input CBU. Variations in CO2 (5% vs. 10%) and dissolved oxygen (DO) setpoints (15% vs. 30%)showed no significant impact on CD34+ expansion. NK cells differentiated in bioreactors under optimal conditions showed >95% CD56+ expression (range: 55-98% CD56+ on Day 28) and demonstrated >75%cytotoxicity against A549 cells at a 1:1 effector-to-target ratio, with donor variability impacting HSC expansion and NK differentiation.

Conclusion

This study successfully optimized and developed CBU-derived HSC expansion and NK cell differentiation in GMP-grade media using the Ambr® 15 bioreactor system. By refining key process parameters, we achieved high-yield, cost-effective CD34+ cell expansion and scalable NK cell production. These findings establish a robust platform, transforming cord blood into a valuable resource for advancing allogeneic NK cell therapies in oncology and immune-related diseases.

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Hematopoietic Stem/Progenitor Cells and Engineering

INHIBITION OF INFLAMMATION AND SENESCENCE ENABLES FUNCTIONALLY PRESERVED EX VIVO EXPANSION OF HUMAN HEMATOPOIETIC STEM & PROGENITOR CELLS

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KEYWORDS: Senescence, Inflammation, Cell Therapy.

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Background & Aim

Limited hematopoietic stem and progenitor cell (HSPC) dose constrains umbilical cord blood transplantation and hematopoietic stem cell engineering. Ex vivo culture induces inflammatory and senescence-associated stress responses that impair stem cell fitness and repopulating capacity, yet most expansion strategies emphasize proliferative signaling rather than stress suppression. We previously identified a novel azole-based small molecule, C7, that mediates robust HSPC expansion. This study aimed to define the mechanism of C7 activity and to test whether inhibition of inflammation and senescence enables preserved HSPC expansion.

Methods, Results & Conclusion

Human CD34+ HSPCs from cord blood, bone marrow, and mobilized peripheral blood were expanded ex vivo with cytokines ± C7. Stem and progenitor composition, proliferation, mitochondrial stress, senescence, and differentiation were assessed by flow cytometry and functional assays. Hematopoietic potential and self-renewal were evaluated by primary and secondary transplantation in NSG mice. Kinase inhibition profiling, BioMAP assays, and single-cell RNA sequencing were used to define mechanisms. C7 preferentially expanded primitive HSPC and phenotypic HSC populations, achieving □4-fold greater expansion of early HPCs and >15-fold greater expansion of HSCs versus cytokine-only cultures, while limiting differentiation and preserving

multilineage output. C7-treated cultures showed increased proliferation, with >40% of early HPCs undergoing ≥5 cell divisions, reduced mitochondrial oxidative stress, and senescence suppression. In vivo, C7-expanded HSPCs demonstrated improved multilineage engraftment, with chimerism comparable to unexpanded grafts in peripheral blood (□28%) and bone marrow (□63%), and preserved self-renewal upon secondary transplantation. Mechanistically, C7 inhibited p38 MAPK together with additional kinase targets and repressed inflammatory and senescence-associated transcriptional programs, including NFκB- and IL-10–related pathways, with strong downregulation of SERPINB2 and CDKN1A. These findings identify inflammation- and senescence-driven stress responses as targetable determinants of HSPC attrition during ex vivo culture. Their suppression enables robust expansion while preserving stem cell function, supporting a shift in hematopoietic stem cell engineering from promoting proliferation alone toward maintaining cellular integrity and establishing a broadly applicable preclinical principle for cell therapy manufacturing.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

RESIDUAL-FREE CLOSED-SYSTEM T CELL SEPARATION PLATFORM ACHIEVING >93% PURITY IN UNDER 30 MINUTES

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KEYWORDS: T-cell, Cell Separation, CAR-T.

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Background & Aim

Precise cell selection is critical for immunotherapy, as the efficacy, safety, and reproducibility of the final product depend on the enrichment of defined immune cell subsets. Current technologies, such as magnetic bead–based separation, can leave residual labels, induce cellular stress, increase costs, and last up to 5 hours. To address these challenges, we developed a pump-driven, closed-system flow-through antibody column technology for negative T cell selection.

Methods, Results & Conclusion

Methods

Peripheral blood mononuclear cells (PBMCs) from healthy donors (n = 5) were used as input for negative T cell separation. Our T-cell separation platform consists of antibodies covalently bound to particles packed within a column and integrated into a closed, pre-filled single-use cartridge. A peristaltic pump maintained constant flow, completing the procedure in under 30 minutes. Post-isolation activation and 9-day expansion were performed using Atract™ T-Cell Activation Kit in G-Rex® 6M culture to assess proliferative capacity within a residual-free workflow. Absence of residual particles was confirmed by microscopy and flow cytometry.

Results

Processing 1×10^8 PBMCs per run, our platform increased $CD3^+$ cell purity from 61% (± 6%) in the starting material to 93% (± 2%), while all unwanted cell populations were reduced to < 2%. $CD3^+$ recovery was 62% (± 12%), with negligible non-target cells and viability >90%. T cells, isolated with our technology, remained highly responsive to Atract™ T-Cell Activation Kit activation, achieving 65-fold expansion with viability >85% and complete absence of residual particles, yielding clinically relevant cell numbers and confirming preserved functional fitness.

Conclusions

Our T-cell separation platform enabled rapid, residual-free T cell enrichment, achieving >93% purity from 1×10^8 PBMCs in a closed workflow completed in under 30 minutes versus up to 5 hours with conventional approaches. Combined with Atract™ T-Cell Activation Kit, isolated T cells demonstrated robust 65-fold expansion and preserved viability, establishing proof of concept for a residual-free selection-to-activation workflow. This single-use cartridge is compatible with standard peristaltic pump systems, supporting integration into existing GMP manufacturing environments. Its modular antibody-binding architecture also enables adaptation to alternative target cell populations, supporting further GMP development and clinical-scale validation.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

ATRACT™: A NOVEL T-CELL ACTIVATION REAGENT

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KEYWORDS: T-cell, activation, CAR-T.

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Background & Aim

Efficient and reproducible T-cell activation is a critical step in the manufacture of cell-based immunotherapies. Many conventional activation systems rely on particulate reagents that require downstream removal, increasing workflow complexity, processing time, and the risk of residual contamination. Reproducibility may also be

compromised in monocyte-rich starting materials, while flexibility is often limited by proprietary system constraints. Atract™ is a residue-free T-cell activation technology developed to address these challenges.

Methods, Results & Conclusion

Methods

Peripheral blood mononuclear cells (PBMCs) from healthy donors (n = 11) were activated using Atract™, a biocompatible composite-based system in which activation antibodies are covalently bound to particles approximately five times larger than cells. This particle size prevents phagocytosis and enables efficient removal by standard filtration. T-cell activation, expansion, viability, and exhaustion marker expression were evaluated and compared with a commercially available activation reagent (TransAct). Compatibility across multiple culture platforms and media formulations was also assessed.

Results

Atract™ effectively activated human T cells, as demonstrated by robust upregulation of activation markers. After 48 hours, CD25 expression averaged 88%, comparable to TransAct (87%). Efficient expansion was observed, with >60-fold T-cell expansion after 7 days for both activation methods. High cell viability (>85%) was maintained, alongside low expression of exhaustion markers, including TIM-3, PD-1, and LAG-3 (<25%). Atract™ was compatible with standard T-cell manufacturing platforms, including well plates, culture bags, and G-Rex systems, as well as a range of culture media, animal-free sera, GMP-compliant formulations, and cytokine conditions.

Conclusions

Atract™ enables effective, residue-free T-cell activation from PBMC starting material while reducing workflow complexity and supporting reproducible performance. This technology represents a flexible and scalable alternative to conventional activation systems for research and translational cell therapy manufacturing.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

ABS CATA-001: A NOVEL CD38/AL BISPECIFIC FOR TREATING LIGHT CHAIN MULTIPLE MYELOMA

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KEYWORDS: multiple myeloma, CD38, bispecific antibodies.

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Background & Aim

In multiple myeloma cases, approximately 15-20% suffer from light chain multiple myeloma (LCMM). Beyond that, clonal plasma cells abnormally secrete free light chain which can evolve to AL amyloidosis leading to amyloid deposition in organs . Current first-line therapy for LCMM follows the same backbone as for typical MM, but with extra urgency for rapid cytoreduction. ABS CATA-001 is a bispecific antibody targeting CD38 and free light chain (CD38/AL BsAb), representing a first-in-class approach with dual functionality of MM cell depletion with the unique catalytic capacity to bind and clear circulating free light chain aggregates.

Methods, Results & Conclusion

ABS CATA-001was designed with a structurally symmetric bispecific antibody. The CD38 binding arm is a humanized VHH antibody discovered from panning from a computer designed pre-humanized llama VHH library. The anti-AL arm was selected from a preexisting mAb targeting aggregated light chain (2A4). The bispecific antibody was further developed using computer-aided design rationale: detuned CD38 binding to enable better safety; effective CD38 binding to lead to MM cell depletion; built-in catalytic function to enable clearance of AL aggregates by both ADPC and catalytic function MOAs; optimized to increase clinical potential backed by on bench validation and clinical POCsIn the discovery of CD38. In order to balance safety and efficacy of CD38 affinity, we detuned the CD38 binding arm to retain MM cell depletion function, without affecting NK cells and activated T cells. *In vitro* ADPC studies show that ABS CATA-001 can deplete H929 cancer cells in the presence of human PBMCs of a healthy donor. *In vivo* studies showed that ABS CATA-001 can effectively and safely deplete and inhibit MM cells without affecting body weight in a human PBMC reconstituted, and H929 engrafted NDG mouse model. The *in vitro* assessments studies show that ABS CATA-001 significantly reduces aggregated

human serum amyloid A1 (hSAA1). LCMM patient serum treated with ABS CATA-001 showed better reduction of serum light chain aggregates in all five LCMM patient donors when compared to Birtamimab. These findings demonstrate that ABS CATA-001 may serve as a next generation therapy.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

A FEEDER-FREE STREAMLINED MANUFACTURING WORKFLOW FOR NK CELL THERAPY USING THE XURI™ CELL EXPANSION SYSTEM

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KEYWORDS: Natural Killer Cell, Allogenic, Manufacturing.

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Background & Aim

Natural killer (NK) cells are a promising immunotherapy for cancer due to their ability to recognize and target tumor cells without major histocompatibility complex (MHC) presentation, making them attractive for allogeneic applications. Preclinical and clinical studies have demonstrated favorable safety profiles and encouraging efficacy in multiple malignancies, including solid tumors. However, large-scale manufacturing remains a major bottleneck. Current processes are labor-intensive, costly, and rely on feeder-cells for expansion, which leads to regulatory complications. To facilitate broader adoption of NK cell therapy, there is a critical need for streamlined, automated, and feeder-free manufacturing solutions that enable both scalability and compliance.

Methods, Results & Conclusion

Methods

NK cells were manufactured using the Xuri™ Cell Expansion System and harvested using the Sefia™ S-2000 system. Cells were isolated from fresh leukopaks of (n = 3) healthy donors by CD3 depletion and CD56 enrichment. Isolated NK cells (300-400 million) were seeded in Xuri™ 2L cellbags (1 x 106 cells/mL) with complete NK MACS media supplemented with IL2 and IL15 proteins, and gentle rocking (2 rpm, 2° angle). Cultures were sampled starting on day 5, and media was added to maintain concentration at 6 x 105 cells/mL. Scale-up to 20L and 50L cellbags were performed as needed. Cell viability and phenotype were quantified throughout expansion. Harvested NK cells were reformulated using the Sefia™ S-2000 system (FlexCell application) and cryopreserved using the VIA Freeze™ controlled-rate freezer and thawed using the VIA Thaw™ dry automated thawer.

Results

NK cell isolation yielded >98% CD56+ purity. In the Xuri™ Cell Expansion System, donor 1 expanded to 27 billion live NK by day 13 (67-fold), donor 2 to 18 billion by day 19 (38-fold), and donor 3 to 17 billion by day 16 (68-fold). Viability remained >91% throughout culture and NK purity at harvest exceeded 99%. Recovery after using the Sefia™ cell processing system was 82 ± 2% and post-wash viability 92 ± 0.3% (~2% drop vs. initial product). Post-thaw viability was 88 ± 2%.

Conclusion

This study demonstrates successful feeder-free NK cell expansion in the Xuri™ Cell Expansion System, achieving allogeneic-scale numbers (>15 billion live NK) from healthy donors. Additionally, automated, closed harvesting using the Sefia™ S-2000 cell processing system showed high recovery and viability, supporting a manufacturing workflow for NK cell therapy.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

VORTEX-ACTUATED CELL SORTING BOOSTS EXPANSION OF CRISPR-EDITED HUMAN REGULATORY T CELLS

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KEYWORDS: Cell Separation, T-Lymphocytes, Regulatory, CRISPR.

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Background & Aim

Regulatory T cells (Tregs) can be genetically modified to enhance suppressive function or specificity using CRISPR-transfection via electroporation. However, electroporation reduces cell viability and the effects of different cell sorting techniques on electroporation-induced cell death are unclear. Highway1 is a GMP-compliant cell sorter that separates cells via vortex-actuated cell sorting (VACS) which may be gentler and improve cell viability compared to conventional sorting methods. We compared immunomagnetic enrichment and stream-in-air fluorescence-activated cell sorting (FACS) with VACS enrichment followed by VACS for the production of gene-edited Tregs.

Methods, Results & Conclusion

Methods

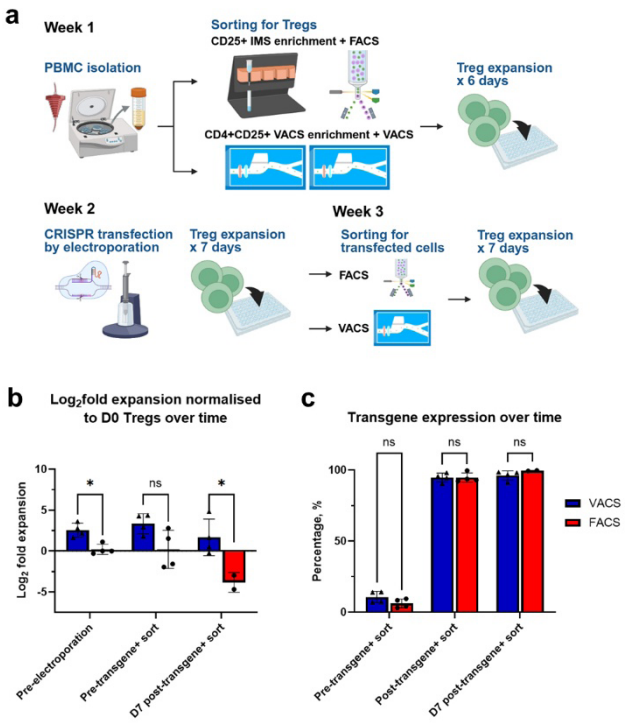
Tregs were sorted from peripheral blood mononuclear cells (PBMCs) derived from healthy donor leukocyte cones by either CD25+ immunomagnetic enrichment followed by FACS (25MF Tregs) or CD4+CD25+ VACS enrichment followed by VACS purity sort (VP Tregs). After 6 days of expansion, cells were electroporated with Cas12a ribonucleoprotein complexes and dsDNA templates. After 7 days of expansion, transfected cells were identified by anti-G4S linker antibodies, sorted by either VACS for VP Tregs or FACS for 25MF Tregs, then expanded for 7 days (Fig 1a). Purity was defined as percentage of target cells in live lymphocytes. Yield was defined as percentage of target cells in the pre-sort material that was isolated.

Results

VP produced Tregs with similar purity (94.9±2.6 vs 95.2±2.0%, mean±SD, n=4 each, p=0.85) and yield (19.3.7±2.9 vs 20.8±3.3%, p=0.43), but required more time (7.5±0.8 vs 1.3±0.3 minutes per 10 x10^6 PBMCs, p=0.0002) than 25MF.
VP Tregs expanded more than 25MF Tregs (2.5±0.9 vs 0.2±0.6 log_2fold expansion, p=0.005, Fig 1b) at day 6. G4S linker expression (10.6±4.0 vs 6.2±3.2%, p=0.14, Fig 1c) and log_2fold expansion (3.34±1.2 vs 0.20±2.3, p=0.07) were similar between VP and 25MF Tregs 7 days post-electroporation, though 25MF Tregs from 2 donors failed to expand.
While sorting for transfected cells, VACS and FACS had similar purity (94.6±0.6 vs 93.3±3.2%, p=0.63), yield (56.9±12.4 vs 37.8±14.2%, p=0.21) and sorting time (4.7±1.8 vs 2.9±0.7 minutes per 10x10^6 cells, p=0.26). VACS-sorted cells expanded more than those sorted by FACS (1.7±2.2 vs -3.8±1.2 log_2fold expansion, p=0.02), with similar purity (96.0±3.4 vs 99.5±0.2%, p=0.13) and Foxp3 expression (89.2±9.1 vs 78.7±0.3% p=0.35) after 7 days.

Conclusion

VACS may improve throughput for Tregs CRISPR-transfected by electroporation.



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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

HUMAN REGULATORY T CELLS WITH A MODULAR RECEPTOR FOR PROGRAMMABLE ANTIGEN TARGETING

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KEYWORDS: T-Lymphocytes, Regulatory, Receptors, Chimeric Antigen, Antigen Specificity.

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Background & Aim

Introduction

Chimeric antigen receptor (CAR) cell therapies are limited by their single antigen specificity. SNAP-CARs can covalently bind different benzylguanine (BG)-conjugated antibodies, thereby redirecting cell specificity against different targets. This strategy may be useful for programming regulatory T cells (Tregs) to target different antigens for use in transplantation with varying HLA mismatches, or in autoimmune diseases with different auto-antigens. We aimed to generate SNAP-CAR Tregs capable of targeting different antigens to broaden the applicability of antigen-specific Treg therapy.

Methods, Results & Conclusion

Methods

Tregs were isolated from peripheral blood mononuclear cells (PBMCs) obtained from healthy donor leukocyte cones, expanded, and transduced using lentiviral vectors to express SNAP-CARs. Transduced cells were sorted for SNAP-CAR Tregs and further expanded (Figure 1). Antibodies were conjugated to BG via an amine coupling reaction.

Stimulation assays were performed by co-culturing SNAP-CAR Tregs (with or without preloading with BG-conjugated antibodies) or autologous, polyclonally expanded, unedited Tregs (apTregs), with or without target antigen-expressing cells. In alloantigen suppression assays, HLA-A2 negative CD3-enriched responder PBMCs were cultured with allogeneic HLA-A2 positive CD3-depleted stimulator PBMCs and Tregs at varying ratios.

Results

SNAP-CAR Tregs and apTregs were phenotypically similar with high demethylation at the Treg-specific demethylation region (Figure 2A and B). SNAP-CAR Tregs preloaded with BG-conjugated antibodies (anti-HLA-A2, anti-HLA-B7 or anti-CD19) showed increased CD25 and CD69 expression with elevated IL-10 secretion when co-cultured with target antigen-expressing cells. This activation was not observed with unloaded SNAP-CAR Tregs, apTregs, or when preloaded cells were stimulated with wild-type K562 cells (Figure 2C-E, n=2-5 donors). SNAP-CAR Tregs preloaded with anti-HLA-A2 antibodies demonstrated a trend towards enhanced suppressive function compared with apTregs (Figure 2F, n=3 donors, p=0.06).

Conclusion

SNAP-CAR Tregs can be specifically activated after preloading with the appropriate antibodies and show evidence of enhanced suppressive function compared to apTregs in an HLA-A2 alloantigen suppression assay. This technology may be harnessed to alter Treg specificity on demand, enabling the targeting of different antigens.

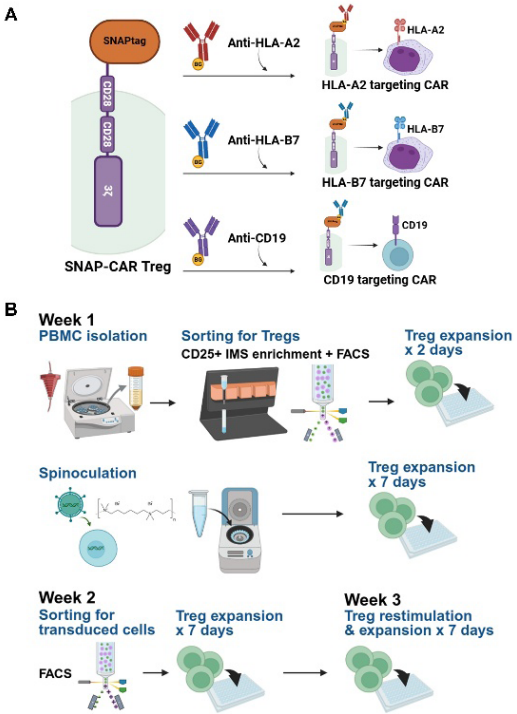


Figure 1. Generation of SNAP-CAR human regulatory T cells (Tregs). (A) Schematic of SNAP-CAR Treg targeting varying antigens using different benzylguanine-conjugated antibodies. **(B)** Workflow for Treg isolation, expansion, lentiviral transduction and enrichment of transduced cells. CAR, chimeric antigen receptor; FACS, fluorescence-activated cell sorting; HLA, human leukocyte antigen; IMS, immunomagnetic separation; PBMC, peripheral blood mononuclear cells

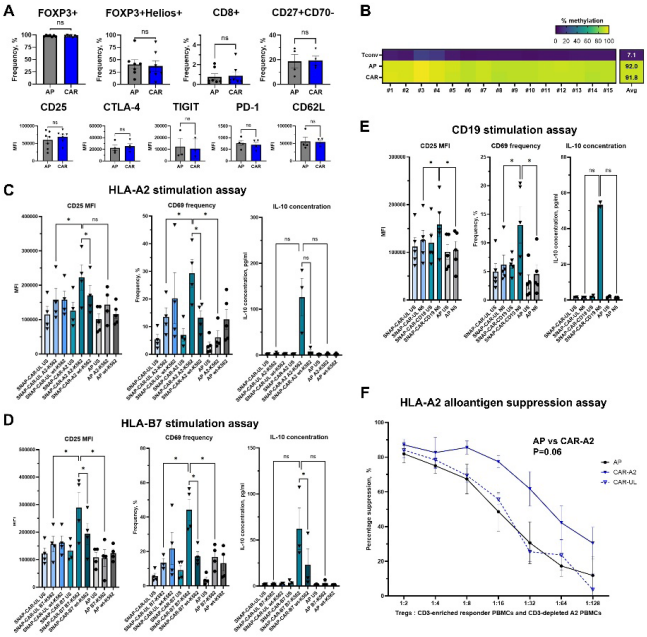


Figure 2. Phenotypic and functional assessment of SNAP-CAR Tregs. (A) Phenotypic markers in SNAP-CAR Tregs vs autologous polyclonally expanded Tregs (AP), gated on live CD4$^+$ cells. n=4–7 donors; each point represents one donor (mean of three technical replicates). Multiple paired t-tests with Holm–Šídák correction. **(B)** Demethylation of the Treg-specific demethylated region (TSDR) in SNAP-CAR Tregs, AP and conventional T cells (Tconv), shown as the average (Avg) across all CpG sites and at each individual site. **(C–E)** Antigen-specific stimulation assay. Unloaded SNAP-CAR Tregs (SNAP-CAR-UL), SNAP-CAR Tregs preloaded with benzylguanine-conjugated antibodies (SNAP-CAR-A2, -B7, -CD19), or AP were left unstimulated (US) or co-cultured with antigen-expressing targets (A2-K562, B7-K562, Nalm-6) or wild-type K562 (wt-K562). CD25 MFI, frequency of CD69$^+$ cells among live CD4$^+$eGFP$^+$ cells, and supernatant IL-10 (ELISA) are shown. Paired t-tests; ns=not significant; * p<0.05. **(F)** HLA-A2 alloantigen suppression assay. Each point represents the mean of three donors (three technical replicates each). Repeated-measures two-way ANOVA between AP and SNAP-CAR-A2 (p=0.06). All error bars represent SEM.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

DECENTRALIZED POINT-OF-CARE CD19 CAR-T MANUFACTURING ENABLES DURABLE RESPONSES IN RELAPSED/REFRACTORY B-CELL MALIGNANCIES: VIETNAM'S FIRST CLINICAL EXPERIENCE

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KEYWORDS: CAR-T cell therapy, Hematological malignancies, Resource-constrained settings.

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Background & Aim

Commercial CAR T-cell therapies remain inaccessible to many patients in low- and middle-income countries due to manufacturing complexity and cost. We evaluated the safety, feasibility, and preliminary efficacy of a point-of-care (PoC) manufactured CD19 CAR T-cell platform for relapsed/refractory (R/R) B-cell acute lymphoblastic leukemia (ALL) and non-Hodgkin lymphoma (NHL) in Vietnam.

Methods, Results & Conclusion

Methods

In the first Phase I CAR T-cell trial conducted in Vietnam (NCT06027957), sixteen patients with R/R B-cell malignancies (8 ALL, 8 NHL) received autologous CD19 CAR T cells manufactured onsite using the automated CliniMACS Prodigy platform. The median infused dose was 1.9 × 10^6 CAR+ T cells/kg. Safety, response rates, progression-free survival (PFS), and overall survival (OS) were assessed.

Results

Manufacturing was successfully completed for all enrolled patients, demonstrating the feasibility of decentralized PoC CAR T-cell production. Treatment was generally well tolerated. Cytokine release syndrome (CRS) occurred in 13/16 patients, with only one grade 3 event. Grade 1 immune effector cell-associated neurotoxicity syndrome (ICANS) occurred in two patients. No severe long-term treatment-related toxicities were observed apart from persistent hypogammaglobulinemia in a subset of patients. Complete remission was achieved in 100% (8/8) of ALL patients and 87.5% (7/8) of NHL patients. Notably, all responding NHL patients maintained complete remission throughout follow-up of up to 34 months, while four ALL patients experienced relapse. Mean progression-free survival was 19.0 months for ALL and 20.3 months for NHL, with corresponding overall survival of 20.7 and 21.2 months. Mean PFS was 19.0 months for ALL and 20.3 months for NHL, while mean OS reached 20.7 and 21.2 months, respectively.

Conclusions

Point-of-care manufactured CD19 CAR T-cell therapy demonstrated favorable safety, durable clinical activity, and reliable manufacturing feasibility in a resource-constrained healthcare setting. These findings support decentralized CAR T-cell production as a scalable strategy to expand access to advanced cellular therapies across Southeast Asia. Building on this platform, clinical programs targeting autoimmune diseases and additional hematologic malignancies are currently underway.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

RADIOTHERAPY-INDUCED NKG2D LIGANDS SENSITIZE TO ARMORED NKG2D-TRUCKS OVERCOMING TGFB1/B7-H3 RESISTANCE IN COLORECTAL CANCER

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KEYWORDS: Natural Killer, Radiotherapy, Colorectal cancer.

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Background & Aim

Radiotherapy (RT) reshapes the tumor immune microenvironment, yet the molecular basis for its synergy with NK/CAR-cell therapy in colorectal cancer (CRC) remains incompletely defined.

Methods, Results & Conclusion

Methods

NKG2D-ligand (NKG2DL) expression was profiled by qRT-PCR, immunoblot, and flow cytometry in CRC lines and in paired patient tumors. Mechanism was dissected using DNA-PK/Rad51 inhibitors, STING knockout, and IRF3 inhibition. NK cells function under TGFβ1 was assessed by cytotoxicity, receptor profiling, GSEA, and mitochondrial-dynamics analysis. An NKG2D-CAR and an armored NKG2D-TRUCK (co-secreting an anti–B7-H3 scFv, a TGFβR decoy, and IL-15) were generated and tested in vitro and in HT29

xenografts.

Results and conclusion

s:

RT upregulated NKG2DLs at the mRNA, protein, and cell-surface levels, and in post-treatment patient tumors (P<0.001). High post-treatment ULBP4 or ULBP2/5/6 predicted superior disease-free survival (n=100, p<0.05). Induction required RT-driven DNA damage and STING–TBK1–IRF3 signaling; DNA-PK or Rad51 inhibition further amplified NKG2DLs and NK killing, whereas STING knockout or IRF3 inhibition abolished it. However, RT concurrently elevated tumor TGFβ1 and B7-H3 (r=0.34, P=0.049), which impaired NK cytotoxicity by skewing the inhibitory/activating-receptor balance and suppressing the IFN-γ response and oxidative phosphorylation through DRP1-mediated mitochondrial fission; TGFβR inhibition or DRP1 inhibition restored NK-mediated killing. Transposon-based NKG2D-CAR cells preferentially lysed irradiated CRC cells, and transposon-based NKG2D-TRUCK achieved the strongest cytotoxicity even against TGFβ1-overexpressing targets. In vivo, RT (with or without Rad51i) combined with NKG2D-CAR/TRUCK is being evaluated in HT29 xenograft NSG models for tumor control and survival. Taken together, RT licenses CRC for NKG2D-directed killing via STING-dependent NKG2DL induction but co-induces TGFβ1/B7-H3-mediated resistance. An armored NKG2D-TRUCK that simultaneously neutralizes both, combined with RT and DNA-repair inhibition, provides a rational off-the-shelf strategy for CRC.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

THERAPEUTIC EFFICACY OF IGF-1R/CD3 BISPECIFIC ANTIBODY-ARMED T CELLS COMBINED WITH PD-L1 BLOCKADE IN SORAFENIB-RESISTANT HCC

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KEYWORDS: Sorafenib-Resistant HCC, IGF-1R Armed T, PD-L1 Blockade.

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Background & Aim

Hepatocellular carcinoma (HCC) is a leading contributor to cancer mortality worldwide. The emergence of resistance to tyrosine kinase inhibitors, particularly sorafenib, substantially compromises therapeutic efficacy and highlights the need for alternative treatment strategies. This study investigated the therapeutic potential of combining IGF-1R/CD3 bispecific antibody-armed T cells (IGF-1R/CD3 Armed-T) with PD-L1 blockade in high IGF-1R-expressing sorafenib-resistant HCC (HCC_R), and further examined the clinical significance and mechanistic basis of this combinatorial approach.

Methods, Results & Conclusion

Publicly available HCC patient datasets were analyzed to evaluate IGF-1R and PD-L1 expression profiles and their clinical relevance. Antitumor activity was assessed in vitro using both two-dimensional culture systems and three-dimensional organoid models, and in vivo efficacy was examined in xenograft models. Elevated expression of IGF-1R and PD-L1 was associated with more aggressive clinicopathological features, earlier recurrence, and poorer survival outcomes in patients with HCC. Mechanistic analyses demonstrated that IGF-1R/CD3 Armed-T cells exhibited sustained engagement with HCC_R cells and induced increased cytokine production. In xenograft tumors, Armed-T cells showed enhanced intratumoral infiltration and persistence, accompanied by increased local IFN-γ release and greater tumor cell apoptosis. Notably, the combination of IGF-1R/CD3 Armed-T cells and PD-L1 blockade exerted synergistic antitumor effects in sorafenib-resistant HCC models in vitro and in vivo. Collectively, these findings support the potential of IGF-1R/CD3 Armed-T therapy in combination with PD-L1 blockade as a promising treatment strategy for sorafenib-resistant HCC.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

MODULAR AUTOMATED PROCESSING, FORMULATION, AND FILL-FINISH FOR DIVERSE CAR-ENGINEERED CELL THERAPIES

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KEYWORDS: CAR-T, CAR-NK, Manufacturing.

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Background & Aim

As engineered cell therapy pipelines broaden, manufacturing processes must be able to manage variability in cell type, target dose, final formulation volume, and fill format. Manual processing and fill–finish operations can contribute to process variability, contamination risk, and workflow inefficiency, especially in multi-step autologous manufacturing. Closed, automated, and modular systems provide a strategy to improve reproducibility and scalability

while maintaining product quality. This study assessed an integrated modular workflow that combines automated cell concentration and washing with automated formulation and fill–finish for multiple CAR-engineered cell therapy models and clinically relevant dose configurations.

Methods, Results & Conclusion

Methods

Model CAR-T and other engineered cell types were processed using an automated counterflow centrifugation platform to support cell concentration and buffer exchange. The processed cell material was then transferred within a closed workflow to an automated formulation and fill system. Formulation and dispensing were performed in cryopreservation media across a broad fill-volume range of 0.5–750 mL, including multi-output and higher-dose configurations. Final product was dispensed into bags or vials. Key assessments included cell recovery, viability, and phenotype before and after processing, as well as dispense-volume accuracy, variability in cell concentration across outputs, and post-dispense viability.

Results

Automated concentration and washing produced high cell recovery while preserving viability and phenotypic marker expression. Automated formulation and fill–finish showed consistent dispense performance across evaluated formats, with fill-volume deviations of ≤10% and cell concentration variability below 10% across outputs from 0.5 to 750 mL. Viability and key phenotype markers were maintained after formulation and dispensing across multiple engineered cell types. The integrated workflow supported multi-output dose formats and remained compatible with adjacent modular upstream and downstream operations.

Conclusion

This study demonstrates the feasibility of a closed, modular automated workflow for processing, formulation, and fill–finish of diverse CAR-engineered cell therapy products. The workflow maintained critical cell quality attributes while enabling accurate dispensing and flexible final product configurations, supporting its potential use in scalable and reproducible engineered cell therapy manufacturing.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

MODULAR AUTOMATION AS A FOUNDATION FOR NEXT-GENERATION AUTOLOGOUS AND ALLOGENEIC CELL THERAPY MANUFACTURING

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KEYWORDS: CAR-T, CAR-ipSC derived iNK, cell processing, gene editing, fill finish, immunotherapy, closed modular automated manufacturing.

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Background & Aim

The transition of cell therapies from development to commercial scale manufacturing requires robust, modular, and automated workflows that minimize manual intervention while maintaining product quality and consistency. In this work, we present integrated methods and instrumentation that enable closed, modular automated cell therapy manufacturing from cell isolation and genome engineering through formulation and fill–finish, supported by GMP grade reagents systems.

Methods, Results & Conclusion

Methods and results

We highlight through this work an end-to-end flexible and modular cell therapy ecosystem that seamlessly integrates upstream and downstream processes. Key technologies include CTS™ DynaBeads™ and the Gibco™ CTS™ Rotea™ Counterflow Centrifugation System for flexible, closed cell isolation, washing, and concentration; Neon™ NxT and CTS™ Xenon™ Electroporation Systems for scalable gene delivery from discovery through GMP; and CTS™ TrueCut™ HiFi Cas9 Protein with GMP compliant media systems for reproducible genome engineering.
Two representative use cases are presented here. First, an autologous CAR-T workflow demonstrates closed enrichment of PBMCs and automated buffer exchange into gene delivery reagents using Rotea, followed by CRISPR-based engineering to generate model anti CD19 CAR-T cells using the Xenon Electroporation System and Cas9 RNP, achieving CAR knock-in efficiencies > 40%. Downstream processing is streamlined through integrated buffer exchange, formulation, and fill–finish using Rotea and a novel automated fill–finish instrument, the Gibco™ CTS™ Compleo™ System with overall preserved cell viability and phenotype.
Second, an iPSC-to-CAR-iNK workflow illustrates closed-system processing of adherent iPSCs expanded in multi-layer Nunc™ Cell Factory™ System, with direct integration of the Gibco™ CTS™ Rotea™ System enabling automated harvest, washing, and concentration prior to cell banking, maintaining > 90% cell viability. The iPSCs were engineered using the CTS™ Xenon™ Electroporation System and CRISPR–Cas9 RNPs, achieving anti-mesothelin CAR knock-in efficiencies of up to 30%. Engineered

CAR-iPSCs were subsequently differentiated using CTS™ StemPro™-34 SFM XF medium and expanded as functional CAR-iNK cells in CTS™ NK-Xpander™ Medium.

Conclusion

Together, these workflows demonstrate how a modular, closed, and automated ecosystem supports scalable, high-quality manufacturing of both autologous and allogeneic cell therapies.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

INTEGRATIVE PROGENITOR TCR STRATEGY FOR SUSTAINED ANTI-CANCER RESPONSES

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KEYWORDS: TCR, stem cell, Cancer.

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Background & Aim

Re-engineering of patients' T cells has shown to be promising as cancer therapy but unfortunately the anti-tumor effect is largely short-lived. In an effort to generate tumor-associated antigen(TAA) specific T cells we have identified NY-ESO-1 as the prototypic target and have developed a T Cell Receptor(TCR)-based cellular immunotherapy platform. Our central hypothesis is that MHC-II-TCR engineered human hematopoietic stem/progenitor cells(hHSC) will lead to durable in vivo supply of fully active T cells with anti-tumor activity, and provide sustained help to co-injected MHC-I-TCR transduced (mature) effector T cells (which will serve to immediately "debulk" the tumor), leading to long-lasting tumor rejection.

Methods, Results & Conclusion

We performed the cloning, construction and generation of lentiviral viral vectors with two unique NY-ESO-1 TCRs (MHC-II restricted HLA-DR1 and DP4), as well as, another novel MHC-I-HLA-A2.1 TCR for NY-ESO-1. Transduction efficiency of hHSC was high with transgene expression levels of 40-51% (0.5-1 vector copies/cell); and 65-92% tetramer+ for mature T cells. We confirmed specific functional activity of all TCRs with various tumor targets (SKMEL-37, MZ19, or aAPC: K562/DR1/DP4/A2.1+/- cognate peptides). For this project we generated new transgenic mouse models based on NSG background with expression of human MHC-II-DP4 and DR1 in order to study hHSC differentiation/function in vivo. We injected CD34+hHSC transduced with MHC-II-TCR and confirmed generation of engineered TCR-expressing-human T cells by FACS. We then tested anti-tumor efficacy in vivo against human melanoma (MZ19) or ovarian carcinoma (A2780/A2/NY) injected with MHC-II-TCR transduced or non-transduced-control-hHSC and low dose(5x10^5cells) of NY-ESO-1-HLA-A2.1-CD8TCR-transduced hPBMC. Remarkable tumor control was obtained ($p<0.05$) with TCR-transduced-hHSC (tumor size=28mm^2; SE+/-11) versus untransduced-hHSC (152.7mm^2; SE+/-24) or control untreated (no hHSC, no CD8 T cell ACT) (196mm^2; SE+/-40).
Therefore we demonstrated for the first time that a combined ACT approach of MHC-II-TCR-transduced hHSC with MHC-I-TCR-transduced PBMC leads to a synergistic and efficient in vivo control of tumor burden, paving the way for a novel adoptive cell immunotherapy platform to benefit patients with advanced solid tumors.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

PERFUSION-ENABLED CAR-T MANUFACTURING IN STIRRED-TANK BIOREACTORS ACHIEVING100+ DOSES PER BATCH

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KEYWORDS: CAR-T Cells, Automation, Perfusion.

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Background & Aim

Industrializing allogeneic CAR-T therapies requires scalable, cost-efficient, and automation-ready manufacturing platforms capable of delivering high cell yields within short timelines. Many current systems lack predictive scale-down models, real-time analytics, and integrated downstream workflows, limiting efficient translation. Here, we establish a serum-free perfusion CAR-T process in stirred-tankbioreactors that integrates predictive scale-down, in-line viable cell monitoring, and automated harvest to enable data-driven scale-up.

Methods, Results & Conclusion

Methods

Anti-CD19 CAR-T cells were expanded for 7 days in a 2 L single-use stirred-tank bioreactor (STR) using serum-free medium with ATF-based perfusion (1.0 VVD from Day 2). In parallel, 250 mL Ambr 250 STRs were operated at matched volumetric power input (P/V approximately 8.78 W per m3) to validate scale-down model (SDM)predictivity, while G-Rex systems served as static controls. Online pH and dissolved oxygen were controlled, and a multifrequency capacitance probe enabled in situ viable cell estimation supported by MVDA and OPLS modeling. Downstream processing was performed using Ksep 400 for automated harvest, washing, and concentration, with viability, phenotype, exhaustion and activation markers, differentiation state, cytotoxicity, and cytokine release benchmarked against manual sampling.

Results

The 2 L perfusion process reached ~3.0 × 10^7 cells/mL in 7 days, yielding 49.7 ± 3.2 × 10^9 viable cells (~113 therapeutic doses at 34% CAR-positive). Performance and quality matched the 250 mL scale-down model. Perfusion STRs achieved ~34% greater expansion than static culture while maintaining >90% viability and favorable metabolic profiles. Real-time capacitance correlated with viable cell density (R2 = 0.98; Q2 =0.96). Automated downstream processing using Ksep 400 achieved ~91% recovery and nine-fold volume reduction without impacting phenotype, cytotoxicity, cytokine secretion, or exhaustion, yielding products with balanced CD4:CD8 ratios and enriched naive and central memory CD8-positive cells.

Conclusion

A 7-day, multi-litre perfusion STR workflow incorporating predictive scale-down models, real-time capacitance analytics, and automated harvest consistently produced more than 100 CAR-T doses per batch while preserving critical quality attributes. This integrated approach provides a practical path to scalable, cost-efficient, and clinically relevant manufacturing aligned with the needs of allogeneic CAR-T programs.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

ENGINEERING NEXT-GENERATION BCMA-TARGETED CAR-T CELLS USING IN SILICO–DESIGNED DE NOVO BINDERS FOR MULTIPLE MYELOMA IMMUNOTHERAPY

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KEYWORDS: in silico design of *de novo* binders.

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Background & Aim

Background

B-cell maturation antigen (BCMA)-targeted chimeric antigen receptor T-cell (CAR-T) therapies have shown strong clinical efficacy in relapsed/refractory multiple myeloma, leading to two approved products. Despite high initial response rates, durable remissions remain a significant challenge and most patients relapse through mechanisms unrelated to antigen loss. These observations highlight the importance of optimizing antigen recognition and CAR functionality to improve therapeutic durability. We therefore sought to identify

and engineer high-performance BCMA binders through an integrated workflow combining functional screening, structural modelling, and developability-guided optimization.

Methods, Results & Conclusion

Methods

Hybridoma clones were screened using a BCMA-blocking assay to identify functionally engaging antibodies. Structural docking and protein visualization were then used to characterize predicted single-chain variable fragments-BCMA interactions, focusing on ionic contacts and binding geometry.

Results

Screening of 11 BCMA CAR constructs identified murine GB9 as the lead candidate based on superior cytotoxicity across all effector-to-target ratios tested. Humanization of GB9 reduced tumor-killing activity. Structural docking analyses revealed differences in predicted binding interactions and electrostatic complementarity between murine and humanized variants likely impairing BCMA engagement. Targeted amino acid substitutions, from developability analyses, were then introduced into the humanized framework to address these issues, successfully restoring cytotoxic function comparable to a benchmark BCMA CAR control levels while retaining the benefits of a humanized format.

Conclusions

Our findings demonstrate that framework-dependent changes can significantly impair CAR performance after humanization but are addressable through rational engineering. The optimized BCMA binders represent strong candidates for next-generation CAR-T approaches, including dual-target BCMA/CD19 platforms, with the potential to improve tumor coverage and durability of response.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

TOWARDS A UNIVERSAL LIPID NANOPARTICLE (LNP) PLATFORM FOR MULTIPLEX ENGINEERING OF NEXT-GENERATION EX VIVO CELL THERAPIES

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KEYWORDS: DNA delivery, LNPs , T-cells.

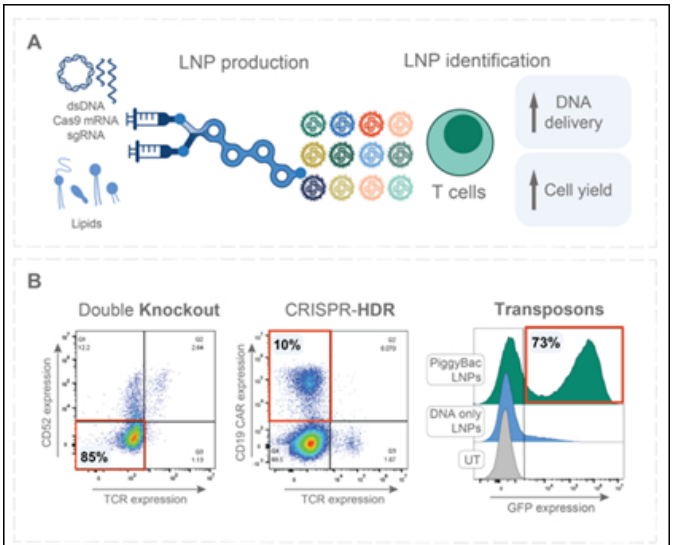
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Background & Aim

Ex vivo cell therapies for solid tumors could require multiplex genetic engineering to improve function within the tumor microenvironment. Allogeneic therapies need simultaneous chimeric antigen receptor (CAR) expression and removal of genes coding for proteins associated with graft-versus-host disease. In principle, these gene modifications can be achieved through the co-delivery of multiple nucleic acid types. In practice, however, safe and efficient delivery, particularly when targeting multiple genes, remains challenging with conventional viral vectors or electroporation (EP).

Methods, Results & Conclusion

Here, we report progress toward developing an LNP platform for RNA and DNA delivery to primary T cells. LNPs were produced using NxGen™ mixing technology. LNP physical characteristics were measured by dynamic light scattering and RiboGreen assay. For gene knockout studies, Cas9 mRNA and sgRNA were encapsulated. For homology-directed repair (HDR), a DNA template was included. For transposon gene integration, a piggyBac transposase mRNA and DNA transposon were encapsulated. Primary T cells were transfected with LNPs at the defined timepoints and doses. Gene knockout, gene expression, viability, cell yield, and cell killing were measured using flow cytometry.
More than 100 LNP formulations containing different novel ionizable lipids, stabilizers, and lipid molar ratios were screened. Lead candidates were selected based on LNP physical characteristics and T cell performance and further evaluated using CRISPR-mediated gene knockouts, with leads showing > 90% TCR knockout and 90% TCR and CD52 double knockouts. Next, lead LNPs were used to insert both small and large genes using CRISPR HDR and transposons, resulting in >30% HA tag integration at *CD5* and > 10% CAR integration at *TRAC*. CAR+ T cells demonstrated high *in vitro* killing > 80% of leukemia cells at a 1:1 effector-to-target ratio. Using transposons, LNPs enabled > 60% GFP integration. Cell viability and proliferation remained high across all experiments and exceeded EP in benchmark experiments.
These results show that LNPs enable the delivery of diverse nucleic acid types and sizes to primary T cells through a simple, one-step cell culture protocol, while maintaining high efficiency and cell yield. This capability supports flexible multiplex engineering strategies, including simultaneous or temporally separated gene modifications, and advances the development of solid tumor and allogenic T cell therapies.



Screening of LNP formulations for T cell DNA delivery. **(A)** LNP libraries carrying both DNA and RNA cargo were screened in primary T cells to identify formulations that maximize DNA delivery and cell yield (HDR+ T cells). **(B)** Representative flow cytometry readouts quantifying functional editing outcomes, including double knockout (TCR–/CD52–), CRISPR-HDR (CD19 CAR), and transposon-mediated (GFP) integration.

Figure 1. Screening of LNP formulations for T cell DNA delivery

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

FROM BLOOD TO TREG THERAPY IN 10 DAYS: THE NEXT-GENERATION TREG MANUFACTURING

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KEYWORDS: Treg, blood, dynacellect.

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Background & Aim

Treg cell therapy is rapidly emerging as a promising treatment for autoimmune diseases, inflammatory disorders, and transplant rejection. Despite its therapeutic potential, widespread clinical adoption has been hindered by significant manufacturing challenges. These include variability in leukapheresis derived starting material, non-standardized isolation of rare target populations, difficulties achieving therapeutic doses, contamination with unwanted cell types, and prolonged culture periods that increase the risk of phenotypic drift. As a result, Treg manufacturing remains highly inconsistent across the field.
At our centre, conventional Treg manufacturing process begins with a 500 mL blood collection, followed by PBMC isolation using CTS Rotea counterflow centrifugation system. $CD25^+$ cells are then enriched on CliniMACS Prodigy, followed by $CD4^+$ CD127low cell sorting using MACSQuant Tyto platform. Purified Tregs are subsequently activated, engineered, and expanded over 21 days to achieve therapeutic dose. This workflow requires >12h of initial sample processing and three weeks manufacturing, creating substantial cost and operational burden.

Methods, Results & Conclusion

To address these limitations, we developed an advanced Treg manufacturing workflow that is faster, simpler and more scalable. Following a 500 mL blood collection completed in just 15mins, $CD4^+$ cells are directly enriched using CTS DynaCellect platform. This step consistently achieves >90% recovery, >97% viability, and ~99% purity. Subsequent $CD25^+$ and/or $CD127^-$ magnetic bead selection eliminates the need for cell sorting and the associated cellular stress. The isolated Tregs undergo brief activation, genetic engineering and expansion, reaching therapeutic dose within 10 days. The final product consistently achieves >600 fold expansion, >90% viability, >95% $CD4^+CD25^+CD127$low purity, and >80% $FoxP3^+$. Overall sample processing time is <8h, while manufacturing time has been shortened to just 10 days, with the potential for increased dose by extending culture to 14 days.
Using fresh blood alleviates pressure on leukapheresis services, simplifies logistics, improves starting material quality and significantly lowers manufacturing costs. Eliminating cell sorting enhances cell viability, while shortened culture minimizes phenotypic drift, driving better therapeutic outcome. Together, these advances redefine Treg manufacturing and provide a practical, standardized pathway to expand patient access to Treg-based therapies.

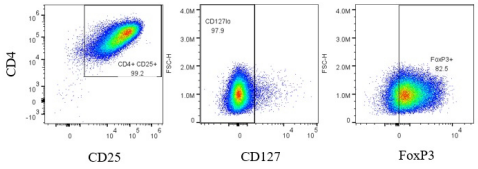


Figure A: Healthy donor HC134 Treg phenotype processed from fresh blood post expansion achieving >95% $CD4^+$ $CD25^+$ $CD127^{low}$ and >80% $FoxP3^+$ on flow cytometry analysis.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

NEXT-GEN CHEMICALLY DEFINED SOLUTION TO REPLACE SERUM IN T CELL MANUFACTURING

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KEYWORDS: Chemically defined ingredients, Serum alternative, Immune cells.

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Background & Aim

T cell expansion in T cell immunotherapy manufacturing traditionally relies on human AB serum to support proliferation and functional performance. However, the use of human serum is associated with challenges including batch variability, supply limitations, high cost, and potential risks associated with human-derived components. In recent years, increasingly stringent regulatory expectations have driven a shift towards chemically defined (CD), xenofree cell culture ingredients to improve consistency and safety. To address the unmet need for serum alternatives with lower risk profile, we developed and optimized a formulation composed of recombinant proteins and other CD ingredients.

Methods, Results & Conclusion

Methods

We tested combinations of recombinant proteins and chemically defined (CD) additives to derive CD formulations that can replace serum in human cell culture. A prototype formulation (CDSA-T) was further optimized as a drop-in replacement for human AB serum. This supplement is designed to be a 1:1 replacement of human AB serum and can be integrated seamlessly into existing cell culture or manufacturing workflow without major process redesign. CDSA-T performance was evaluated in commercial T cell media using primary human T cells from multiple healthy human donors, with assessments focused on cell expansion, cell viability and phenotype distribution.

Results

CDSA-T supplementation enhanced T cell expansion by 3.5 fold at day 10 of *in vitro* culture, when compared to media supplemented with 5% human AB serum. This translates into a shorter culture period required to reach the desired T cell dose for cell therapy. Cell viability remained consistently high, exceeding 90% throughout the culture period. Notably, CDSA-T also promoted a more favorable phenotype, doubling the total number of naïve T cells compared to serum supplementation.

Conclusion

Our prototype CDSA-T formulation has been demonstrated to be a robust alternative to human AB serum in the culture of T-cells. Besides boosting cell proliferation, CDSA-T improves the consistency, scalability, and regulatory compliance in T cell manufacturing. This approach can improve consistency in cell therapy production. Our serum alternative may also be applicable to other immune cell types that require human serum for cell expansion, significantly aiding in addressing regulatory challenges associated with the use of human-derived materials in cell therapy production.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

FEASIBILITY OF AUTOMATED GMP MANUFACTURING OF TUMOR-REACTIVE T CELLS FROM ANTIGEN-NAÏVE HEALTHY DONOR AND TRANSPLANT RECIPIENTS

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KEYWORDS: Tumor Reactive T Cells, Prodigy, GREX.

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Background & Aim

Tumor-reactive T cells (TRT) have demonstrated clinical efficacy in hematologic malignancies and solid tumors, but conventional manufacturing relies on labor-intensive, manual processes performed in high-grade GMP facilities. Automated closed GMP-compliant platforms may improve scalability and inter-institutional adoption. We evaluated the feasibility of producing clinical-grade TRT using the CliniMACS Prodigy system, with optional expansion in a closed GREX-CS device to maximize throughput and minimize clean-room dependence.

Methods, Results & Conclusion

For full-scale GMP validation, leukapheresis products from healthy antigen-naïve donors (n = 3; 0.6–1.3e9 mononuclear cells [MNC]) were stimulated for 36–40h with peptide pools targeting PRAME, Survivin, and WT1 in the presence of CD28 costimulation. Activated CD137+ T cells were enriched by immunomagnetic selection and expanded using irradiated feeder cells,

high-dose IL-2, and CD3 stimulation. To assess feasibility using engrafted T cells and to validate GREX expansion, 100 mL of peripheral blood from an allogeneic umbilical cord blood transplant recipient was processed at 1:10 scale (1.0e8 starting MNC) using manual enrichment and closed-system GREX 10M-CS expansion.
Initial stimulation activated 2.41–10.58% viable CD3+ cells (vCD3). Prodigy-based CD137+enrichment yielded 0.33–6.01e6 vCD3 (21.2–79.5% efficiency), which expanded to 81.9–1,963e6 vCD3 within 10–12 days. Manual enrichment from 1.0e8 MNC yielded 0.29e6 CD137+ vCD3 (4.7% efficiency) which were expanded in GREX to 20.4e6 vCD3 over 14 days.
All final products met predefined release criteria, including sterility, endotoxin, and mycoplasma testing, and demonstrated antigen-specific functional activity. Cytokine secretion and activation marker expression exceeded background controls for both CD4+ and CD8+ subsets: CD4+ T cells showed IFN-γ (2.46–7.79 vs 0.16–0.19), TNF-α (9.47–28.57 vs 0.43–1.74), CD137 (8.32–25.03 vs 0.41–0.54), and CD154 (6.95–28.36 vs 0.97–1.90), while CD8+ T cells demonstrated IFN-γ (1.18–23.58 vs 0.06–0.24), TNF-α (0.65–26.12 vs 0.39–1.55), and CD137 (11.89–43.62 vs 3.29–18.71). Notably, TRT products manufactured by this method were also enriched for γδ T cells (31.59 – 42.11% of CD3+ cells). We produced clinical-grade TRT from both antigen-naïve donors and allogeneic transplant recipients using Prodigy platform with optional GREX expansion in unrated laboratory space, supporting scalable and decentralized manufacturing.

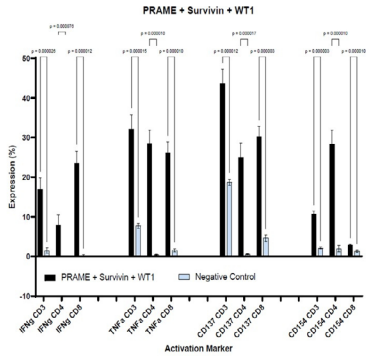


Figure 1. Expression of activation markers (IFNg, TNFa, CD137, CD154) in CD3, CD4 and CD8 populations of expanded TRT following in-vitro re-stimulation with mixed tumor-associated peptide pools (PRAME, Survivin, WT1 PepTivators®). Negative control was performed with media only (no PepTivators® added). Data shown reflects testing of the final product of one representative TRT manufacturing run, performed in 9 replicates. Unpaired t test with Welch correction, bar graphs denote the mean +/- SD.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

HIGH-THROUGHPUT COMBINATORIAL SCREENING IDENTIFIES NOVEL TRANSCRIPTION FACTOR COCKTAILS FOR THE DIRECT REPROGRAMMING OF IPSCS TO NATURAL KILLER CELLS

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KEYWORDS: Direct Reprogramming, NK cells, Transcription Factor.

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Background & Aim

A major bottleneck in the clinical translation of induced pluripotent stem cell (iPSC)-derived Natural Killer (NK) cells as "off-the-shelf" immunotherapies is the complex, multi-stage directed differentiation protocols that require up to 40 days, rely on expensive cytokines, and often yield cells lacking critical functional receptors like CD16. To address these manufacturing constraints, we developed a streamlined 26-day production platform driven by a synergy of transcription factor (TF) expression and targeted cytokine signalling.

Methods, Results & Conclusion

For this purpose, we executed a combinatorial screen of 20 candidate NK-specific TFs utilizing the CombiCult platform to identify novel synergistic TF networks capable of optimizing and accelerating NK cell fate commitment. Bulk culture validation successfully identified multiple novel 3-TF combinations capable of driving the direct reprogramming of iPSCs to CD45+CD56+ NK cells (repNK cells). Notably, these repNK cells exhibit robust expansion and a mature phenotypic profile, including the expression of NKp30, NKp44, NKp46, and NKG2D. Crucially, we observed significant expression of the mature marker CD16 by Day 26, which remains remarkably low or absent even at later endpoints in standard differentiation protocols. *In vitro* functional assays further confirmed that repNK cells possess potent cytotoxicity against tumor targets. We conclude that by leveraging a high-throughput screening approach, we condensed the manufacturing timeline by nearly 35% compared to conventional methods, thus providing a superior, highly scalable platform for next-generation allogeneic cell therapies.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

A DEFINED SERUM-FREE SUPPLEMENT ENABLES ROBUST FEEDER-FREE EXPANSION OF FUNCTIONAL NK CELLS

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KEYWORDS: NK cells, Manufacturing, Immunotherapy.

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Background & Aim

Natural killer (NK) cells continue to be a promising immunotherapy with numerous clinical trials demonstrating favorable safety profiles and encouraging efficacy, particularly in hematologic malignancies such as acute leukemia. Chimeric antigen receptor -engineered NK (CAR-NK) cells are further advancing NK cell immunotherapy as a potential "off the shelf" option. Recent technical advances including improved ex-vivo NK cell expansions systems, more efficient genetic engineering and advanced CAR designed optimized for NK Cell signal transduction have improved the scalability and potency of the NK cell products.
Despite these advances, several manufacturing challenges remain. Many NK cell culture systems require the use of human AB (hAB) serum for robust expansion and functionality. However, hAB serum poses many challenges including undefined composition, lot to lot variability, regulatory and safety concerns related to adventitious agents, and supply chain constraints.

Methods, Results & Conclusion

Here we describe a serum free supplement specifically developed for feeder- free NK cell expansion that maintains superior NK cells expansion, phenotype and function. With the NK Cell Serum Replacement, T cell depleted cultures can be expanded to >150-fold in two weeks. These expanded NK cells maintain high activation marker expression, such as DNAM-1, CD16, and NKG2D and express low levels of inhibitory markers PD-1 and CD158. Importantly, these NK cells remained functionally active, with robust IFN-g production and demonstrating efficient cytotoxicity against K562 target cells within a two-hour period. These results support the use of a defined, serum-free supplement as a scalable and reproducible alternative for hAB serum for NK cell manufacturing, enabling consistent expansion of highly functional NK cells suitable for immunotherapy applications.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

SYSTEMS BIOLOGY ANALYSIS OF ONCOLYTIC VIRUS-MEDIATED TUMOR PRIMING FOR CAR NK THERAPY IN HEAD AND NECK CANCER

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KEYWORDS: Oncolytic virotherapy, Head and Neck Cancer , CAR NK.

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Background & Aim

Limited immune cell trafficking and an immunosuppressive tumor microenvironment remain major barriers to CAR-NK efficacy in solid tumors. Oncolytic virotherapy (OIVT) has the potential to remodel the tumor microenvironment and enhance susceptibility to adoptive cellular therapies. This research is aimed at identifying molecular pathways and immune signatures induced by OIVT that may promote CAR-NK cell recruitment, activation, and anti-tumor activity in Head and Neck Squamous Cell Carcinoma (HNSCC).

Methods, Results & Conclusion

Transcriptomic datasets from OIVT-treated tumors and public HNSCC cohorts were analyzed using an integrated systems biology approach. Differential expression and pathway enrichment analyses (GO, KEGG, Reactome) identified OIVT-induced molecular changes. Immune-cell composition was inferred through computational deconvolution, while cytokine/chemokine and protein–protein interaction networks were used to identify pathways and key regulators associated with immune recruitment, NK-cell activation, and tumor susceptibility. A CAR-NK permissiveness signature was developed incorporating genes involved in chemokine-mediated trafficking (CXCL9, CXCL10, CXCL11, CCL5), antigen presentation (HLA-I, B2M, TAP1/2), interferon signaling, and NK-cell activating ligands. In silico analyses predicted enrichment of interferon-related inflammatory pathways, antigen processing and presentation machinery, and chemokine networks involved in lymphocyte trafficking following oncolytic virus exposure. Network analysis identified IFNγ, STAT1, IRF1, CXCL10, and CCL5 as key regulatory nodes potentially linking viral infection with immune activation. Computational immune deconvolution further suggested increased abundance of cytotoxic lymphocytes and NK cells in OIVT-associated transcriptomic profiles. Integration of pathway

activity scores with a CAR-NK permissiveness signature revealed a predicted increase in tumor immunogenicity, characterized by enhanced chemokine signaling, antigen presentation, and interferon responses. Collectively, these in silico findings suggest that OIVT may promote a more immune-inflamed tumor microenvironment through activation of interferon signaling, antigen presentation pathways, and immune-cell trafficking networks. The identified regulatory hubs and predictive biomarkers can provide mechanistic insights into potential OIVT-mediated enhancement of CAR-NK therapy and may support the rational design of future translational and experimental studies in Head and Neck Cancer.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

SCALABLE PROCESS DEVELOPMENT FOR GMP-COMPLIANT MANUFACTURING OF CORD BLOOD-DERIVED CAR GAMMA DELTA (ΓΔ) T CELLS VIA DESIGN OF EXPERIMENT (DOE) OPTIMIZATION

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KEYWORDS: CAR γδ T cells, Process Development, Scalable GMP Manufacturing.

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Background & Aim

CAR gamma delta (γδ) T cells derived from umbilical cord blood represent a promising off-the-shelf platform for cancer immunotherapy, but their clinical translation depends on robust, scalable and GMP-compliant manufacturing. Here, we describe scalable process development for GMP manufacturing of cord blood-derived CAR γδ T cells. We focused on two critical components of the manufacturing workflow: (i) generation of irradiated feeder cell banks required to support γδ T-cell expansion, and (ii) optimization of the CAR-γδT manufacturing process.
Across both components, our key approach was to apply Design of Experiment (DoE) methodology to optimize critical process parameters in a scale-down model, followed by at-scale studies to validate the optimal process parameters under manufacturing-relevant conditions. For irradiated feeder cell bank generation, DoE was applied in the scale-down GREX cell culture platform to optimize parameters such as seeding density, media replenishment and culture duration, maximizing critical quality attributes (CQA) including expansion-fold, peak cell density and viability.

Methods, Results & Conclusion

Feeder cells cultured under DoE-optimized conditions consistently displayed superior CQA, achieving peak cell culture concentration of >1×10^7 cells/cm^2 with over 87% cell viability. Subsequent at-scale runs in GREX100M and GREX500M confirmed the validity of the DoE model and demonstrated the robustness and scalability of the approach resulting in 1380.7 ± 230 cumulative fold-expansion. The expanded feeder cells were then irradiated and cryopreserved as a cGMP working cell bank (WCB) using controlled-rate freezers.
For CAR-γδT manufacturing, DoE was likewise employed in a scale-down model to optimize key process parameters, including culture media, the aAPC (irradiated feeder) ratio and cytokine concentration, among others, with the optimal parameters subsequently validated in at-scale studies. Together, this DoE-driven, scale-down-to-at-scale strategy provides an accelerated and reproducible route to a scalable, GMP-compliant process for manufacturing cord blood-derived CAR γδ T cells to support clinical application.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

TARGETED USE OF ANTI–CD19 AND ANTI–CD22 CAR–T CELL PRODUCTS FOR DUAL–ANTIGEN TARGETING IN B–ALL: A FEASIBLE AND COST–EFFICIENT STRATEGY FROM THE ALACART TRIAL

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KEYWORDS: CAR-T cells, B-ALL.

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Background & Aim

Anti–CD19 CAR–T cells have revolutionized the treatment of ALL but in some patients a fraction of leukemic cells do not express CD19. The approach of ALACART (NCT05038696) is to identify these patients prior to CAR–T cell therapy and supplement anti–CD19 CAR–T cells with anti–CD22 CAR–T cells if the CD19negative leukemic cells also express CD22.

In this study, we assessed the cost-effectiveness of this targeted approach to the use of CAR–T cell specificities.

Methods, Results & Conclusion

Methods

All CAR–T products were manufactured from autologous leukapheresis using identical protocols within a Biospherix isolator in a GMP–certified Grade D facility. If anti–CD19 and anti–CD22 CAR–T cells are indicated, both products were produced in parallel, except for one patient due to logistical considerations. Manufacturing data were analyzed retrospectively from batch and inventory records. Cost analysis included comparison with a theoretical non–targeted manufacturing approach in which all patients would have received both CAR–T products.

Results

Forty–one pediatric patients (median weight 31.1 kg; range 10–85 kg) were treated: 32 received anti–CD19 CAR–T cells alone, and 9 received both anti–CD19 and anti–CD22 CAR–T cell products. All 50 CAR–T products manufactured between July 2017 and August 2025 met release and dose specifications. With the ALaCART approach, substantial cost savings were achieved as compared with a theoretical non–targeted model in which all patients would receive both CAR–T cells. The median manufacturing cost per patient was USD 38,851 in the ALaCART approach versus USD 71,068.69 for 2 CAR–T cell products. Based on median per–patient values, the total projected cost would be USD 2.84M for a non–targeted approach as compared to the real–world actual total cost of USD 1.78M, representing cost savings of USD 1.06M.
Operational efficiencies paralleled the cost savings, with lower isolator utilization (10.5 vs 15.1 h), total processing time (12.5 vs 19 h), manpower (28 vs 33 man units), and labor time (331.7 vs 362.8 man–hours).

Conclusion

Overall, the targeted ALaCART manufacturing model achieved substantial cost reductions while maintaining product quality, demonstrating a practical, and cost–efficient strategy for dual–antigen CAR–T cell therapy in B–ALL.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

MAPPING THE MULTIPLE MYELOMA MICROENVIRONMENT: STAGE-SPECIFIC IMMUNE DYSREGULATION AS A BLUEPRINT FOR CELLULAR THERAPY

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KEYWORDS: Multiple Myeloma, Tumor Microenvironment, Nk Cells.

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Background & Aim

Multiple myeloma (MM) is an incurable hematological malignancy characterized by clonal plasma cell proliferation within the bone marrow. The tumor microenvironment (TME) plays a crucial role in immune evasion and disease progression by suppressing anti-tumor immunity and supporting tumor growth. Understanding immune cell dynamics across different disease states is essential to identifying therapeutic vulnerabilities and developing effective immunotherapies. This study aims to comprehensively profile the distribution of immune cell subsets in healthy controls (HC), newly diagnosed multiple myeloma (NDMM), and relapsed/refractory multiple myeloma (RRMM) to unravel the stage-specific immunological landscape alterations associated with MM progression.

Methods, Results & Conclusion

Methods

Single-cell RNA sequencing (scRNA-seq) and multi-parametric flow cytometry were employed to analyze immune cell subsets across HC, NDMM, and RRMM cohorts. Immune cell proportions were normalized to allow for comparative analysis across conditions. Additionally, multi-parametric flow cytometry was utilized to validate the findings obtained from scRNA-seq, ensuring robust, reliable, and reproducible characterization of immune cell distributions within the bone marrow TME.

Results

NDMM samples exhibited significant immune cell deficits compared to HC, including a dramatic reduction in dendritic cells (0.71% vs. 2.47%), T_CD4_memory cells (5.03% vs. 11.49%), and classical monocytes (9.22% vs. 14.32%). B cells, in contrast, were markedly elevated in NDMM (56.78% vs. 18.94% in HC), reflecting a potential adaptive or pathological

response. RRMM showed partial restoration of dendritic cells (4.96%) and classical monocytes (22.61%), highlighting immune reprogramming during disease progression.

Conclusion

The immune microenvironment in MM evolves dynamically, with distinct deficits in NDMM and partial recovery in RRMM. The observed loss of dendritic cells and T_CD4_memory subsets underscores the importance of targeting these populations to restore immune balance. This study provides a foundation for developing immunotherapies aimed at reprogramming the tumor microenvironment in MM.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

EVALUATION OF THE CYTOTOXIC EFFECT OF ANTI-BSMA CAR-NK CELLS OF UMBILICAL CORD BLOOD IN VITRO

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KEYWORDS: Car-nk, Cord blood, Cytotoxic

1. SanGMU, Samara, Russian Federation.

Background & Aim

This work was carried out as part of a research and development contract with JSC Firma Evroservis, research and development contract No. 55n/2024 dated March 25, 2024.
The aim of the study was to investigate the cytotoxicproperties of a new genetic construct of anti-BSMA CAR-NK cells in vitro to assess the cellular product.

Methods, Results & Conclusion

Material and methods

Whole umbilical cord blood from donors was used as a source of NK cells. The mononuclear cell fraction was isolated from cord blood using the standard method of density gradient separation of Ficoll. The ability of the obtained anti-BCMA CAR-NK cells to eliminate RPMI 8226 (target cells of the human myeloma line) was evaluated using flow cytometry on a CELLRIVER (Labvision, Russia) using antibodies against CD 269 and 7-AAD.
The purified NK cells were transduced with a lentiviralvector encoding the TurboGFP variant of the baboon virus (BaEV) pseudotype. NK-cells were cultured without the use of feeder cells on NK MACS Medium, human (Miltenyi Biotec, Germany), in 6-well plates. To obtain BaEV-LV – vector, pre-transfection of HEK 293 cells line with three plasmids. RPMI8226 culture cells (target cells) were cultured with CAR-NK cells (effector cells), non-transduced NK cells (control cells) in a 1:1 ratio in 12- and 24-well plates for 2 days in 10 independent experiments. Untransduced NK cells were used as a control group to assess non-specific effects in the same ratios as CAR-NK cells.

Results

The viability of CD269+ RPMI 8226 target cells decreased to 53.86±2.58% (50.42-58.66), after 24 hours to 30.6±4.05% (23.11-35.88), and after 48 hours to 1.99±0.98% (1.01-3.8). At the same time, the untransduced cells used as a non-specific control did not have a cytotoxic effect on CD296+ RPMI8226 and, when co-cultured in the same ratios, the viability of 7-AAD practically did not change and was 12 hours later. 97,05±1,19% (95,43-99,20), after 24 hours, 97.05±1.56% (94.13-99.01), and after 48 hours 94,01±2,36% (89,1-97,16).

Conclusions

The cytotoxicity tests showed that the anti-BCMA CAR-NK cells eliminated BCMA-positive RPMI-8226 cells within 48 hours at an E:T ratio of 1:1.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

REMODELING OF THE INTESTINAL CELLULAR LANDSCAPE IN A MULTI-DRUG REFRACTORY ULCERATIVE COLITIS PATIENT WITH SUSTAINED REMISSION UPON CD19-DIRECTED CAR T-CELL THERAPY

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KEYWORDS: CAR T-cells, Ulcerative Colitis, CAR-T.

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9. Miltenyi Biotec, Bergisch Gladbach, Germany.

Background & Aim

CD19-directed Chimeric Antigen Receptor (CAR) T-cell therapy has revolutionized the treatment of relapsed/refractory hematological malignancies and is now increasingly demonstrating efficacy in B-cell mediated autoimmune diseases. Recent studies have suggested that dysregulated B cells and plasmablasts are involved in the pathogenesis of ulcerative colitis (UC). We have treated a patient with severe, multidrug-resistant UC with in-house manufactured CAR T cells, resulting in clinical and endoscopic remission (Müller et al., NEJM 2025). Herein, we report on the longitudinal impact of CAR T-cell therapy on the peripheral and mucosal cell composition in the drug-free, remittent patient over an extended follow-up time.

Methods, Results & Conclusion

Methods

Blood samples and colonic mucosa biopsies were collected at multiple time points and analyzed using high-dimensional flow cytometry and single-cell RNA sequencing. In addition, structural changes in the mucosal landscape were validated by spatial imaging.

Results

CAR T-cell therapy induced rapid clinical, biochemical and histological remission, which was sustained throughout a drug-free follow-up period of 14 months. CAR T cells peaked at 350 cells/µl on day +10, followed by a contraction phase and low-level persistence over 7 months. Circulating B cells and plasmablasts were completely depleted within days and recovered 8 months after therapy, displaying an immature B-cell phenotype, indicating a full B-cell reset with new egress of early B-cell differentiation stages from the bone marrow. Spatial imaging and single-cell profiling confirmed deep and durable depletion of B cells and plasma cells in mucosal biopsies, paralleled by shifts in the T-cell and myeloid cell compartments. Moreover, epithelial cells and fibroblasts exhibited reduced inflammatory signalling, diminished leukocyte recruitment and activation of tissue remodeling and secretory pathways following CAR T-cell therapy.

Conclusion

Taken together, these findings highlight the central role of dysregulated B cells and plasmablasts in the pathogenesis of UC and provide first-in-human evidence that deep B-cell depletion induces coordinated immune and mucosal remodeling. Additional patients and longer follow-up are needed to evaluate the full therapeutic potential of CAR T-cell therapy in UC.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

AN INTEGRATED END-TO-END CAR-T MANUFACTURING WORKFLOW FOR FLEXIBLE AND STREAMLINED MANUFACTURING

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KEYWORDS: Autologous CAR-T, Manufacturing Workflow, Automation.

1. Terumo Blood and Cell Technologies, Singapore, Singapore.

Background & Aim

Background

As autologous CAR-T therapies continue to expand globally, improving manufacturing readiness and patient access is increasingly important. However, many manufacturing programs still rely on fragmented workflows involving multiple manual handoffs and labor-intensive processes from PBMC collection through final fill-and-finish. These challenges increase operational complexity, limit

process standardization, and reduce manufacturing efficiency. Modular, integrated, and automated workflow strategies provide a practical approach to improving efficiency, scalability, process consistency, and workflow streamlining while maintaining manufacturing flexibility.

Aims

To evaluate an integrated end-to-end autologous CAR-T manufacturing workflow developed by Terumo Blood and Cell Technologies (TBCT), integrating modular technologies across key steps to support flexibility, automated process control, and streamlined manufacturing while maintaining cell quality.

Methods, Results & Conclusion

Methods

Healthy donor-derived T cells were processed using a TBCT-designed end-to-end workflow integrating automated technologies across key CAR-T manufacturing steps, including cell collection, activation, transduction, expansion, concentration, and final formulation. Cell yield, viability, transduction efficiency, phenotype, and cytotoxic activity were evaluated using flow cytometry and functional assays.

Results

The workflow generated approximately one billion CAR-T cells within 7–9 days, achieving cell viability above 80% and transduction efficiency exceeding 40%. Expanded cells maintained high TSCM levels and demonstrated potent in vitro cytotoxic activity. The resulting cell yield is clinically relevant for many autologous CAR-T applications. The modular workflow architecture enabled flexible process configuration while reducing manual handling, streamlining workflow execution, and supporting workflow standardization.

Conclusions

This integrated end-to-end CAR-T workflow generated clinically relevant cell doses while maintaining robust cell quality and function. By combining modular workflow flexibility and automated process execution, the workflow provides a practical framework for flexible, scalable, and streamlined autologous CAR-T manufacturing, supporting broader manufacturing adoption and patient access.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

TATMYCTOFUSP (TAT-MYC) FUSION PROTEIN ENHANCES T CELL ACTIVATION, PREVENTS EXHAUSTION, AND DEMONSTRATES ANTI-TUMOR ACTIVITY ACROSS MULTIPLE SOLID TUMOR TYPES

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KEYWORDS: Tatmyctofusp, T cell exhaustion, Autologous cell therapy.

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3. NUS, Singapore, Singapore.
4. Oncofibro, Singapore, Singapore.

Background & Aim

T cell exhaustion — driven by prior chemotherapy, checkpoint inhibitor exposure, or advanced disease — remains a critical barrier to effective immunotherapy. Tatmyctofusp (Tat-MYC) is a recombinant fusion protein combining the MYC transcription factor with the HIV-1 Tat protein transduction domain, enabling receptor-independent, transient intracellular delivery into immune cells without gene editing or viral vectors. This study aimed to evaluate its capacity to enhance T cell function, prevent exhaustion, and drive anti-tumor responses in preclinical and clinical settings.

Methods, Results & Conclusion

Methods

Activated T cells were treated with tatmyctofusp and assessed for proliferation (cell count, alamarBlue assay), activation and exhaustion marker expression (CD69, CD25, TIM-3, PD-1) by flow cytometry, and transcriptomic changes by RNA-seq. In vivo efficacy was evaluated in a murine melanoma (C57BL/6) model using a single infusion of tatmyctofusp-treated cells. Clinically, autologous PBMCs treated with tatmyctofusp were administered to patients with stage IV metastatic breast cancer and standard-of-care-refractory non-small cell lung cancer (NSCLC), with tumor response assessed by imaging.

Results

Tatmyctofusp rapidly penetrated the T cell nucleus within 1–3 hours and produced significant, sustained increases in proliferation. Flow cytometry showed upregulation of CD69 and CD25 alongside reduction of TIM-3 and PD-1, indicating enhanced activation and prevention of exhaustion. RNA-seq revealed upregulation of cell cycle, DNA replication, JAK-STAT signaling, and CD8+ T cell differentiation pathways. In the melanoma model, treated mice achieved 60% long-term survival beyond 210 days versus 0% in

controls, with strong MART-1-specific CTL and antibody responses. Clinically, target lesions in the breast cancer patient decreased from 43.0 mm to 25.6 mm and 26.3 mm to 17.7 mm across two visits. The NSCLC patient showed clear shrinkage of the primary lung tumor mass following 7 doses (1E6 cells/kg).

Conclusion

These preliminary data establish tatmyctofusp as a non-genetic immunotherapeutic platform capable of improving T cell function and preventing exhaustion, with translational evidence of anti-tumor activity across multiple solid tumor types.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

HIGH CONFIDENCE TUMOR-SPECIFIC T CELLS DISCOVERY USING THE TROVO TIL ISOLATION SYSTEM

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KEYWORDS: TIL Isolation, Personalized Immunotherapy, Tumor-Specific T Cells.

1. Enrich Biosystems Inc., Branford, CT, United States.

Background & Aim

The identification of potent tumor-infiltrating lymphocyte (TIL) clones remains a critical bottleneck in the development of personalized adoptive cell therapies. Conventional screening approaches often rely on bulk phenotypic or molecular readouts, which can miss rare but highly functional T cell clones and provide limited linkage between tumor killing activity and recoverable therapeutic candidates.

Methods, Results & Conclusion

Methods

We developed TroVo, an automated, high-throughput single-cell co-culture platform for functional TIL clone discovery. Individual TILs or small TIL clusters are co-cultured with dissociated autologous or model tumor cells in programmable PEGDA hydrogel microwell arrays. The platform enables longitudinal brightfield and fluorescence imaging to quantify tumor cell loss, T cell proliferation, and dynamic T cell–tumor interactions. A normalized Z-score–based ranking workflow compares each microwell against matched control wells, allowing objective identification of wells enriched for tumor-reactive T cells. Selected microwell contents can then be selectively recovered for downstream expansion, sequencing, or validation.

Results

TroVo enables scalable functional screening across thousands to over one million microwells, supporting both short-term cytotoxicity profiling and multi-day monitoring of T cell–tumor co-culture dynamics. In proof-of-concept studies, the system identified top-performing killer T cell populations based on longitudinal tumor clearance and T cell expansion metrics. The integrated analysis workflow distinguished wells with significant functional activity from background tumor attrition, supporting prioritization of rare TIL clones with high therapeutic potential.

Conclusion

The TroVo platform provides a scalable strategy for rapid, functional, and phenotype-guided TIL clone identification and recovery. By directly linking dynamic tumor killing behavior with recoverable T cells, TroVo may accelerate the discovery of clinically relevant TIL clones for personalized cell therapy development.

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

SUSTAINED CD7 EXPRESSION CONTRIBUTES TO IMPROVED PROLIFERATION OF CORD BLOOD DERIVED NK CELL BY K562 FEEDER CELL EXPRESSING MEMBRANE BOUND IL-21

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KEYWORDS: K562 feeder cell, NK cell, CD7.

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Background & Aim

Autologous CAR-T therapy has transformed haematologic oncology but is constrained by individualised manufacturing, long production timelines, and high costs. NK cells offer a compelling alternative — innate effectors capable of eliminating malignant cells without causing graft-versus-host disease, and amenable to scalable, off-the-shelf development. However, generating large numbers of functional NK cells reproducibly and cost-effectively remains challenging. While K562-based feeder-cell systems have improved expansion, comparative data on IL-15 versus IL-21 platforms remain conflicting. This study established K562 feeder lines co-expressing CD137L with either IL-15 or IL-21, comparing their capacity to support NK-cell expansion, survival, and function from cord

blood mononuclear cells (CBMCs), while exploring phenotypic and mechanistic differences.

Methods, Results & Conclusion

Methods

K562-IL15-CD137L and K562-IL21-CD137L feeder lines were generated by retroviral transduction. NK cells were expanded ex vivo from CBMCs, with expansion efficiency, viability, and cytotoxicity evaluated. Flow cytometry characterised post-expansion immunophenotypic changes. CD7 emerged as a candidate marker of enhanced expansion and was investigated via knockdown experiments in the IL-21 platform.

Results

Both feeder lines supported robust NK-cell expansion. The IL-21-based system produced superior proliferation, survival, and cytotoxic activity against tumour targets. IL-21-expanded NK cells better maintained expression of CD7, CD57, CD25, CD71, CD54, CD62L, and NKG2A, while CD69, TIGIT, and CD70 declined more rapidly than in IL-15-expanded cells. CD7 knockdown significantly impaired expansion in the IL-21 system, implicating CD7 in mediating IL-21-driven proliferative capacity.

Conclusions

K562-IL21-CD137L feeder cells outperform their IL-15 counterparts in supporting NK-cell proliferation, survival, and cytotoxic function. Sustained CD7 expression appears mechanistically linked to IL-21-driven NK-cell fitness. These findings support IL-21-based platforms for large-scale NK-cell manufacturing and advance the clinical translation of next-generation NK-cell therapies.

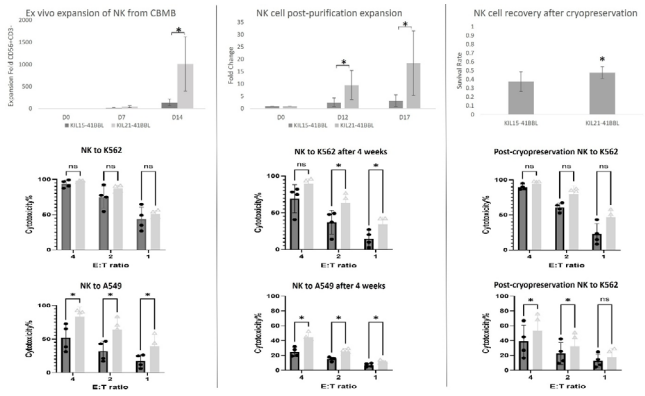


Figure 1. IL21-feeder-NK cell shows superior proliferation, survival, cytotoxicity and post-cryopreservation recovery than IL15-feeder-NK

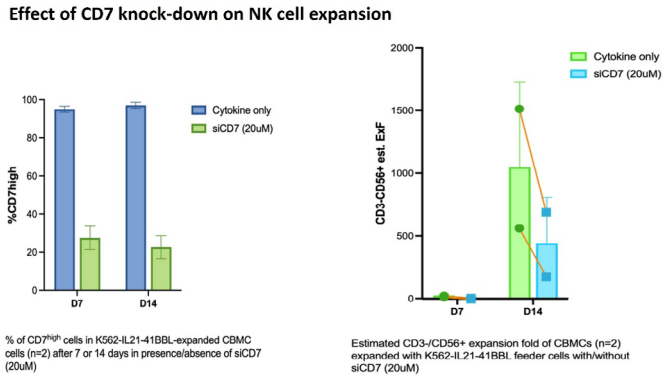


Figure 2. CD7 knock-down impairs IL21-feeder-NK cell expansion

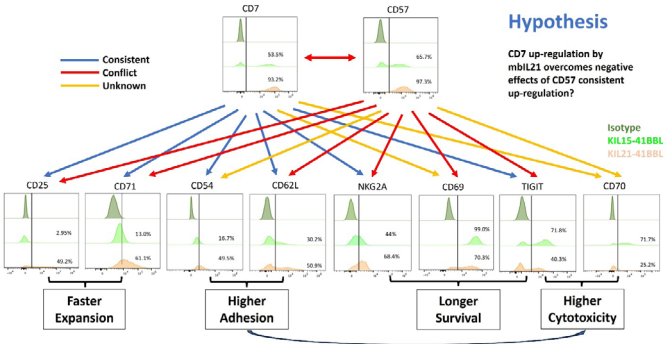


Figure 3. Summary of hypothesis

Table 1: NK cell surface marker panel

Classification	Marker	Classification	Marker
Activating Receptor	CD27	Cytokine Receptor	CD25
	CD253		CD122
	CD16		CD132
	CD226		CD215
	CD314		CD71
	CD159c	Maturation Marker	CD7
	CD69		CD57
Activating and Inhibitory Receptor	CD70	Identity Marker	CD3
			CD56
Inhibitory Receptor	CD279	Adhesion Marker	CD62L
	CD159a		CD54
	CD366		LFA-1
	TIGIT		CD2

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Immunotherapy (CAR-T, T Reg, NK Cells etc.)

EFFICIENT CD3 DEPLETION USING MAGNETIC BEADS TO ENHANCE ROBUSTNESS AND FLEXIBILITY IN T CELL MANUFACTURING

E. R. Zynda[1]

KEYWORDS: Allogeneic, T cell depletion, automation.

1. Cell Therapy, Thermo Fisher Scientific, Grand Island, NY, United States.

Background & Aim

Chimeric antigen receptor (CAR) T cell therapies have demonstrated remarkable clinical efficacy; however, their manufacturing remains complex, especially in the context of allogeneic workflows that require the removal of cells expressing endogenous T cell receptors. Here, we present a new magnetic bead–based CD3 depletion technology designed to enable efficient and scalable removal of CD3+ cells, supporting robust and flexible allogeneic CAR T cell manufacturing workflows. The Gibco Dynabeads CD3 Depletion Prototype beads leverage high-affinity antibodies conjugated to (para)magnetic Dynabeads beads to support a rapid and reproducible depletion of CD3+ cells across a range of input cell compositions.

Methods, Results & Conclusion

Performance was evaluated using healthy donor leukapheresis material, assessing depletion efficiency, cell recovery and viability. The Gibco Dynabeads CD3 Depletion Prototype beads enabled consistent and effective CD3 depletion while maintaining high viability and recovery of target cell populations. The technology is compatible with the Gibco CTS DynaCellect Magnetic Separation System for closed and automated manufacturing, aligning with current Good Manufacturing Practice (cGMP) requirements and scalable production needs. In summary, this new CD3 depletion bead technology provides a robust tool for cell processing in allogeneic CAR T cell manufacturing. By enabling efficient removal of CD3+ cells the Gibco Dynabeads CD3 Depletion Prototype supports enhanced process control, flexibility, and scalability, addressing key challenges in the manufacture of next-generation cell therapies.

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iPSC

ESTABLISHMENT OF A GMP-COMPLIANT PROCESS FOR MULTI-ETHNIC ASIAN INDUCED PLURIPOTENT STEM CELL BANKING FOR FUTURE CELL THERAPY APPLICATIONS

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KEYWORDS: Cell Therapy, Induced Pluripotent Stem Cells, Biobanking.

1. BetaLife Pte Ltd, Singapore, Singapore.

Background & Aim

Human induced pluripotent stem cells (hiPSCs) are an invaluable resource for biomedical research for drug development, disease modelling and cell therapy. Development of a centralised hiPSC reserve provides access to diverse high quality hiPSC lines, for research applications and informed selection of cell lines for allogenic cell-based therapies. The current iPSC repositories predominantly consist of cell lines with Caucasian or Japanese ancestry, with a limited representation of Asian ethnicities which impacts the translational relevance across Asian populations. Here, we aim to establish a well characterised multi-ethnic Asian iPSC biobank composed of healthy and disease-affected donors under a GMP-controlled environment.

Methods, Results & Conclusion

Peripheral blood mononuclear cells (PBMCs) were collected with informed consent from multi-ethnic donors (Chinese, Indian, and African). PBMCs were reprogrammed using a non-integrating Sendai virus-based reprogramming and clonally selected in GMP-compatible culture conditions. Resultant hiPSC lines were evaluated for safety, pluripotency, genomic integrity, and clearance of reprogramming vectors. Furthermore, selected cell lines were used to develop end products from multiple lineages such as iPSC-derived mesenchymal stem cells (iMSCs) and iPSC-derived islets. The entire process of hiPSC derivation and differentiation to iMSCs was conducted under xeno-free, feeder-free culture conditions in a Grade A+B cleanroom facility under a quality management system (QMS).
We successfully generated 59 hiPSC cell lines from 15 donor-derived PBMCs. All cell lines cleared residual virus vectors from passages P11-P13. The cell lines showed positive pluripotency marker expression and were negative for microbiological and endotoxin contamination. Selected hiPSCs could be differentiated into iMSC and iPSC-islets using distinct 2D and 3D culture methods respectively. The iMSCs show plastic adherence, MSC marker expression and could differentiate towards

osteogenic lineage. The iPSC-derived islets were positive for islet markers insulin, PDX-1 and NKX-6.1 and were responsive to glucose stimulation.
We successfully established a multi-ethnic iPSC biobank comprising healthy and disease-affected donor-derived cell lines complying with GMP-readiness. The biobank supports downstream differentiation into functional and clinically-relevant cell types, demonstrating their utility in disease modelling, drug development and regenerative medicine for Asian populations.

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iPSC

FUNCTIONAL AND PHENOTYPIC COMPARISONS BETWEEN PSC-DERIVED AND PRIMARY NK CELLS

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KEYWORDS: iPSC, NK cells, Scalable.

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2. Thermo Fisher Scientific Inc, Waltham, MA, United States.

Background & Aim

The cell therapy field has expanded rapidly as a therapeutic modality. However, scalable production of functional immune effector cells remains a key limitation. Natural killer (NK) cells are cytotoxic innate lymphoid cells of interest for cancer immunotherapy due to their ability to eliminate malignant cells without HLA matching. Clinical NK cell therapies may require up to 1×10^8 NK cells per kilogram of body weight, motivating the development of renewable NK cell sources that closely resemble primary human NK cells.

Methods, Results & Conclusion

Here, we describe a directed differentiation strategy using pluripotent stem cells (PSCs) to generate induced NK (iNK) cells designed to closely resemble the phenotypic, transcriptomic, and functional properties of primary NK cells. CTS™ StemScale™ PSC culture medium enabled efficient expansion of stable, undifferentiated PSCs maintained as spheroids and served as a robust platform for downstream differentiation. PSCs were transitioned to CTS™ StemPro™-34 SFM XF for hematopoietic differentiation, followed by maturation of progenitors into functional iNK cells using a CTS™ NK-Xpander™ Medium/MEMα blend. Across multiple PSC lines, differentiation yielded approximately 10–50 iNK cells per seeded PSC.
Phenotypic characterization demonstrated comparable expression of key NK cell markers between PSC-derived iNK cells and primary NK cells. Transcriptomic profiling revealed a high degree of transcriptional concordance between PSC-derived iNK cells and primary NK cells, supporting shared NK cell identity. Functional assessment showed robust cytotoxic activity of iNK cells that was comparable to primary NK cells.
Together, these results demonstrate that PSC-derived iNK cells generated using a CTS™ StemScale™-based differentiation workflow closely resemble primary NK cells across phenotypic, transcriptomic, and cytotoxic dimensions. This work supports the potential of PSC-derived NK cells as a renewable and consistent starting material for clinically relevant NK cell therapy applications.

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iPSC

LNP-DELIVERED NEAT1 SIRNA SUPPRESSES CYTOPLASMIC TDP-43 AGGREGATION AND RESCUES MOTOR DYSFUNCTION IN ALS NEUROMUSCULAR ORGANOIDS

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KEYWORDS: iPSC, Amyotrophic lateral sclerosis , LNP-siRNA.

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Background & Aim

Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disorder marked by progressive motor neuron loss and the pathological accumulation of cytoplasmic TDP-43 inclusions. Although TDP-43 proteinopathy is a defining feature of ALS, the upstream molecular events that drive its cytoplasmic mislocalization, phase transition, and aggregation remain incompletely understood. Moreover, whether these early pathogenic processes can be therapeutically intercepted remains an important unresolved question.

Methods, Results & Conclusion

Here, we established patient-specific ALS models using induced pluripotent stem cells (iPSCs) from three individuals carrying the familial TDP-43^{M337V} mutation, alongside their isogenic gene-corrected controls. Through this platform, we identified the ALS-associated long non-coding RNA NEAT1 as a disease-relevant regulator and potential therapeutic target. In ALS iPSC-derived MNs, NEAT1 exhibited aberrant cytoplasmic accumulation rather than its expected nuclear localization. Cytoplasmic NEAT1 promoted TDP-43 condensates that preceded pathological aggregation.
To evaluate the therapeutic relevance of this mechanism, we applied lipid nanoparticle (LNP)-

formulated NEAT1 siRNA to ALS iPSC-derived MNs and neuromuscular models. NEAT1 silencing effectively reduced cytoplasmic TDP-43 pathology, preserved neuromuscular junction integrity, enhanced muscle contraction, and mitigated the progression of motor dysfunction in Neuromuscular Models.
Collectively, our findings reveal that aberrantly mislocalized cytoplasmic NEAT1 acts as an upstream driver of TDP-43 proteinopathy in ALS MNs. Therapeutic silencing of NEAT1 using LNP-delivered siRNA suppresses pathological TDP-43 aggregation, thereby protecting neuromuscular function and offering a potential RNA-targeted therapeutic strategy for ALS.

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iPSC

COMBINING GENETIC ENGINEERING AND SCALABLE PRODUCTION OF STEM CELL-DERIVED PANCREATIC ISLETS TO ENABLE ALLOGENEIC CELL REPLACEMENT THERAPY IN INSULIN-DEPENDENT DIABETES

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KEYWORDS: Pancreatic islets, hypoimmune, iPSC.

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Background & Aim

Human islet transplantation is a curative treatment for T1D patients. However, shortage of cadaveric donors and the need for immunosuppression limit its impact. Human induced pluripotent stem cell (hiPSC)-derived islets offer an off-the-shelf, on-demand, cell therapy for diabetes. Yet, to truly achieve an off-the-shelf therapy addressing a chronic disease, a scalable manufacturing system is required to produce large batches of islets consistently. hiPSC-derived islets can also be engineered to be immune tolerant to prevent the need for patients to undergo intensive immunosuppression in an allogeneic treatment.
Our study aims to generate genetically-engineered, immune-evasive hiPSC-derived islets for allogeneic cell therapy on a scalable culture platform.

Methods, Results & Conclusion

In our Asian-derived hiPSC lines, we conducted complete removal of MHC class I/II molecules through genome editing and further knocked in the expression of multiple immune modulators in proprietary genomic safe harbour sites that conferred stable and efficient expression of large payloads. We generated hiPSC-derived pancreatic islet cell clusters through a multi-step directed differentiation process using an entirely scalable 3D suspension culture-based bioreactor platform. The hiPSC-derived islets were validated in both *in vitro* and *in vivo* assessments for their functional performance.
We demonstrated successful generation of hypoimmune hiPSCs without affecting the differentiation capacity of the cells. The genome-edited hiPSCs were shown to have stable knockout of MHC molecules and targeted expression of immune cloaking factors with >80% efficiency. The immune tolerance properties of the hiPSC-derived islets were validated using *in vitro* co-culture assays with human peripheral blood mononuclear cells (PBMCs), and in immunocompetent mouse models that revealed at least 70% reduction in immune activation pathways. hiPSC-derived islets were also differentiated as 3D spheroids in a suspension bioreactor culture platform to generate functional islets expressing key islet markers (INS, GCG, PDX1, NKX6.1) with positive glucose-stimulated insulin secretion outcomes at high yield.
Overall, successful generation of hypoimmune hiPSC-derived islets, especially when combined with a fully controlled and scalable production platform, will bring us a step closer to the goal of producing an unlimited source of human islet cells for allogeneic treatment of diabetes, ideally without the need for intensive immunosuppression.

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SCALABLE PRODUCTION OF UNIFORM CELL AGGREGATES USING DISSOLVABLE CAPSULES GENERATED BY IN-AIR MICROFLUIDICS

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KEYWORDS: Encapsulation, iPSC, Cell Therapy.

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Background & Aim

The rapidly expanding cell and gene therapy market demands scalable and controllable manufacturing technologies. Using in-air microfluidics, we produced size controlled protective cell culture capsules that enable efficient formation and culture of uniform spheroids and cell aggregates in a shear-protected environment. This approach enables controlled 3D culture and aims to support consistent, scalable production of cell aggregates in bioreactors. By improving process robustness and reproducibility, it addresses key manufacturing challenges in cell therapy and facilitates the translation of advanced cell-based therapies.

Methods, Results & Conclusion

Methodology

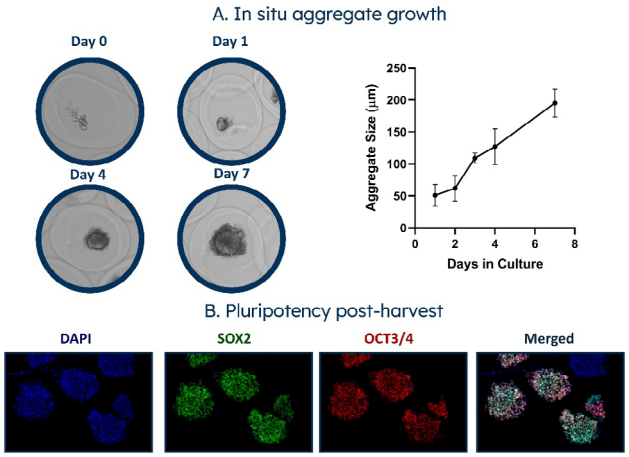
In-air microfluidics was used to produce dissolvable, cell-laden capsules. 3D cell encapsulation studies were performed using pluripotent stem cells encapsulated in xeno-free, calcium-alginate-based capsules. Encapsulated cells were cultured in suspension to form monodisperse cell aggregates. Experiments were partially conducted in collaboration with DBE and AST groups at the University of Twente, the Netherlands.

Results

In-air microfluidics enabled the generation of >1,000 cell-laden capsules per second. Encapsulated cells stained positive for pluripotency markers, including Sox2 and Nanog, and formed uniform cell aggregates with low size variability (CV <10%). At the end of culture, cell aggregates were efficiently released from the capsules using mild conditions, such as phosphate-buffered saline (PBS) or EDTA, while maintaining viability, integrity and functionality, as demonstrated by successful differentiation towards functional, beating cardiac spheroids.

Conclusion

In-air microfluidics enables scalable production of uniform, dissolvable cell culture capsules that support controlled cell aggregate formation while preserving pluripotency, viability, and functionality. Taken together with the ability to harvest cells from the capsules using mild, standard reagents, this innovation addresses key manufacturing challenges, such as scalability and reproducibility, enabling improved cell aggregate-based cell therapy production.



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ENGINEERED HGF-OVEREXPRESSING IPSC-DERIVED MESENCHYMAL STROMAL CELLS ALLEVIATE LUNG INFLAMMATION AND FIBROSIS

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KEYWORDS: iPSC, HGF-overexpressing, pulmonary fibrosis.

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Background & Aim

Idiopathic pulmonary fibrosis (IPF) is a progressive and fatal interstitial lung disease with limited therapeutic options. Although approved antifibrotic therapies can slow disease progression, IPF remains a life-threatening disease with substantial unmet medical needs. Hepatocyte growth factor (HGF) has been implicated in epithelial repair, anti-inflammatory regulation, and antifibrotic activity. Here, we developed NCR101, an investigational HGF-overexpressing induced pluripotent stem cell-derived mesenchymal stromal cell (HGF-iMSC) product, and evaluated its therapeutic potential, manufacturability, and safety in preclinical models of IPF.

Methods, Results & Conclusion

NCR101 was generated from a qualified human iPSC bank by targeted integration of the HGF transgene , followed by directed differentiation into mesenchymal stromal cells under a GMP-compliant manufacturing process. Cell identity, differentiation potential, and HGF secretion were assessed using phenotypic, functional, and secretion assays. Therapeutic efficacy was evaluated in a bleomycin-induced mouse model of pulmonary fibrosis. Mechanistic assessments included inflammatory cytokine profiling, profibrotic pathway analysis, extracellular matrix deposition, and histopathological evaluation. Biodistribution, pilot-scale manufacturing comparability, tumorigenicity, tumor-promoting potential, systemic toxicity, and immunogenicity were further assessed in relevant preclinical models, including non-human primates (NHPs).
NCR101 maintained a stable mesenchymal phenotype and sustained HGF secretion. In the bleomycin-induced pulmonary fibrosis model, NCR101 demonstrated greater antifibrotic activity than wild-type iMSCs, as shown by reduced inflammatory cytokine expression, suppression of profibrotic signaling, decreased extracellular matrix deposition, and improved lung histopathology. Biodistribution studies indicated prolonged pulmonary retention after administration, suggesting enhanced local therapeutic exposure. Pilot-scale manufacturing preserved key phenotypic and functional attributes, supporting process scalability. Safety studies showed no evidence of tumorigenicity in sensitive spike-in assays or promotion of c-MET-high tumor growth.
In NHPs, NCR101 administration was generally well tolerated, with no systemic toxicity or clinically significant immunogenicity observed. Together, these findings support NCR101 as a scalable investigational regenerative cell therapy candidate for pulmonary fibrosis.

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A GMP-COMPLIANT IPSC-DERIVED MSC THERAPY WITH IMMUNOMODULATORY AND CHONDROPROTECTIVE POTENTIAL FOR KNEE OSTEOARTHRITIS

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KEYWORDS: iPSC, mesenchymal stromal cells, Knee osteoarthritis.

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Background & Aim

Knee osteoarthritis (KOA) is a common degenerative joint disease characterized by chronic inflammation, cartilage degradation, pain, and impaired joint function. Current treatments are largely symptomatic and have limited disease-modifying effects. iPSC-derived mesenchymal stromal cells (iMSCs) offer a renewable and standardized cell source that may overcome the variability of donor-derived MSCs. This study evaluated the nonclinical pharmacology and safety of NCR100, an investigational iMSC product, for KOA.

Methods, Results & Conclusion

NCR100 was generated by directed differentiation of human iPSCs into mesenchymal stromal cells, followed by standardized expansion under a GMP-compliant manufacturing process. In vitro, immunomodulatory activity was assessed using activated lymphocyte assays. In vivo efficacy was evaluated following intra-articular administration in rat and rabbit models of KOA, including cartilage degeneration. Assessments included pain-related functional outcomes, gross cartilage evaluation, histopathology and inflammatory cytokine levels. Safety was assessed through safety pharmacology, single- and repeated-dose toxicity, genotoxicity, hemolysis, immunogenicity, and immunotoxicity studies.
NCR100 exhibited typical MSC characteristics, including expression of canonical MSC surface markers, and trilineage differentiation potential. In vitro, NCR100 showed marked immunomodulatory activity by regulating lymphocyte activation and inflammatory factor release. Following inflammatory stimulation, NCR100 expressed high levels of IDO and secreted trophic factors associated with tissue repair. In rat and rabbit models of KOA, intra-articular administration of NCR100 improved pain-related functional outcomes, reduced cartilage degeneration, preserved cartilage matrix, and decreased inflammatory cytokines, including TNF-α, IL-1β, and IL-6. In the osteochondral defect model, NCR100 promoted repair of damaged cartilage and supported cartilage regeneration. These effects were associated with improved cartilage matrix preservation and suppression of joint inflammation. Toxicology studies showed no significant NCR100-related safety concerns, with no evidence of systemic toxicity, genotoxicity, hemolysis, hypersensitivity, or significant immunotoxicity, and low immunogenicity observed.
Together, these findings support NCR100 as a standardized iPSC-derived MSC therapy candidate with immunomodulatory, chondroprotective, and cartilage repair potential for KOA.

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iPSC

DEVELOPMENT OF GMP-COMPLIANT IPSC-DERIVED NATURAL KILLER CELLS WITH BROAD ANTITUMOR ACTIVITY

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KEYWORDS: iPSC, Natural killer, Tumor.

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Background & Aim

Natural killer (NK) cell therapy is an emerging strategy for cancer treatment, but donor-derived NK cells are limited by donor variability, restricted scalability, and inconsistent functional potency. iPSC-derived NK cells (iNK) provide a renewable and standardized source for developing off-the-shelf NK cell products. This study aimed to evaluate the anti-tumor activity and safety of an investigational iPSC-derived NK cell product (product ID: NCR300).

Methods, Results & Conclusion

NCR300 was generated from human iPSCs through a GMP-compliant stepwise differentiation process into hematopoietic progenitors, naïve iNK cells, and mature iNK cells expressing NK-associated markers, including CD56, NKG2D, and NKp30, while lacking CD3 expression. *In vitro* cytotoxicity was assessed against multiple hematologic and solid tumor cell lines and compared with peripheral blood NK (PBNK) cells. *In vivo* anti-tumor activity was evaluated in xenograft tumor models using single- and repeated-dose administration. Tumor burden, survival, dose-response effects, and NK-related effector molecules were analyzed. Safety was assessed through single- and repeated-dose toxicity, tumorigenicity, hemolysis and coagulation testing, local tolerance, hypersensitivity, and immunogenicity studies.
In vitro, NCR300 showed broad and potent cytotoxic activity against both hematologic and solid tumor cell lines, with time- and dose-dependent tumor lysis. Under comparable conditions, NCR300 demonstrated stronger cytotoxicity than PBNK cells across multiple tumor cell lines. NCR300 also released NK-related effector molecules in a dose-dependent manner, supporting a mechanism involving cytotoxic granule-mediated tumor killing.
In vivo, NCR300 markedly reduced tumor burden and prolonged animal survival in multiple xenograft tumor models. Anti-tumor activity was observed after both single and repeated administration and increased with higher dose levels, indicating a dose-dependent efficacy profile. Mechanistic analyses showed increased levels of granulysin, perforin, IFN-γ, and granzyme A, suggesting that NCR300 exerted antitumor effects through activation of NK cytotoxic effector pathways. NCR300 showed no evidence of toxicity, tumorigenicity, hemolysis, coagulation effects, injection-site irritation, immunogenicity. Together, these findings support NCR300 as a standardized iPSC-derived NK cell therapy candidate with broad antitumor activity and a favorable nonclinical safety profile.

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Mesenchymal Stem/Stromal Cells

TARGETING THE IL-6–DRIVEN INFLAMMATORY PHENOTYPE IN KNEE OSTEOARTHRITIS: THERAPEUTIC POTENTIAL OF MSC SECRETOME FOR PRECISION REGENERATIVE MEDICINE

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KEYWORDS: knee osteoarthritis, interleukin-6, mesenchymal stromal cells.

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Background & Aim

Knee osteoarthritis (KOA) is increasingly recognized as a whole-joint disorder in which inflammation drives symptoms and structural progression. Interleukin-6 (IL-6) has emerged as a key mediator associated with synovial inflammation, cartilage degradation, and pain sensitization, while mesenchymal stromal cell (MSC)-based therapies show promising clinical outcomes. Growing focus on MSC-derived secretome and extracellular vesicles (EVs) reflects a shift toward cell-free, mechanism-driven therapeutics that offer more standardized orthobiologic approaches while preserving MSC immunomodulatory and regenerative properties. This scoping review examines IL-6–associated pathways in KOA and outcomes of MSC therapies, highlights secretome-mediated effects, and proposes a translational framework for future trials evaluating MSC secretome or EV-based therapies in IL-6–stratified KOA populations.

Methods, Results & Conclusion

This scoping review followed PRISMA-ScR guidelines. Literature searches were conducted in MEDLINE/PubMed, Embase and the Cochrane Library, with additional screening of Scopus, Web of Science and trial registries (ClinicalTrials.gov and WHO ICTRP). The analysis was restricted to human studies, and the findings were synthesized narratively due to the heterogeneity in biomarker assessment, osteoarthritis definitions, and MSC product characteristics. Consistent evidence from systematic reviews, meta-analyses and observational studies shows elevated

IL-6 levels in the synovial fluid and/or serum of patients with symptomatic KOA. Increased IL-6 levels are associated with synovitis, inflammatory joint activity and pain severity. Meta-analyses of intra-articular MSC therapies report improvements in pain and function, including reduced WOMAC and VAS scores. Mechanistic studies suggest MSC effects are largely mediated through paracrine signaling. This supports the plausibility of secretome and EV-based therapies. However, direct clinical evidence for standardized MSC secretome or EV products in KOA remains limited compared with cellular MSC injections. Current evidence supports IL-6 as a key biomarker of an inflammatory KOA phenotype. The benefits of MSC-based therapies and their paracrine mechanisms suggest that biomarker-stratified trials of MSC secretome or EV interventions are warranted. Future studies should integrate inflammatory biomarkers and imaging to optimize patient selection and trial interpretability.

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Mesenchymal Stem/Stromal Cells

FUNCTIONAL EVALUATION OF HUMAN UMBILICAL CORD MESENCHYMAL STEM CELLS CULTURED IN SERUM-CONTAINING AND SERUM-FREE MEDIA

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KEYWORDS: Umbilical cord-derived mesenchymal stem cells, Multilineage differentiation potential, Clinical grade MSCs.

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Background & Aim

Umbilical cord-derived mesenchymal stem cells (UC-MSCs) are among the most promising sources of multipotent stem cells due to their easy availability, minimal ethical concerns, low immunogenicity, and strong proliferative and differentiation potential. Most studies focused on fetal bovine serum-supplemented media (SCM) for cell expansion, but it has proven to be unsuitable for therapeutic use. Hence, serum-free medium (SFM) and optimized isolation, expansion, and functional evaluation are essential for ensuring the safety, efficacy, and functionality of UC-MSCs. Therefore, the present study aimed to evaluate the functional properties of UC-MSCs in SCM and SFM conditions.

Methods, Results & Conclusion

UC-MSCs were evaluated for cellular and biological characteristics (morphology, viability, growth kinetics, surface markers, and pluripotency markers), potency (colony-forming ability, alkaline phosphatase activity [ALP]), and senescence activity. Finally, multilineage differentiation potential, including adipogenic, osteogenic, chondrogenic, and pancreatic β-cell lineages, was assessed in SCM and SFM. Established UC-MSCs exhibited a small, spindle-like appearance, higher proliferation rate, greater colony-forming ability and ALP activity, a lower population doubling time, and senescence activity in SFM. Flow cytometry analysis showed higher levels of surface markers CD44, CD73, and CD90, and very low expression of CD34, CD45, and HLA-DR in both media. Further, UC-MSCs differentiated into adipocytes, osteocytes, and chondrocytes were confirmed by oil red, alizarin red, and alcian blue stain, respectively, and they showed differential expression of adipose-related genes (aP2, PPARγ2, LPL), bone-related genes (osteocalcin, osteonectin, and osteopontin), and cartilage-related genes (Collagen type II α1, aggrecan, SOX9). UC-MSC-differentiated pancreatic β-cells stained positively with dithizone and showed a good response to varying glucose concentrations in SFM. Later, the cells exhibited differential expression of gene markers, including PDX1, Nestin, Insulin, Glut-2, NKX6.1, and C-Peptide. UC-MSCs cultured in SFM maintained their biological properties and multilineage differentiation potential comparable to cells cultured in SCM. These findings demonstrate that serum-free culture conditions can effectively support the expansion and functional properties of UC-MSCs, highlighting their potential as a safer and more standardized alternative for the production of clinical-grade MSCs.

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Mesenchymal Stem/Stromal Cells

THE MACROPHAGE COLONY-STIMULATING FACTOR STIMULATED IMMUNOMODULATORY PROPERTIES OF MESENCHYMAL STEM CELLS

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KEYWORDS: Mesenchymal stem cells, Macrophage colony-stimulating factor, immunomodulation.

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Background & Aim

Mesenchymal stem cells (MSCs) have been recognized for their dual roles in immunomodulation. These cells have the capacity to transition between pro-inflammatory and anti-inflammatory phases, a process that is influenced by the inflammatory environment. The cytokine composition and their levels are the major determinants. The immunomodulatory potential of different cytokines varies significantly. Macrophage colony-stimulating factor (M-CSF) is a cytokine that is secreted during periods of inflammation. It is most prominent for its roles in hematopoiesis and the differentiation of monocytic lineages. The substance exhibits a dualistic property, manifesting both pro-inflammatory and anti-inflammatory characteristics. The influence of M-CSF on MSC properties, especially their immunoregulatory characteristics, remains to be elucidated. In this study, we aimed to investigate the effects of M-CSF on the immunoregulatory properties of MSCs.

Methods, Results & Conclusion

M-CSF was applied to the primary human Wharton's jelly MSCs cell culture for 8 hours and 24 hours. MSCs and the culture media were harvested for gene expression analysis and ELISA for measuring secreting cytokine levels. Exogenous M-CSF did not alter proliferative properties and the expression of stemness genes. The stimulation of M-CSF led to an increase in the expression of the Mcsf gene, suggesting that MSCs respond to M-CSF and initiate a positive-feedback response on transcription levels. The treatment of MSCs with M-CSF led to a significant inhibition in the production of pro-inflammatory mediators, such as IL-8. Concurrently, the treatment resulted in a substantial augmentation in the production of anti-inflammatory cytokines, including IL-10. However, the expression of *Tlr3* gene was not significantly increased by the presence of M-CSF, suggesting that the promotion of immunomodulation effects was not mediated by MSC2 polarization. The findings of this study suggest the potential for mesenchymal stem cell-based therapy in treating a range of immune-related diseases, including inflammation and autoimmune diseases.

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Mesenchymal Stem/Stromal Cells

CLINICAL-STAGE ALLOGENEIC ADSC THERAPY: AN INTEGRATED TRANSLATIONAL EVIDENCE FRAMEWORK ACROSS OSTEOARTHRITIS AND CHRONIC KIDNEY DISEASE

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KEYWORDS: Mesenchymal Stem Cell, Osteoarthritis, Chronic Kidney Disease.

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Background & Aim

Mesenchymal stem cell (MSC) therapies show therapeutic potential across diverse disease indications. However, integrating of product characterization, biological mechanisms, and clinical outcomes into a coherent translational strategy remains a major challenge. To address this, we development an integrated translational evidence framework to support the clinical development of an allogeneic adipose-derived stem cell (ADSC) therapy for osteoarthritis (OA) and chronic kidney disease (CKD).

Methods, Results & Conclusion

Evidence was integrated from OA and CKD clinical studies, external real-world CKD cohorts, nonclinical disease models, mechanistic investigations, and assessments of mechanism-linked potency attributes. Biological activities relevant to immunomodulatory and tissue-protective functions were evaluated alongside selected potency markers. In OA, ELIXCYTE treatment demonstrated sustained improvements in pain and functional outcomes through 96 weeks, indicating durable clinical benefit. In CKD, 88.2% of patients exhibited stable or improved renal function trajectories over 48 weeks. Compared with external real-world cohorts, ELIXCYTE treated patients demonstrated a reduced risk of clinically meaningful renal function decline, including a lower risk of ≥30% eGFR reduction (HR=0.276), supporting potential disease-modifying activity.
Nonclinical studies consistently demonstrated therapeutic activity across both indications. In OA models, ELIXCYTE treatment attenuated inflammation and cartilage degeneration, whereas in CKD models treatment reduced renal fibrosis and

preserved renal tissue architecture. Despite distinct disease indications, convergent findings across clinical and nonclinical studies supported common immunomodulatory and tissue-protective biological activities.
Mechanism-linked potency attributes representing complementary biological functions demonstrated significant associations with cellular activity, including IDO activity with T-cell suppression (r=0.894), HGF secretion with macrophage modulation (r=0.912), and PGE2 expression with macrophage modulation (r=0.821).
Collectively, these findings integrate clinical outcomes, real-world evidence, nonclinical efficacy, proposed mechanisms of action, and mechanism-linked potency attributes into a coherent translational evidence framework. This work demonstrates how integrated clinical, mechanistic, and potency evidence can support mechanism-informed development of clinical-stage MSC therapies across diverse indications.

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Mesenchymal Stem/Stromal Cells

POLYDEOXYRIBONUCLEOTIDE MODULATES DPSC–MACROPHAGE CROSSTALK UNDER PULPITIS-MIMICKING INFLAMMATORY CONDITIONS.

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KEYWORDS: PDRN, Pulpitis, DPSC–macrophage crosstalk.

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Background & Aim

Pulpitis is associated with persistent inflammation and impaired repair of the dentin–pulp complex. Although polydeoxyribonucleotide (PDRN) has been clinically used as a tissue repair-promoting agent, its role in regulating the inflamed pulp microenvironment remains unclear. We investigated whether PDRN primarily suppresses inflammatory signaling in dental pulp stem cells (DPSCs) or instead modulates DPSC-associated repair responses and DPSC–macrophage crosstalk under pulpitis-mimicking conditions.

Methods, Results & Conclusion

Human DPSCs were stimulated with lipopolysaccharide and treated with PDRN, and cell viability, wound closure, inflammatory cytokine expression, inflammatory signaling-related proteins, and intracellular ROS levels were evaluated. Stromal–immune interaction was further assessed using a transwell co-culture system with macrophages, followed by migration assay and additional analyses of macrophage-related responses and DPSC-associated gene expression. Under the present experimental conditions, PDRN was associated with preserved DPSC viability and enhanced wound closure, whereas its effects on canonical inflammatory cytokines and signaling-related proteins were limited, and marked ROS reduction was not observed. In the co-culture setting, PDRN-treated conditions were additionally associated with changes in macrophage migration and macrophage-related responses. Taken together, these findings suggest that, in this model, PDRN may be associated more closely with modulation of DPSC-associated repair responses and stromal–immune interaction than with strong direct suppression of inflammatory signaling.

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Mesenchymal Stem/Stromal Cells

MESENCHYMAL STROMAL CELLS AND ANTI-MICROBIAL PEPTIDES WORKING IN CONJUNCTION TO TARGET UPEC MEDIATED INFECTION: PRELIMINARY VALIDATION AND A PATH TO TRANSLATION

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KEYWORDS: Mesenchymal Stromal Cells, Anti-microbial Peptides, Uropathogenic E.coli.

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Background & Aim

The increasing prevalence of infectious diseases and the limited effectiveness of conventional therapies highlight the urgent need for novel approaches to combat bacterial infections, including urosepsis. Prolonged antibiotic use fosters antimicrobial resistance, posing a global health threat. Mesenchymal stem/stromal cells (MSCs) offer promising therapeutic potential owing to regenerative, immunomodulatory, anti-inflammatory, and antimicrobial properties by secreting antimicrobial peptides (AMPs). This study explored combinatorial effect of MSCs and AMPs in combating Uropathogenic E.coli (UPEC) CFT073-mediated pathogenesis.

Methods, Results & Conclusion

To begin with, total 6 AMPs were docked with HisC

(PDB ID: 1fg7) using HDOCK webserver followed by MD simulations using gmx_qk software (Fig 1A). Wharton-Jelly derived MSCs (WJ-MSCs) were cultured for 48 h and conditioned medium was collected (Fig 1B). WJ-MSCs were characterized for their pan markers using flow cytometry. The peptide and WJ-MSCs-derived double-concentrated conditioned medium (DCM) was tested against CFT073 as per CLSI guidelines. Membrane disruption was evaluated by scanning electron microscopy (SEM). For safety and feasibility of interventions, cytotoxicity and hemolytic assay were conducted. To evaluate, immunomodulatory efficacy of only DCM and in presence of CL, PBMCs were activated with UPEC for 24 h followed by treatment for 96h.
C-L peptide, a derivative of existing peptides: Cecropin and LL-37, demonstrated optimum RMSD and RMSF and least Gibbs' free energy (-1125.88 kJ/mol), was chosen for further studies (Fig 2). WJ-MSCs were positive for CD73, CD90, and CD105 markers (Fig 3). Antibacterial assays demonstrated MIC (48 µg/ml) and MBC value (55 µg/ml) for C-L peptide (Fig. 4A), and DCM showed 50% bacterial inhibition (Fig. 4B). In a sequential setup, CL and DCM worked effectively without affecting the antimicrobial property of CL (Fig. 5). Disruption of bacterial morphology was reported in presence of interventions (Fig 6). Both interventions showcased negligible toxicity and hemolytic activity (Fig 7). In terms of immune profile, it showcased the significant recalibration in CD3 profile and cell proliferation, which proves that DCM immune-modulatory capacity is retained in presence of CL (Fig 8).
Hence, this combination represents a strategic convergence of immune modulation and targeted microbial debulking. This approach may serve as a model for future interventions in infection-related inflammatory diseases.

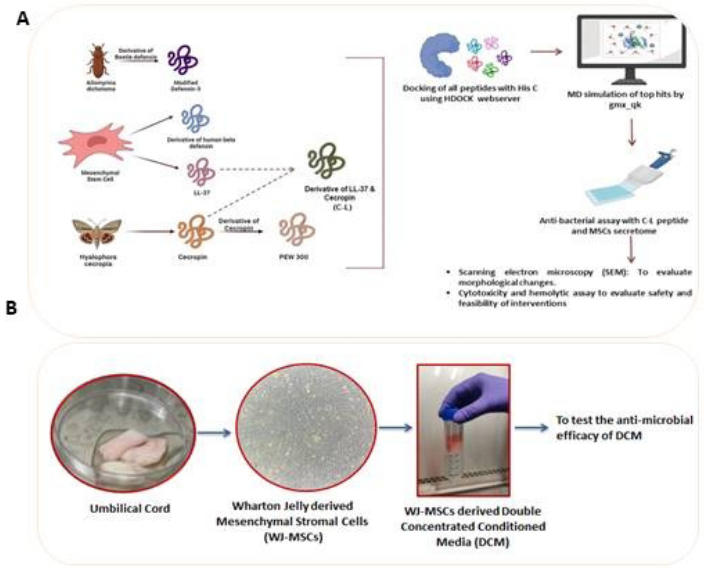
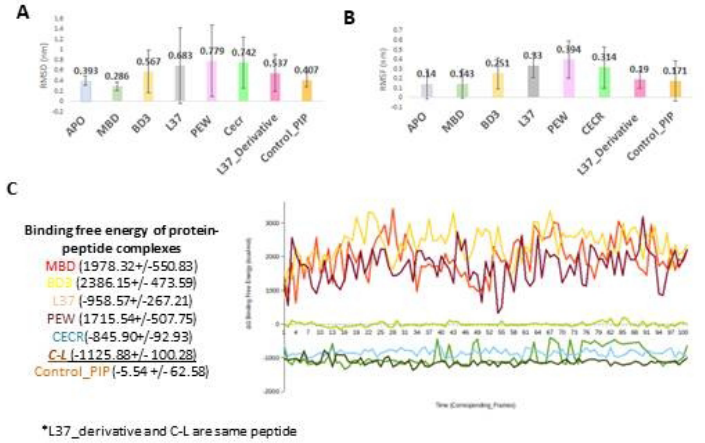


Figure 1: Schematic representation of methodology. (A) Workflow for shortlisting an effective peptide through *in silico* methods and subsequent *in vitro* validation (B) Explant culture of WJ-MSCs and double concentration of WJ-MSCs derived conditioned media. (Created by Biorender.com).



*L37_derivative and C-L are same peptide

Figure 2: In silico validation of shortlisted antimicrobial peptides. (A) Root Mean Square Deviation (RMSD) of Apo and Protein-Peptide complexes, (B) Root Mean Square Fluctuation (RMSF) of Apo and Protein-Peptide complexes and (C) Binding free energy of Protein-Peptide complexes.

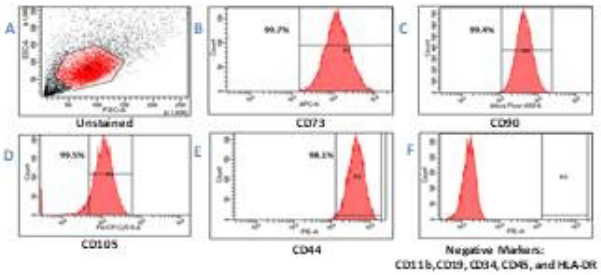


Figure 3: Phenotypic characterization of WJ-MSCs. Flow cytometric analysis indicated that WJ-MSCs stained with respective antibodies were positive for (B) CD73, (C) CD90, (D) CD105, (E) CD44 and negative for (F) CD11b, CD 19, CD34, CD45, and HLA-DR .

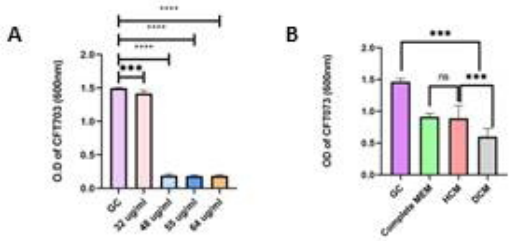


Figure 4: *In vitro* validation to evaluate antibacterial effect of C-L peptide and DCM. (A) Significant bacterial inhibition reported in presence of C-L with Minimum Inhibitory Concentration (MIC)= 48ug/ml and Minimum Bactericidal Concentration (MBC) = 55 ug/ml and (B) 50% bacterial inhibition observed in presence of DCM at OD=600 nm. GC: Growth Control, HCM: Healthy conditioned media, DCM: Double concentrated conditioned media. *** p value = 0.0005, **** P value < 0.0001

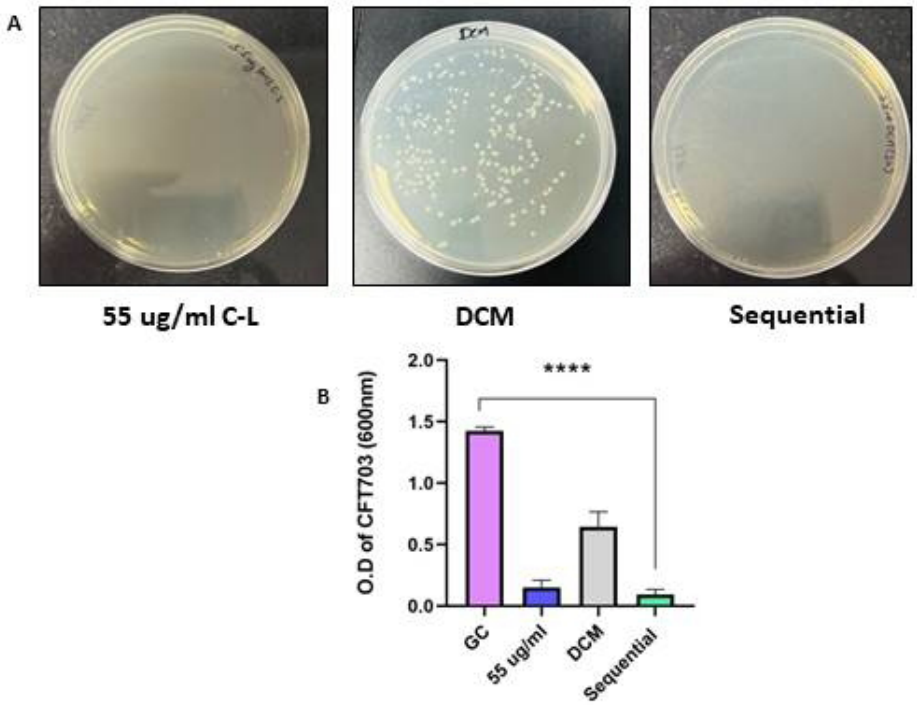


Figure 5: Sequential antibacterial effect of C-L and DCM. (A) 100% cfu reduction was reported in presence of both C-L peptide (55ug/ml) and DCM. (B) Significant bacterial inhibition in sequential setup. *** p value = 0.0005, **** P value < 0.0001

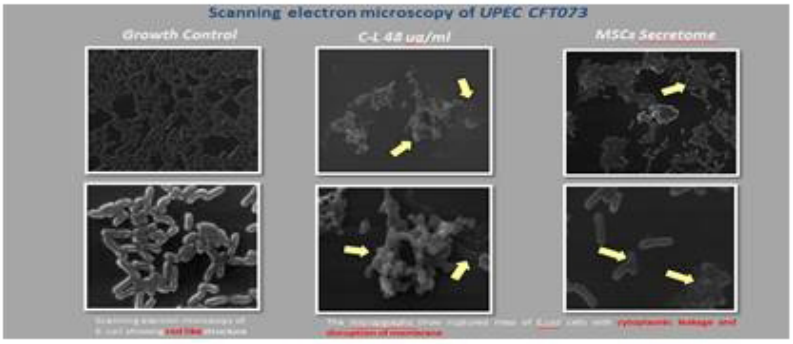


Figure 6: Scanning electron microscopy of UPEC showing rod like structure. Figure B and C shows micrographs of UPEC representing the effect of C-L (48ug/ml) and DCM respectively on bacterial morphology. The micrographs show ruptured mass of *UPEC* cells with cytoplasmic leakage and disruption of membrane.

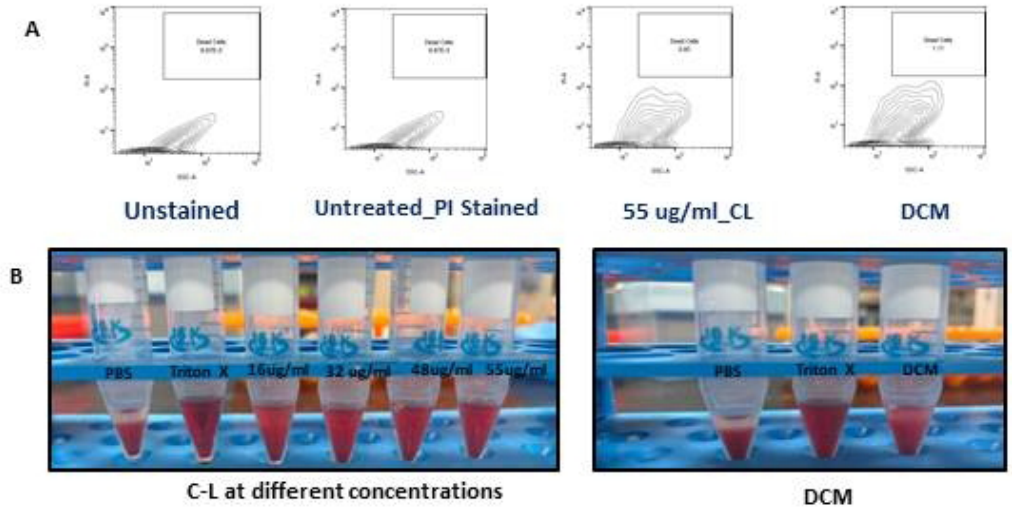


Figure 7: Safety and evaluation of intervention. (A) Representative contour plots showing the effect of the C-L peptide (55ug/ml) and DCM on T-24 cell line using flow cytometer. Percentage of PI stained (dead cells) was negligible in presence of both C-L and DCM. (B) Hemolysis assay of C-L peptide and DCM. The presence of hemoglobin was observed at 540 nm. 5-10% hemolysis was observed in presence of interventions.

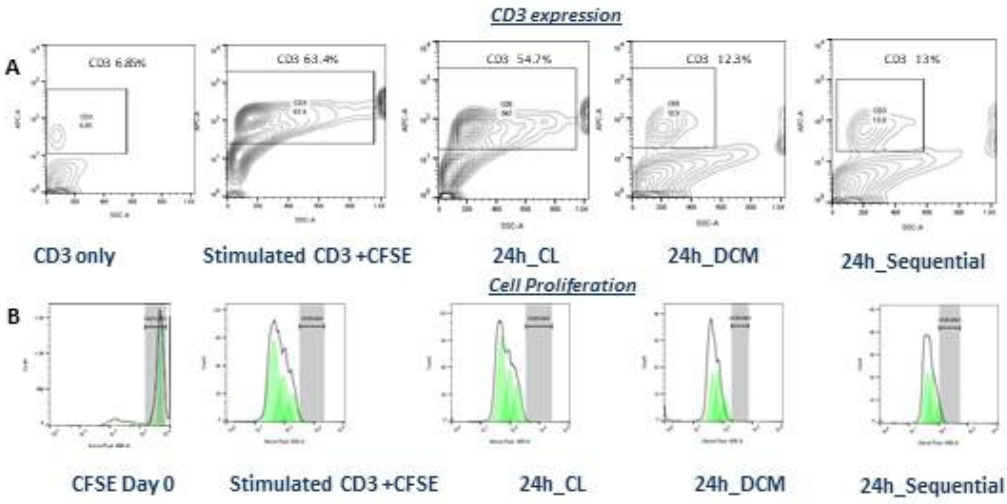


Figure 8: *Immune modulation in presence of C-L peptide and DCM. Activation of PBMCs with UPEC CFT073 followed by sequential treatment with C-L and DCM lead to (A) recalibration of CD3 profile and (B) modulation in CFSE stained cell proliferation.*

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Mesenchymal Stem/Stromal Cells

REVIVE™ SVF ISOLATION DEVICE: A RAPID AND LOW-RISK APPROACH TO HIGH-CONCENTRATION SVF ISOLATION

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KEYWORDS: SVF, Isolation, Stem cell.

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Background & Aim

In regenerative medicine there are various sources of therapeutic cells, among which stromal vascular fraction (SVF) is one of the most promising. Isolation of SVF from adipose tissue is a labour-intensive protocol, of tissue digestion and multiple washing steps, in order to isolate viable cell suspension. This process is automated with Revive™ SVF isolation device by Bio-ReCell and adapted for use in clinics, GMP-facilities and research institutions. The device eliminates the risk of contamination and exposure, and reduces processing time. SVF isolation automated on Revive™ SVF isolation device reproduces the steps of manual process, through utilizing a system of bags, tubes and filters, that separate SVF cell population from oil, adipose tissue, red blood cells and cellular debris, while maintaining a GMP-compliant closed system.

Methods, Results & Conclusion

Adipose tissue was collected from subjects undergoing liposuction and used for SVF isolation with the Revive™ SVF isolation device. The entire SVF isolation is performed inside the Revive™ single use consumable. The setup for the process requires 5 minutes, while the isolation from 40-120 mL of adipose takes approximately 55 minutes. The process starts with enzymatic digestion inside the device, followed by washing and concentration of heterogenous cell mix. The quality of SVF was evaluated with flow cytometry by staining relevant surface markers, as well as using nuclei stain for determination of total nucleated cell (TNC) content. SVF was used for colony-forming unit-fibroblast (CFU-f) assay and cultivating mesenchymal stromal cell (MSC) culture.
The Revive™ SVF isolation process yields on average 1,96*10^6 TNCs/mL of SVF (± 1,47*10^6 TNCs/mL). The automated process of is gentle on cells, resulting in high viability. The content of CD45- (SVF cells, non-blood) cells is 67,8 % (± 11,6 %) and the content of CD90+ cells 78,5 % (± 6,4 %). It contains a high proportion of adipose-derived MSCs, that after cultivation possess all the properties defined by ISCT. On average, the yield of CFU-f assay is 7358 CFU-f/mL of adipose tissue (± 6749 CFU-f/mL of adipose).

Revive™ SVF isolation device produces a high-quality SVF, with high concentration of viable and potent cells that have the ability to facilitate regenerative and anti-inflammatory response. SVF has a high content of adipose-derived MSCs that retain their colony forming ability and have high cultivating potential. The process reduces associated risks and saves time.

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Mesenchymal Stem/Stromal Cells

HUMAN EXFOLIATED DECIDUOUS TEETH (SHED): A POTENT SOURCE FOR REGENERATIVE APPLICATIONS

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KEYWORDS: Stem cells from Human Exfoliated Deciduous Teeth.

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Background & Aim

Stem cells from Human Exfoliated Deciduous Teeth (SHED) are mesenchymal stem cells (MSCs) obtained from naturally shed primary teeth. They are easily accessible through a non-invasive procedure and exhibit high proliferative capacity, multilineage differentiation potential, and immunomodulatory properties. These features make SHED an ethically favorable and promising cell source for regenerative medicine, wound healing, and aesthetic applications At the Stem Cell and Gene Therapy Applied Research Center (STEMREC), research focuses on mesenchymal stem cell isolation, characterization, preservation, and functional evaluation. This poster presents selected research highlights from MSC studies at STEMREC, with emphasis on immunoregulation and hypothermic preservation strategies supporting translational applications

Methods, Results & Conclusion

Method
SHED were isolated from exfoliated deciduous teeth of Vietnamese donors and expanded under standardized culture conditions. MSC identity was confirmed by plastic adherence, surface marker expression via flow cytometry, and in vitro differentiation assays
For preservation studies, SHED were subjected to hypothermic storage using various crystalloid electrolyte and caloric intravenous solutions. Cell viability, morphology, and post-storage proliferative capacity were evaluated
Immunoregulation studies were conducted using UC-MSCs treated with kynurenic acid (KYNA) and quercetin under hyperglycemic conditions. Expression of aryl hydrocarbon receptor (AhR) and interleukin-6

(IL-6) was analyzed by RT-PCR across different concentrations and time points

Result

SHED consistently displayed mesenchymal stem cell characteristics, including appropriate immunophenotype and multilineage differentiation capacity. Preserved SHED maintained stable morphology and functional properties, supporting their suitability for downstream regenerative applications. KYNA and quercetin modulated immunoregulatory gene expression in UC-MSCs, demonstrating concentration- and time-dependent effects on AhR and IL-6 signaling pathways

Conclusion

SHED represents a safe, accessible, and potent MSC source. Through complementary studies, STEMREC has established standardized workflows from isolation and preservation to functional validation, highlighting strong potential for future regenerative and aesthetic applications. Located in the Technology Research and Development Zone in Hanoi, STEMREC is equipped with advanced laboratories and cleanroom facilities to support translational research

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Mesenchymal Stem/Stromal Cells

HUMAN UMBILICAL CORD BLOOD-DERIVED MESENCHYMAL STEM CELLS REGULATE OSTEOCLAST MATURATION AND FUNCTIONAL ACTIVATION IN OSTEOARTHRITIS-ASSOCIATED SUBCHONDRAL BONE REMODELING

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KEYWORDS: Mesenchymal Stem Cells, Osteoclastogenesis, Osteoarthritis.

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Background & Aim

Human umbilical cord blood-derived mesenchymal stem cells (hUCB-MSCs) have shown therapeutic potential in osteoarthritis (OA); however, their effects on osteoclast-mediated subchondral bone remodeling remain incompletely understood. OA is increasingly recognized as a disease of the entire osteochondral unit involving not only cartilage degeneration but also pathological remodeling of the subchondral bone. Given the contribution of enhanced osteoclast activity to abnormal bone remodeling and OA progression, this study aimed to investigate the effects of hUCB-MSCs on osteoclast differentiation, maturation, and functional activation.

Methods, Results & Conclusion

Methods

RAW264.7 cells were stimulated with receptor activator of nuclear factor kappa-B ligand (RANKL) to induce osteoclastogenesis and were co-cultured with hUCB-MSCs using a transwell co-culture system. Osteoclast-related gene and protein expression were analyzed by quantitative PCR and immunocytochemistry, respectively. Osteoclast differentiation, multinucleation, and functional maturation were evaluated by tartrate-resistant acid phosphatase (TRAP) staining and actin ring formation analysis.

Results & Conclusion

RANKL stimulation markedly increased the expression of osteoclastogenesis-associated markers, including NFATc1, OSCAR, and TRAP. Co-culture with hUCB-MSCs significantly suppressed the expression of osteoclast fusion and maturation markers, including DC-STAMP, ATP6V0D2, and CTSK. Consistent with these findings, hUCB-MSC treatment reduced the formation of multinucleated TRAP-positive osteoclasts and significantly inhibited actin ring formation, a hallmark of mature osteoclast functional activation. Importantly, the inhibitory effects of hUCB-MSCs were more pronounced on markers associated with osteoclast fusion and terminal maturation than on early differentiation markers, suggesting preferential regulation of late-stage osteoclast development and functional maturation.
These findings demonstrate that hUCB-MSCs suppress osteoclast fusion, maturation, and functional activation, thereby potentially modulating osteoclast-mediated pathological processes relevant to OA progression. Collectively, our results provide supportive mechanistic evidence that hUCB-MSCs may exert therapeutic benefits in OA not only through cartilage protection but also through regulation of osteoclast-related pathological processes.

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Mesenchymal Stem/Stromal Cells

A COMPARATIVE CASE REPORT OF STEM CELL AND SECRETOME THERAPY FOR POST-STROKE RECOVERY: NOVEL INSIGHTS FROM QUANTITATIVE ELECTROENCEPHALOGRAPHY AND FUNCTIONAL ASSESSMENTS

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KEYWORDS: ischemic stroke, secretome intrathecal, stem cell intrathecal.

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Background & Aim

Stroke remains a major cause of mortality and long-term disability worldwide, including in Indonesia. Mesenchymal stem cell (MSC)-based therapy and MSC-derived secretome therapy are emerging regenerative strategies for post-stroke neurorestoration. This comparative case report evaluates clinical, functional, cognitive, and quantitative electroencephalography (Q-EEG) changes after intrathecal MSC therapy and hypoxic MSC-derived secretome therapy in two ischemic stroke patients.

Methods, Results & Conclusion

Case Summary and Methods

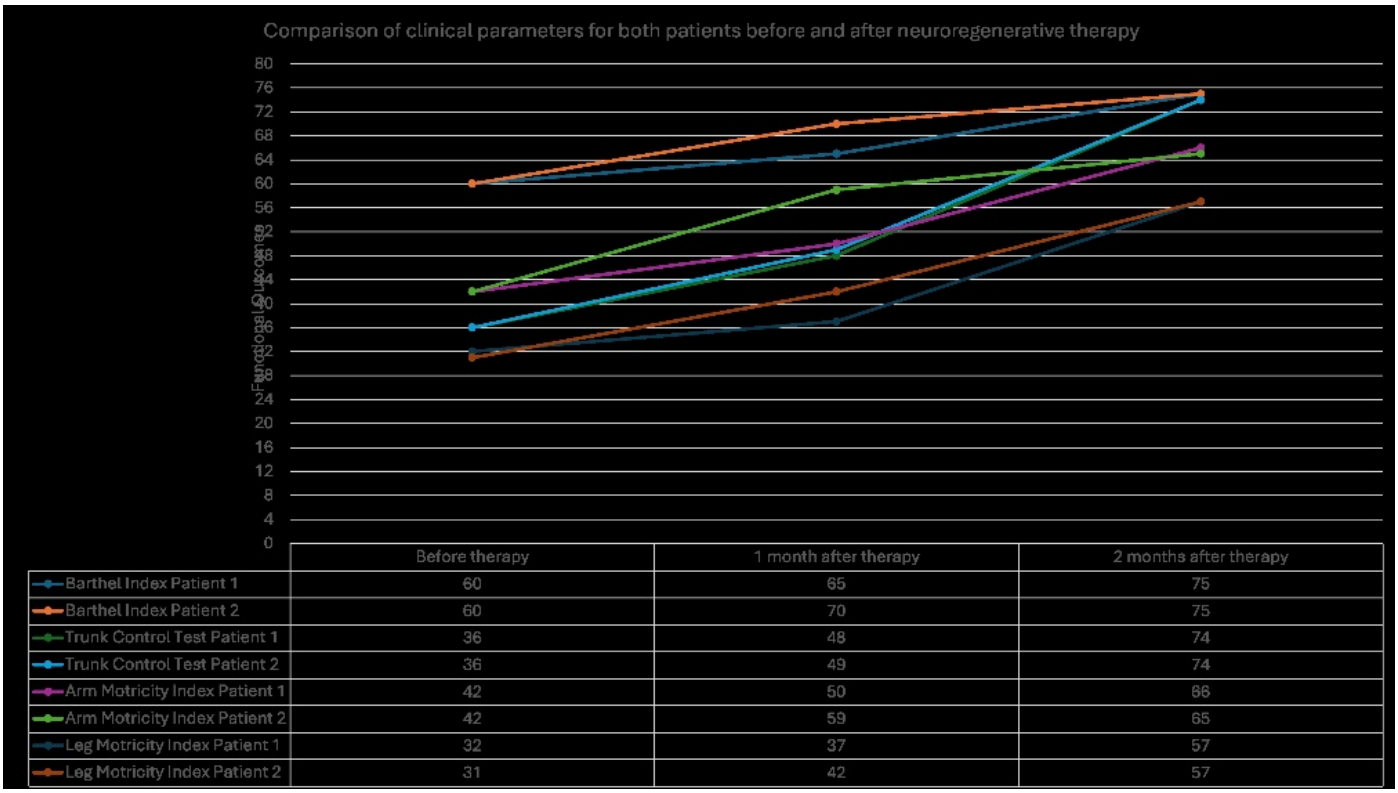
Two 56-year-old right-handed men presented with an 8-hour history of sudden-onset ischemic stroke. Both had long-standing uncontrolled hypertension and controlled diabetes mellitus. The baseline National Institutes of Health Stroke Scale (NIHSS) score was 12, indicating moderate stroke severity. Non-contrast brain CT confirmed right middle cerebral artery (MCA) territory infarction with an Alberta Stroke Program Early CT Score (ASPECTS) of 8, consistent with embolic ischemic stroke. Repeat laboratory examinations were performed approximately 2 weeks after stroke onset. On Day 15, Patient 1 received an intrathecal injection of 2 × 10^7 MSCs, whereas Patient 2 received an intrathecal injection of 300 µL hypoxic MSC-derived secretome. Both were discharged on Day 16 and followed at 1 and 2 months after injection. Outcomes included NIHSS, Barthel Index, Fugl-Meyer Assessment (FMA), Trunk Control Test (TCT), Motricity Index (MI), Montreal Cognitive Assessment-Indonesian version (MoCA-INA), Trail Making Test (TMT), and Q-EEG parameters, including delta activity, beta activity, and delta-theta/alpha-beta ratio (DTABR).

Results

Both patients showed progressive neurophysiological and functional improvement over 2 months. Serial Q-EEG demonstrated gradual normalization of cortical activity, reflected by improvement in abnormal delta, beta, and DTABR values. Functional recovery was observed in daily activities, trunk control, and limb motor strength.

Conclusion

Intrathecal MSC therapy and hypoxic MSC-derived secretome therapy may support neurophysiological and functional recovery after ischemic stroke. Improvements in motor strength, trunk control, activities of daily living, and Q-EEG patterns suggest enhanced post-stroke neuroplasticity. Larger controlled studies with longer follow-up are needed to confirm efficacy, safety, optimal timing, dosing, and patient selection.



	Before therapy	1 month after therapy	2 months after therapy
Barthel Index Patient 1	60	65	75
Barthel Index Patient 2	60	70	75
Trunk Control Test Patient 1	36	48	74
Trunk Control Test Patient 2	36	49	74
Arm Motricity Index Patient 1	42	50	86
Arm Motricity Index Patient 2	42	59	65
Leg Motricity Index Patient 1	32	37	57
Leg Motricity Index Patient 2	31	42	57

Figure 1. Table comparison patient 1 (stem cell intrathecal injection) VS patient 2 (secretome intrathecal injection)

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Mesenchymal Stem/Stromal Cells

ENZYMATIC DETACHMENT OPTIMIZATION FOR QUALITY PRESERVATION IN GMP HUMAN ADIPOSE-DERIVED MESENCHYMAL STROMAL CELL MANUFACTURING

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KEYWORDS: Adipose-derived mesenchymal stromal cells (AD-MSCs), Enzymatic cell detachment, Cell clumping.

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Background & Aim

Enzymatic cell detachment is a critical upstream processing step that directly affects cell yield, viability, and overall product quality, including cell potency. Despite widespread use of enzymatic detachment solution in MSC culture, the influence of practical handling variables, including enzyme pre-warming temperature, exposure time, and incubation temperature, on AD-MSC quality attributes has not been thoroughly characterized. As a result, evidence-based guidance for optimizing these parameters remains limited, particularly in GMP-oriented manufacturing workflows. This study systematically evaluates the impact of TrypLE Select handling conditions, specifically enzyme pre-warming temperature and detachment incubation temperature, on detachment efficiency and quality attributes of human adipose-derived mesenchymal stromal cells (AD-MSCs).

Methods, Results & Conclusion

Cells were expanded to 80% confluency, then processed at a defined pre-warming temperature, exposure time, and incubation temperature to ensure controlled evaluation of these variables and reproducible processing conditions. Cellular outcomes were analyzed using a comprehensive panel of complementary assays, including morphological assessment, cell count and viability analysis, cell clumping assessment, functional adhesion testing, and growth performance. The findings support the development of standardized Critical Process Parameters (CPPs) for MSC processing, thereby improving process consistency, product quality, scalability, and translational readiness in cell therapy manufacturing workflows.

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Mesenchymal Stem/Stromal Cells

ENHANCING MSC EXPANSION ON MICROCARRIER USING SMALL SCALE MEDIA EXCHANGE BIOREACTORS

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KEYWORDS: mesenchymal stromal cell, extracellular vesicle, rapid medium exchange.

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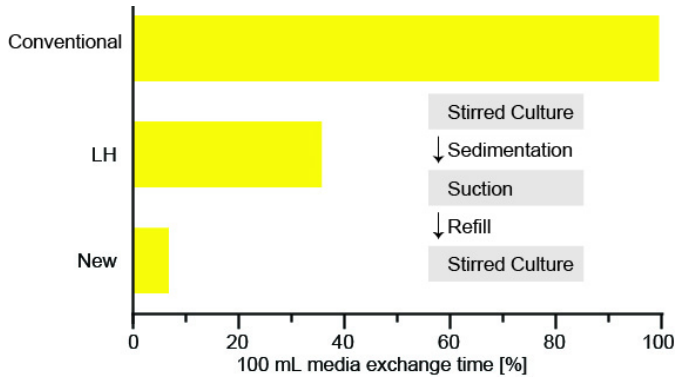
Background & Aim

Medium exchange is common procedure during mesenchymal stromal cell (MSC) expansion by maintaining nutrients and reducing waste products. Automated high-throughput small scale multi-parallel bioreactor system, such as Ambr® 250, could facilitate process development efficiency with liquid handler to reduce labor. However, medium exchange still requires intensive pipetting and is time consuming. This study introduces an efficient media exchange workflow in small-scale bioreactors. By overcoming the limitation of intensive pipetting and risk of contamination in current workflows, this approach minimizes the use of costly reagents and reduces manual operations. The innovative system enhances high-throughput MSC microcarrier expansion process development, optimizing resource utilization and accelerating advancements in bioprocess methodologies

Methods, Results & Conclusion

This work established a rapid medium exchange workflow for high-throughput process development by combining small-scale single-use vessels with long dip-tube connections and the fully automated Ambr® 250 High Throughput (Ambr® 250 HT) system. By connecting bioreactors to external peristaltic pumps using media exchange tubing, full medium removal and addition cycles were performed without manual pipetting or removing bioreactors from culture stations. The method enabled medium recharge within 5 minutes, reducing time and workload by more than 90% compared with conventional procedures, while maintaining cell viability and density.
Thanks to rapid medium exchange workflow and fully automated Ambr® 250 HT system, we conducted design of experiments (DOE) screening to investigate MSC expansion in 12 parallel bioreactors. Results showed that higher medium recharge frequency and increased microcarrier density supported improved MSC expansion. Furthermore, we applied our rapid medium exchange workflow to completely replace MSC growth medium to EV production medium in a semi-automated, multi parallel and high throughput mode. We collected up to 3E10 particles/ml from conditioned

medium, roughly ~6,000 particles/cell/day. Overall, this rapid medium exchange workflow reduces labor and processing time, improves efficiency in MSC microcarrier expansion process development, and simplifies small-scale MSC-EV manufacturing. By increasing throughput while minimizing manual handling, the method has strong potential to accelerate MSC process development.



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Mesenchymal Stem/Stromal Cells

EVALUATION OF SKIN REGENERATIVE PROPERTIES OF CLINICAL -GRADE HUMAN ADIPOSE TISSUE DERIVED STEM CELLS

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KEYWORDS: Adipose tissue-derived stem cells , Growth factors , Inflammatory cytokines.

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Background & Aim

Adipose tissue-derived stem cells (ASCs) are the most promising option among mesenchymal stem cells (MSCs) in tissue engineering applications due to their ease of access and abundance in adipose tissue. ASCs could regulate immunomodulatory properties through cell-to-cell interactions and the secretion of biomolecules, including growth factors, to enhance skin regeneration. Recently, MSC-derived cell sheets have also been generated to enhance tissue regeneration. Hence, the present study investigated morphology, proliferation, surface marker levels, lineage differentiation, immunomodulatory properties, growth factor expression, and biomolecule expression. Further, the ASCs were induced to form a cell sheet and assessed the expression of markers related to extracellular matrix (ECM) remodeling, stemness, angiogenesis, and inflammation.

Methods, Results & Conclusion

ASCs cultured in the serum-free media (SFM) were plastic-adherent and exhibited a fibroblast-like morphology. The cells expressed the MSC-markers (CD73, CD90, CD105) and were negative for hematopoietic stem cell markers (CD34, CD45, HLA-DR). ASCs showed a greater tendency to differentiate into mesenchymal lineages, including osteocytes and adipocytes, as confirmed by cytochemical staining and the expression of lineage-specific mRNA markers. ASCs exhibited the expression of selected growth factors, such as stromal cell-derived growth factor (SDF), epidermal growth factor (EGF), insulin-like growth factor (IGF), vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), platelet-derived growth factor (PDGF), keratinocyte growth factor (KGF), and transforming growth factor-beta (TGFβ). Further, ASCs demonstrated the immunomodulatory features through varied expression of markers, including interleukin (IL)-1β, IL-6, TNF-α, IL-10, and TGF-β. Finally, ASCs successfully generated cell sheets and showed higher expression levels of markers implicated in ECM remodeling (COL1, Integrin β1, and MMP1), stemness (OCT4, SOX2), angiogenesis (VEGF, bFGF), and the inflammatory response (IL-4, IL-6, IL-10, TGFβ). Thus, clinical-grade ASCs could potentially improve therapeutic impact as regenerative factors, modulators of the immune microenvironment, or sources of cell sheets for skin tissue engineering applications.

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Mesenchymal Stem/Stromal Cells

SYSTEMIC ADMINISTRATION OF HUMAN ADIPOSE-DERIVED STEM CELLS IMPROVES MUSCLE QUALITY AND FRAILTY IN NATURALLY AGED SARCOPENIC MICE

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KEYWORDS: Cell Therapy, Aging, Sarcopenia.

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Background & Aim

Sarcopenia, characterized by the progressive loss of skeletal muscle mass and function with age, is prevalent in older adults and is associated with increased risks of cardiovascular disease, diabetes, falls, and mortality. Effective pharmacological treatments specifically targeting sarcopenia remain limited. This study investigated the effects of systemic administration of human adipose-derived mesenchymal stromal cells (hADSCs) on muscle quality and frailty in naturally aged mice, with comparison to voluntary exercise.

Methods, Results & Conclusion

Twenty-one-month-old female C57BL/6 mice received weekly intravenous tail-vein injections of hADSCs or PBS for two months. Three-month-old mice served as young controls. A separate cohort was subjected to voluntary wheel-running exercise. Outcomes were assessed by DXA scanning, muscle histology and wet weight, grip strength, ex vivo contractile function and fatigue testing, multiplex cytokine arrays, and a frailty index. hADSC treatment increased skeletal muscle mass, myofibre cross-sectional area, and contractile performance. Compared with exercise, hADSCs were associated with greater gains in muscle wet weight and superior anti-fatigue capacity, whereas exercise produced better recovery after fatigue. Both interventions yielded comparable improvements in grip strength and hanging endurance. In addition, both hADSC administration and exercise attenuated age-related elevations in circulating pro-inflammatory cytokines and reduced frailty index scores. These findings indicate that systemic hADSC delivery can improve muscle quantity and quality while reducing frailty in naturally aged sarcopenic mice, with overall effects comparable to voluntary exercise. The results support further investigation of hADSC-based therapy as a potential approach for age-related muscle decline.

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Mesenchymal Stem/Stromal Cells

IDENTIFICATION OF MORPHOLOGICAL FEATURES ASSOCIATED WITH A VEGF-PRODUCING MSC SUBPOPULATION BY IMAGE-BASED ANALYSIS

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KEYWORDS: Mesenchymal stromal/stem cells, Single-cell RNA sequencing, Morphological image analysis.

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Background & Aim

Human mesenchymal stromal/stem cells (MSCs) possess the ability to produce vascular endothelial growth factor (VEGF) under ischemic conditions and are therefore considered promising candidates for the treatment of ischemic diseases. However, functional evaluation of MSCs generally relies on invasive and off-line assays, such as gene expression analysis and quantification of secreted factors. In this study, to facilitate future automated manufacturing of MSC-based products, we aimed to establish a non-invasive method for predicting VEGF-producing capacity under ischemic conditions based solely on cell morphology obtained during MSC culture.

Methods, Results & Conclusion

We previously identified a distinct MSC subpopulation (Cluster3) that contributes to VEGF secretion under ischemic conditions using single-cell RNA sequencing (scRNA-seq) (Miura et al., *Stem Cells Translational Medicine*, 2023). In the present study, to identify morphological features of human MSCs associated with the Cluster3 subpopulation, a machine-learning approach, Learning from Label Proportions (LLP), was employed to learn the relationship between single-cell morphological profiles and the proportion of Cluster3 cells determined by scRNA-seq.
As a result, LLP analysis successfully identified morphological features associated with Cluster3. Interestingly, evaluation of these morphological features using imaging datasets revealed that the cells corresponding to Cluster3 displayed characteristics typical of mesenchymal cells. This result was also consistent with DotPlot analysis of scRNA-seq data, which demonstrated enrichment of mesenchymal cell-related gene expression signatures

in Cluster3. Furthermore, knockdown experiments targeting genes highly expressed in Cluster3 indicated that suppression of several candidate genes altered the identified morphological features, suggesting that these genes are involved in the regulation of Cluster3-specific cell morphology.
In conclusion, these findings suggest that morphology-based imaging analysis can serve as a non-invasive method for identifying MSC subpopulations associated with VEGF production under ischemic conditions. Therefore, the label-free and non-destructive approach for characterizing cellular functions may provide a practical strategy for raw material cell selection and in-process quality monitoring during the manufacturing of MSC-based cell therapy products.

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Mesenchymal Stem/Stromal Cells

CHARACTERIZATION OF CLINICAL-GRADE HUMAN MESENCHYMAL STROMAL CELLS FROM DIFFERENT TISSUE ORIGINS FOR THERAPEUTICS

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KEYWORDS: Clinical grade MSCs, Plasticity, Lineage Differentiation.

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Background & Aim

Human mesenchymal stem/stromal cells (MSCs) from postnatal and adult tissues offer promising candidates for regenerative medicine and tissue engineering applications. However, the similarities and differences in their stemness and plasticity still need to be clearly understood. In this view, the present study evaluated the stemness and plasticity features of human MSCs derived from umbilical cord blood (CB-MSCs), bone marrow (BM-MSCs), infrapatellar fat pad (IFP-MSCs), and dermis tissue (DMSCs).

Methods, Results & Conclusion

MSCs were isolated from cord blood and tissues using plastic-adherent culture techniques and expanded to up to 5 passages. MSCs were assessed for growth kinetics, expression of pluripotent and phenotypic markers, colony-forming unit (CFU) ability, alkaline phosphatase (ALP) activity, and their ability to differentiate into osteocytes, adipocytes, and chondrocytes. All MSCs exhibited a characteristic fibroblast-like morphology, high proliferative potential, and CFU ability and ALP activity. The MSCs were positive for CD29, CD44, CD73, CD90, and CD105, but with varying levels of expression. However, all MSCs were negative for hematopoietic stem cell markers, CD34, CD45, and HLA-DR. The examined MSCs showed reduced expression of stemness markers Oct4, Sox2, and Nanog. All MSCs demonstrated their capacity to differentiate into mesenchymal lineage cells, with varying propensities during the induction period, as confirmed by cytochemical staining. Osteogenesis was confirmed by the expression of ALP, RUNX2, and osteocalcin markers. The expression of aP2, PPARγ2, and lipoprotein lipase corroborated the adipogenesis. Further, the expression of aggrecan, collagenase type-II α1, and SOX-9 evidenced the chondrogenic potential. However, no remarkable differences in expression levels were observed among different MSCs. The results revealed both similarities and differences in potency, phenotype maintenance, and multilineage differentiation among clinical-grade MSCs derived from different tissues. The findings underscore that the tissue source of MSCs is an important consideration for therapeutic applications in human medicine.

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Mesenchymal Stem/Stromal Cells

GMP-MANUFACTURED UMBILICAL CORD MSC-CONDITIONED MEDIUM AS ADJUNCTIVE THERAPY IN PAEDIATRIC DRUG-RESISTANT EPILEPSY: A REAL-WORLD REGISTRY OF SAFETY, SEIZURE, FUNCTIONAL, AND BIOMARKER OUTCOMES

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KEYWORDS: Pediatric Drug Resistant Epilepsy, Mesenchymal Stem Cell, Conditioned Medium.

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Background & Aim

Paediatric drug-resistant epilepsy (DRE) is etiologically heterogeneous but increasingly viewed as a neuroimmune network disorder, in which IL-6-driven signalling amplifies synaptic dysfunction and impairs neurodevelopment, while inflammatory tone is reflected by high-sensitivity C-reactive protein (hs-CRP). Preclinical studies suggest that cell-free umbilical cord mesenchymal stem cell-conditioned medium (UC-MSC-CM) may exert immunomodulatory and neurorestorative effects through paracrine mechanisms; however, clinical evidence remains limited. We evaluated the feasibility, safety, and clinical and biomarker outcomes associated with adjunctive UC-MSC-CM in children with DRE.

Methods, Results & Conclusion

Methods

A real-world paediatric DRE registry (April 2025-May 2026) was analysed. Exposure, feasibility, and safety were summarised across all treated children. GMP-manufactured UC-MSC-CM was characterised using available Certificate of Analysis data. A biomarker-linked matched case-control subset compared children receiving adjunctive UC-MSC-CM (10 serial intravenous injections, n=45) with standard-care controls (n=43) over 6 months. Outcomes included monthly seizure frequency, EEG findings, GMFM-66, Bayley-4, serum IL-6, hs-CRP, and tolerability.

Results

The registry comprised 88 children with DRE and neurodevelopmental comorbidities (median age at first administration, 4.2 years). The product contained quantifiable HGF (1152-1290 pg/mL), TGF-beta1 (438-577 pg/mL), bFGF (89-144 pg/mL), KGF (70-116 pg/mL), and procollagen I alpha-1 (467-512 ng/mL), supporting a multi-factorial paracrine profile plausibly relevant to neuroregeneration and immunomodulation. In the matched subset, ≥35% seizure frequency reduction occurred in 62.5% of treated children versus 31.2% of controls (p=0.048), with resolution of epileptiform discharges on EEG in 44.2% versus 24.8% (p=0.032). GMFM-66 improvement ≥5 points occurred in 25/45 versus 10/43 children (p=0.007), and Bayley-4 composite scores rose by +7.2±3.1 versus +2.1±2.8 points (p<0.001). At 6 months, treated children had lower IL-6 (9.1±5.25 vs 15.22±7.23 pg/mL; p=0.002) and hs-CRP (0.88±0.52 vs 4.22±2.11 mg/L; p=0.032) than controls. No major safety signals were identified.

Conclusion

Adjunctive UC-MSC-CM was feasible and well tolerated, and was associated with greater seizure and functional improvements alongside favourable IL-6/hs-CRP shifts. These findings support future prospective, biomarker-stratified trials incorporating batch analytics.

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Mesenchymal Stem/Stromal Cells

DISSOLVABLE MICROCARRIERS ENABLE HIGH-YIELD, SCALABLE MSC MANUFACTURING IN SUSPENSION BIOREACTORS

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KEYWORDS: Microcarrier, Stem Cell, Bioreactor.

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Background & Aim

The recent approval of mesenchymal stromal cell (MSC) therapies has intensified the need for efficient and scalable manufacturing processes. A key bottleneck at scale is the use of conventional microcarriers, which complicate cell recovery, reduce yield, and require challenging separation steps. We developed dissolvable microcarriers as an alternative to overcome these limitations for bioreactor-based MSC expansion and demonstrate their use in an automated bioreactor.

Methods, Results & Conclusion

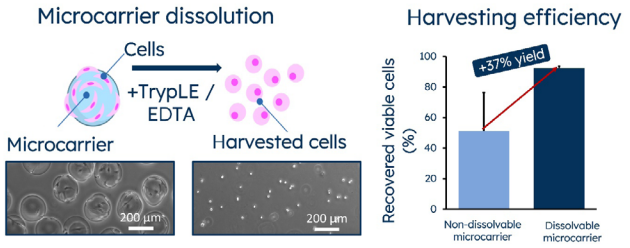
Methodology

In-air microfluidics was employed to produce dissolvable microcarriers composed of alginate with a high-purity gelatin coating. Their performance was evaluated using bone-marrow derived MSCs (BM-MSCs) and benchmarked against two industry standard microcarriers in an Osilaris bioreactor. The bioreactor volume was increased from 125 mL to 1.2L over 14 days by unfolding the expandable bag. Microcarrier surface area was maintained at 21 cm^2/mL, and was doubled on day 8, after which the culture was continued until

growth plateaued.
Cultures were regularly sampled to assess glucose, lactate, cell viability and cell count. Cells were harvested by dissolving microcarriers using TrypLE and EDTA, then cryopreserved and later analysed for MSC identity and potency by flow cytometry (CD73, CD90, CD105, CD14, CD19, CD34, CD45) and trilineage differentiation using histological staining. Experiments were partially conducted in collaboration with Fraunhofer ISC and IBMT institutes.

Results

Exponential cell growth was achieved on the dissolvable microcarriers, with >90% viability maintained and a cell yield of 1.3 billion cells within 14 days of culture with a cell recovery of >90%. The dissolvable microcarriers outperformed industry standard dissolvable microcarriers (1.2 billion cells after 19 days) and non-dissolvable microcarriers (0.8 billion cells after 22 days) in terms of cell yield.
Flow cytometry confirmed maintenance of the BM-MSCs phenotype, with high expression (>90%) of CD73, CD90 and CD105 and low expression (<5%) of CD14, CD19, CD34 and CD45. Trilineage differentiation potential was preserved, as demonstrated by histological stains.
Dissolvable microcarriers offer an efficient way to scale MSC culture using suspension bioreactors, combining high yield (>1 billion in 14 days of culture) while simplifying downstream processing by eliminating the need for physical microcarrier separation and enabling harvest using standard cell culture reagents, enabling GMP compatibility by design.



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Mesenchymal Stem/Stromal Cells

MESENCHYMAL STEM CELL-DERIVED SECRETOME COMBINED WITH NEGATIVE PRESSURE WOUND THERAPY FOR LARGE PERINEAL AND GLUTEAL SOFT TISSUE LOSS WITH URETHRAL AND ANORECTAL RUPTURE: A CASE REPORT

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KEYWORDS: Secretome, Mesenchymal Stem Cell, Perineogluteal soft tissue loss.

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Background & Aim

Background

Extensive perineal and gluteal soft tissue loss associated with urethral and anorectal rupture represents a complex reconstructive challenge, particularly when the wound is exposed to urinary and fecal contamination. Flap reconstruction is commonly considered for large soft tissue defects; however, it may carry a high risk of complications in contaminated wounds and requires complex vascularized tissue transfer.

Aim

This case report aims to describe the clinical outcome of mesenchymal stem cell-derived secretome (MSC-secretome) combined with negative pressure wound therapy (NPWT) as a non-flap treatment approach for managing extensive traumatic perineal and gluteal soft tissue loss complicated by urethral and anorectal rupture.

Methods, Results & Conclusion

Case Presentation

A 33-year-old male presented with massive perineal and gluteal soft tissue loss following a road traffic accident in which he was run over by a truck. The injury was complicated by urethral and anorectal rupture. Initial management included surgical debridement, cystostomy, and colostomy. Due to the extensive open wound and the high risk of contamination from urine and feces, flap reconstruction was not performed. The patient was subsequently managed as an outpatient using MSC-secretome treatment combined with NPWT.

Intervention and Outcome

The MSC-secretome was derived from allogeneic umbilical cord mesenchymal stem cells cultured

under hypoxic preconditioning. MSC-secretome was administered once weekly at a dose of two vials per session. The treatment was repeated 30 times over a period of 30 weeks. NPWT was applied to promote wound bed preparation, granulation tissue formation, and wound contraction. Progressive wound healing was observed throughout the treatment period, with gradual reduction in wound size and improved tissue coverage. Complete wound closure was achieved after 30 weeks without the need for flap reconstruction.

Conclusion

This case demonstrates that the combination of MSC-secretome and NPWT may serve as a feasible non-flap treatment strategy for selected patients with extensive traumatic perineal and gluteal soft tissue loss, particularly when flap reconstruction carries a high risk due to wound contamination.



Figure 1. treatment course of extensive traumatic perineogluteal soft tissue loss using mesenchymal stem cell-derived secretome combined with negative pressure wound therapy. **(A)** Urethral rupture is shown by the light blue arrow, and anorectal rupture is shown by the pink arrow. **(B)** Massive perineal and gluteal soft tissue loss with peri-anorectal rupture and high risk of fecal contamination is indicated by the dark blue arrows. **(C)** Negative pressure wound therapy dressing was applied after initial wound management. **(D)** During outpatient follow-up, serial debridement of necrotic tissue was performed, followed by repeated secretome administration and reapplication of negative pressure wound therapy. Necrotic areas are indicated by the yellow arrows. **(E)** At week 17, progressive wound healing was observed, characterized by wound contraction, granulation tissue formation, and neo-epithelialization, indicated by the green arrows. **(F)** Combined secretome and negative pressure wound therapy was continued until week 30.

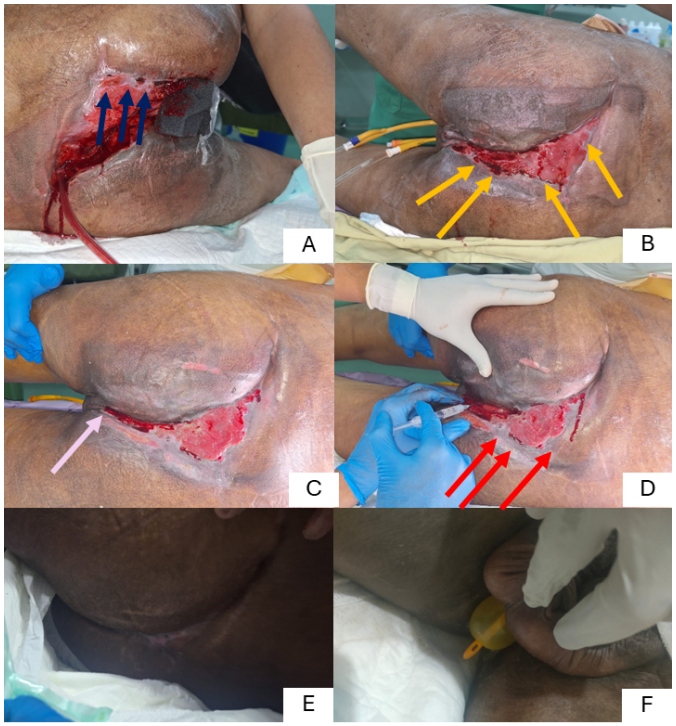


Figure 2. Serial wound healing progression after combined mesenchymal stem cell-derived secretome therapy and negative pressure wound therapy. **(A)** At week 20, the wound showed substantial contraction with newly formed epithelial tissue at the wound margin, indicated by the dark blue arrows. **(B)** At week 24, the residual open wound area continued to decrease. **(C-D)** At week 26, progressive granulation tissue formation, soft tissue coverage, and neoepithelialization were observed, indicated by the red arrows. Gradual closure of the perianorectal wound region is indicated by the pink arrow. **(E-F)** Final clinical appearance showing complete wound closure, minimal residual scarring, and satisfactory soft tissue healing without flap reconstruction.

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Mesenchymal Stem/Stromal Cells

ADJUNCTIVE STEM CELL–DERIVED SECRETOME IN PRIMARY AND SECONDARY SPONTANEOUS PNEUMOTHORAX: AN EXPLORATORY CASE SERIES

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KEYWORDS: Stem Cell–Derived Secretome, Spontaneous Pneumothorax, Adjunctive therapy.

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Background & Aim

Spontaneous pneumothorax presents with a variable clinical course, ranging from self-limiting disease in primary cases to more complex and prolonged recovery in secondary cases with underlying lung pathology. Stem cell–derived secretome has emerged as a potential regenerative approach due to its paracrine effects, including immunomodulation and promotion of tissue repair, as demonstrated in preclinical lung injury models. However, clinical evidence in pneumothorax remains limited.
To explore the potential role of stem cell–derived secretome as an adjunctive therapy in patients with primary and secondary spontaneous pneumothorax.

Methods, Results & Conclusion

We report two cases of spontaneous pneumothorax managed with standard treatment, including chest tube insertion, combined with adjunctive administration of stem cell–derived secretome. Secretome was administered intramuscularly at a dose of 1 mL per injection, three times per week for two consecutive weeks (total of six injections). Clinical symptoms and serial chest radiographs were evaluated.
The cases included a 28-year-old female with primary spontaneous pneumothorax and a 62-year-old male with secondary spontaneous pneumothorax complicated by hydropneumothorax and multiple comorbidities. In the primary case, radiographic improvement was observed by day 5 following chest tube insertion, with complete lung re-expansion achieved by days 12. In the secondary case, radiographic improvement was observed by day 3 after initiation of treatment, with complete re-expansion achieved by day 9. The patient also reported subjective improvement in dyspnea within approximately one day. No adverse events related to secretome administration were observed.
Adjunctive secretome therapy was well tolerated and associated with clinical and radiologic improvement in both cases. The relatively favorable clinical course observed in the secondary pneumothorax case, despite underlying lung disease, may warrant further investigation. However, causality cannot be established due to the self-limiting nature of pneumothorax and concurrent standard treatment. These findings should be considered hypothesis-generating, and further controlled studies are needed.

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Mesenchymal Stem/Stromal Cells

SERIAL IMPROVEMENT OF RENAL BIOMARKERS FOLLOWING REPEATED INTRAMUSCULAR ADMINISTRATION OF MSC-DERIVED CONDITIONED MEDIUM IN CHRONIC KIDNEY DISEASE: A LONGITUDINAL CASE REPORT

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KEYWORDS: Chronic Kidney Disease, Mesenchymal Stem Cell, Renal Biomarkers.

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Background & Aim

Chronic kidney disease (CKD) is a progressive condition characterized by persistent inflammation, fibrosis, microvascular injury, and gradual loss of renal function. CKD with severely decreased Glomerular Filtration Rate (GFR) remains difficult to manage because currently available therapies largely delay progression rather than restore renal function. MSC-derived conditioned medium is a cell-free regenerative therapy with potential anti-inflammatory and renoprotective effects in preclinical in vitro and in vivo studies. However, clinical data describing serial biomarker responses after repeated administration remain limited. This case report aimed to evaluate serial changes in renal biomarkers following repeated intramuscular (IM) administration of MSC-derived conditioned medium in a patient with CKD. This case report may contribute to the clinical evidence supporting cell-free regenerative therapy as a potential strategy for slowing disease progression in patients with CKD.

Methods, Results & Conclusion

The patient was diagnosed with CKD-G4 (severely decreased GFR) according to KDIGO 2024 criteria, three months before treatment and had been receiving standard-of-care management since diagnosis. MSC-derived conditioned medium (supplied by Regenic, Indonesia) was administered intramuscularly on days 0, 7, 14, and 21. Renal biomarkers was monitored longitudinally using serial measurements of serum creatinine, estimated-GFR (eGFR), ureum, and urinary albumin-to-creatinine ratio (UACR). Biomarkers were evaluated over a

35-day follow-up period. Progressive improvement in renal biomarker was observed after MSC-derived conditioned medium administration. Serum creatinine decreased from 3.84 to 2.80 mg/dL, accompanied by an increase in eGFR from 15.80 to 21.41 mL/min/1.73 m^2. UACR declined from 1,198 to 623 mg/g, whereas ureum remained relatively stable (44-56 mg/dL) throughout follow-up. Longitudinal analysis demonstrated a consistent trend toward improved kidney biomarkers and reduced urinary albumin excretion. The concurrent reduction in albuminuria and improvement in renal function may suggest a potential biological response to this therapy. Although interpretation is limited by the single-patient design and absence of a control group, these findings support further investigation of MSC-derived conditioned medium as a cell-free regenerative strategy for CKD.

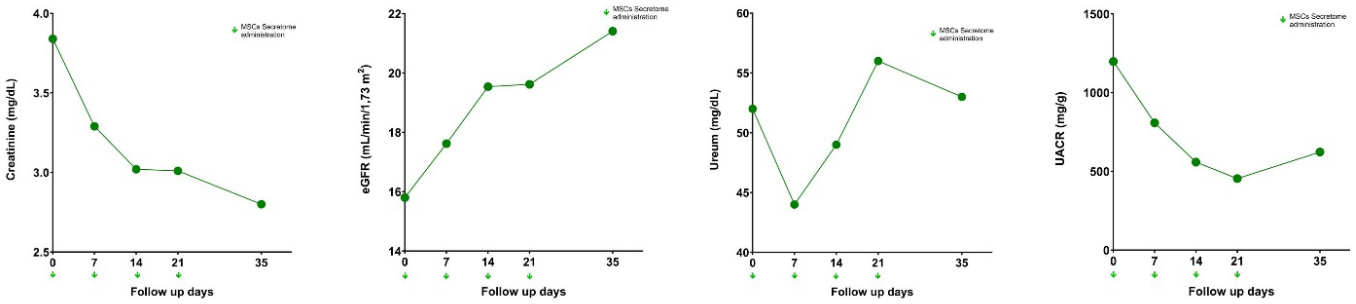


Figure 1. Longitudinal changes in renal biomarkers following repeated intramuscular administration of MSC secretome in a patient with CKD-G4. Serial measurements demonstrated a progressive reduction in serum creatinine and UACR, accompanied by an increase in eGFR over the 35-day follow-up period. Ureum levels remained relatively stable. Green arrows indicate the timing of MSC-derived conditioned medium administration (days 0, 7, 14, and 21).

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Mesenchymal Stem/Stromal Cells

A 50L BIOREACTOR CULTURE SYSTEM UTILIZING SHOWNIN NCMISSION™ MSC CLUTURE MEDIUM AND MICROCARRIERS FOR THE LARGE-SCALE EXPANSION OF HUMAN MESENCHYMAL STROMAL CELLS TO YIELD OVER 50 BILLION CELLS

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KEYWORDS: mesenchymal stromal cells, scale up to 50L, 3D culture of MSC.

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Background & Aim

Human mesenchymal stromal cells (hMSCs) are extensively utilized in regenerative medicine research and clinical translation. With over 10 MSC-based therapies approved commercially worldwide, the large-scale expansion of MSCs remains a critical bottleneck in the industry. Efficiently manufacturing higher-quality MSCs in a single batch is a paramount challenge in the global regenerative medicine sector. To address this, Shownin Biotechnologies has developed a 3D MSC culture system capable of harvesting over 50 billion hMSCs within a 50L bioreactor.

Methods, Results & Conclusion

Methods

A large-scale hMSC manufacturing system was established utilizing a 50L bioreactor system paired with NcMission™ MSC Culture Medium and Shownin's proprietary microcarriers. At harvest, the expanded cells were dissociated using unique lysis buffer and collected via a continuous-flow centrifugation system. Finally, the cells were formulated and cryopreserved using an automated filling system with Shownin's hMSC Cryopreservation Medium. Post-thaw cell viability, recovery rate, and quality attributes were comprehensively evaluated.

Results

Initiating the culture on Day 0 with an inoculation of 2.2×10^9 hMSCs, a total yield of 6×10^10 cells was harvested within a 4-day culture period. The harvested cells were formulated into ready-to-use MSC products at a density of 5×10^7 cells/vial, supporting direct intravenous infusion immediately post-thaw. Over the 4 days, the hMSCs achieved a 27.6-fold expansion with a consistent viability profile above 98%. Phenotypic analysis demonstrated that the expression of CD73, CD90, CD105 exceeded 99%, while CD45, CD34, CD14, CD19, HLA-DR remained below 1%. Trilineage differentiation proceeded normally, and the cells exhibited an immunosuppressive capacity of 92.5%. Residual microcarrier testing returned negative results. Furthermore, the cryopreserved cells exhibited a post-thaw viability exceeding 90% with a 99% cell recovery rate.

Conclusion

Shownin's MSC culture system enables the one-step expansion and harvest of over 50 billion high-quality hMSCs in a 3D 50L bioreactor system, equivalent to 1,000 clinical doses (5×10^7 cells/dose). Compared to traditional 2D culture methods, this system increases MSC yield by 5 to 10-fold while reducing quality control and testing costs by 5 to 10-times. This platform holds the potential to be further scaled up to 100–200L, which can accelerate the large-scale commercial application of MSC-based therapeutics.

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Process Development, and Manufacturing & Commercialization

VALIDATION OF THE AUTOMATED MICROBIAL DETECTION SYSTEM FOR STERILITY TESTING ACROSS THE MANUFACTURING PROCESS OF HUMAN ADIPOSE-DERIVED MESENCHYMAL STROMAL CELLS

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KEYWORDS: Sterility Testing, Automated Microbial Detection System, Method validation.

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2. Excellence Center for Advanced Therapy Medicinal Products (EC-ATMPs), King Chulalongkorn Memorial Hospital, The Thai Red Cross Society, Bangkok, Thailand.

Background & Aim

Sterility testing is critical to ensuring the safety and quality of Advanced Therapy Medicinal Products (ATMPs) prior to clinical administration. For small-volume cell therapies, conventional compendial methods (e.g., Ph. Eur. 2.6.1 or USP <71>) are often impractical due to large volume requirements and a mandatory 14-day incubation period, which is incompatible with short-shelf-life products. This study validated the BACTEC™ FX40 automated microbial detection system as a rapid alternative sterility test across critical stages of the human adipose-derived mesenchymal stromal cell (AD-MSC) manufacturing workflow.

Methods, Results & Conclusion

Method suitability testing was performed in triplicate across four distinct product matrices: the aqueous

layer of lipoaspirate, cell stock in cryopreservation medium, final drug MSC product in 0.9% NaCl-based solution, and used expansion culture media. Samples were inoculated with six compendial challenge microorganisms (aerobic, anaerobic, and fungal species at a low inoculum of <33 CFU) into BACTEC™ Aerobic, Anaerobic, and Myco/F Lytic culture vials to evaluate microbial recovery and potential matrix interference. This system successfully met all predefined acceptance criteria, demonstrating robust microbial recovery across all four matrices without false negatives or inhibitory interference. Time-to-detection (TTD) was highly efficient, with all bacterial strains detected within 3 days and fungal strains within 5 days of incubation. All negative controls (sterile water and uninoculated matrices) remained negative throughout the study period. Performance validation of the automated Microbial Detection System provides a rapid, sensitive, and volume-efficient alternative to conventional sterility testing for AD-MSCs, in accordance with Ph. Eur. 2.6.27 guidelines. By significantly reducing turnaround time from 14 days to a maximum of 5 days, this method supports the timely, safe, and efficient release of short-shelf-life cellular products.

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Process Development, and Manufacturing & Commercialization

INVERTED FLOW MONOLITH MEDIA FOR PURIFICATION OF LARGE PLASMID DNA REQUIRED FOR CELL AND GENE THERAPY

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KEYWORDS: Plasmid DNA, Cell and gene therapy, Monoliths.

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3. BOKU University, Vienna, Austria.
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Background & Aim

Plasmid DNA (pDNA) is a critical raw material for viral vector manufacturing and for direct transfection in cell and gene therapy (CGT). The quality of pDNA often determines the quality of viral vectors and the outcome of therapeutic interventions. For CGT applications, the large size of pDNA and its inherent viscosity pose significant challenges for downstream purification. Established bead-based resins suffer from low binding capacity and long cycle times, compromising both productivity and quality.

Monolithic stationary phases that utilize convective mass transport within open-pore structures can help address these limitations. This study evaluates a novel monolithic media featuring an 'inverted flow morphology'—hollow spheres interconnected by large pores with porosities reaching 80%. Its wider pores allow unhindered access for large pDNA molecules to functional binding sites, facilitating a faster, more robust, and scalable purification process at significantly lower backpressures than current state-of-the-art monoliths.

Methods, Results & Conclusion

A quaternary amine (QA)-functionalized media was evaluated against market-leading QA columns for purification of pDNA ranging from 3 to 12 kb (pUC19, pRep2Cap9 pHelper). To assess process robustness, crude bacterial lysates were sourced from various preparation workflows. Post-purification, pDNA fractions were quantitatively analyzed for step yield, supercoiled content (% SC), absorbance ratios (A260/A280), and residual host-cell impurities. Pressure flow curves for established and new monoliths were generated.

The media consistently delivered high yields (>70%) and high-resolution separations across the pDNA size range tested even at flow rates up to 20 CV/min, underscoring suitability for high throughput manufacturing. The purified pDNA exhibited >90% of supercoiled pDNA content and A260/A280 ratios between 1.8-2.0, meeting stringent quality criteria. Furthermore, the process achieved significant clearance of host-derived impurities, including endotoxins and RNA.

The 'inverted flow' media represents a new category of chromatography media, enabling purification of large plasmids at high flow rates with only one-third the pressure drop of established monoliths. Taken together, these data show that monolithic materials can be rationally designed to couple low-pressure operation with high-resolution separation of supercoiled pDNA, providing a promising platform for the scalable manufacture of plasmids for CGT applications.

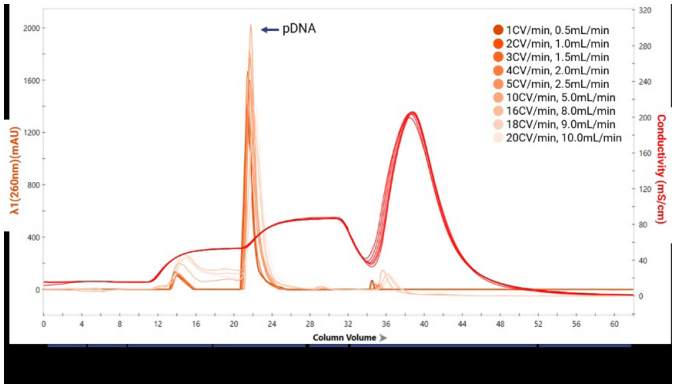


Figure 1. Chromatographic overlays of pRep2Cap9 purification

runs using AXISFLOW™ QA (0.5 mL) at varying flow rates, ranging from 1 CV/min to 20 CV/min.

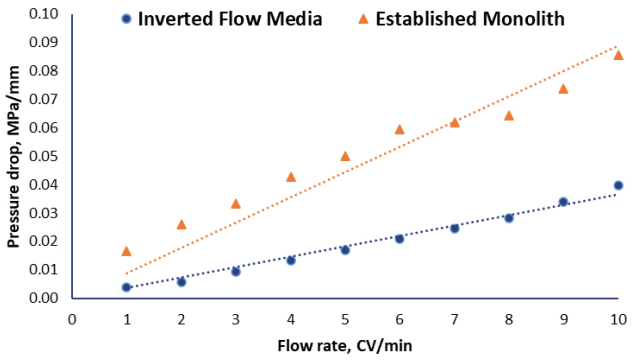


Figure 2. Normalized pressure drop (MPa/mm) of columns across various flow rates.

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Process Development, and Manufacturing & Commercialization

A NOVEL MEMBRANE-FREE IN-LINE MICROFLUIDICS MEDIA EXCHANGER FOR CONTINUOUS 3D IPSC AGGREGATES MANUFACTURING

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KEYWORDS: iPSC manufacturing, Closed bioprocessing, Single-use technologies.

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Background & Aim

Three-dimensional (3D) induced pluripotent stem cell (iPSC) aggregate culture is promising for scalable cell manufacturing. However, fed-batch media exchange is labor-intensive and can cause aggregate loss, shear damage, and contamination, while membrane-based perfusion is prone to fouling and clogging. Here, we present a portable membrane-free microfluidic system for automated, closed media exchange in continuous 3D iPSC manufacturing. The device operates at 1-1.5 mL/min and is designed for continuous media perfusion for pilot- to small scale-bioreactors (0.5 to 2L).

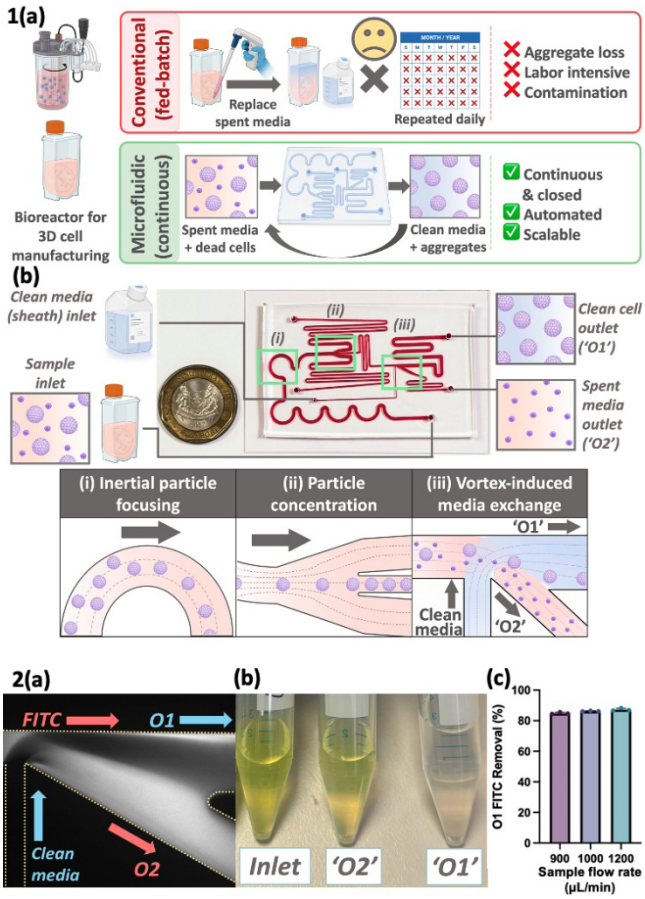
Methods, Results & Conclusion

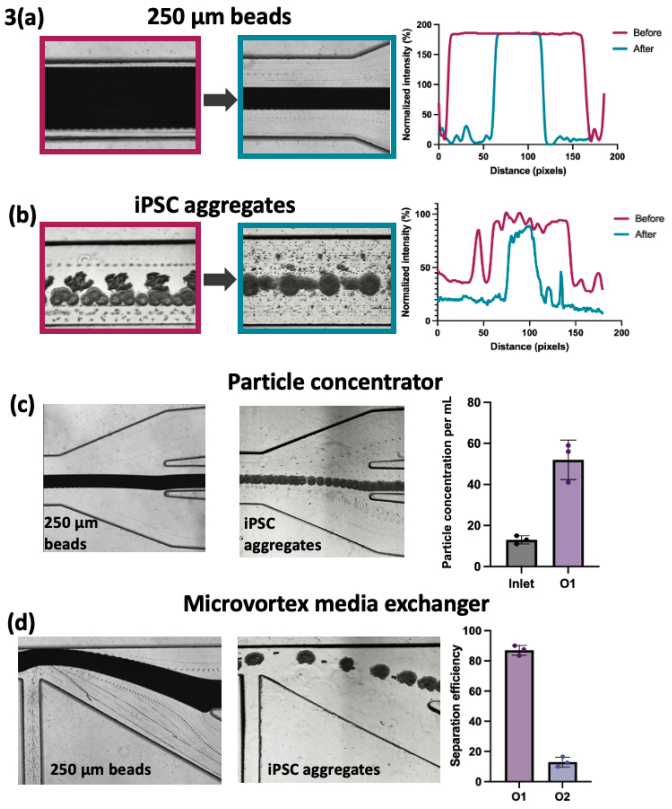
The PDMS device has three functional regions (Fig. 1). First, microcarriers and cell aggregates (~50-300 µm) are focused in a serpentine channel. Excess particle-free spent media is removed through side outlets in the concentrator region. Clean media is introduced at an asymmetric junction to create a microvortex that directs smaller debris and spent media to the waste outlet (O2), while larger aggregates continue to the cell outlet (O1) and are resuspended in clean media, enabling membrane-free media exchange.

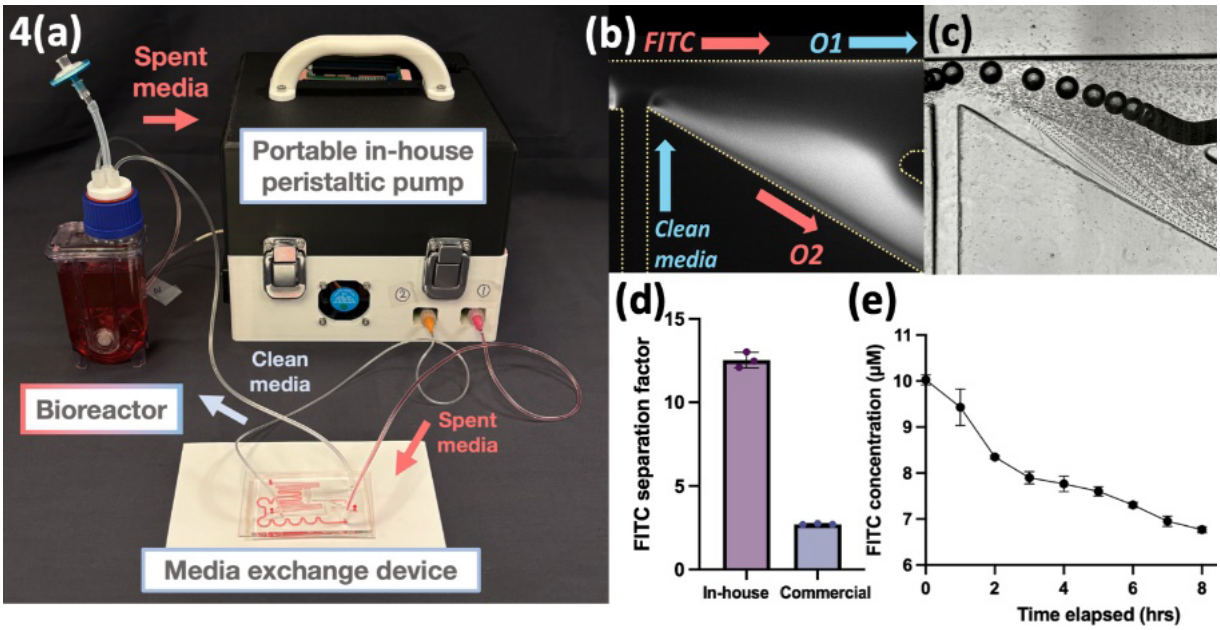
Media exchange was first evaluated using fluorescein isothiocyanate (FITC) as spent-media (Fig. 2). Fluorescence imaging showed clear separation between FITC-containing spent media and clean media, with FITC-depleted media collected at O1. Particle focusing and concentration were assessed using 250 µm polystyrene beads and iPSC aggregates (~50-200 µm) (Fig. 3). High-speed imaging and line scans confirmed focusing after the serpentine region, enabling removal of particle-free spent media through side outlets. At the exchange region, particles and aggregates were focused toward O1, achieving ~87% bead recovery.

For continuous operation, the chip was integrated with a portable in-house dual-channel peristaltic pump with flow-sensor feedback in a closed bioreactor setup (Fig. 4). Compared with commercial syringe and peristaltic pumps, the system improved FITC separation through automated flow-rate control while maintaining similar aggregate focusing. As proof-of-concept, 8 h of media exchange at 1 mL/min was demonstrated in a 1 L bioreactor which showed a gradual decrease in FITC concentration. .

Overall, this work shows the potential of a portable membrane-free microfluidic perfusion platform for scalable 3D iPSC manufacturing. Ongoing work compares iPSC expansion under manual fed-batch and microfluidic continuous perfusion to assess feasibility for closed-system cell therapy bioprocessing.


1(a)
Conventional (fed-batch)
Replace spent media
Repeated daily
Aggregate loss
Labor intensive
Contamination
Microfluidic (continuous)
Spent media + dead cells
Clean media + aggregates
Continuous & closed
Automated
Scalable
Bioreactor for 3D cell manufacturing
(b)
Clean media (sheath) inlet
Sample inlet
Clean cell outlet ('O1')
Spent media outlet ('O2')
(i) Inertial particle focusing
(ii) Particle concentration
(iii) Vortex-induced media exchange
'O1'
'O2'
Clean media
2(a)
(b)
(c)
FITC
O1
Clean media
O2
Inlet
'O2'
'O1'
O1 FITC Removal (%)
Sample flow rate (µL/min)


3(a)
250 µm beads
Normalized intensity (%)
Distance (pixels)
Before
After
(b)
iPSC aggregates
Particle concentrator
(c)
250 µm beads
iPSC aggregates
Particle concentration per mL
Inlet
O1
Microvortex media exchanger
(d)
250 µm beads
iPSC aggregates
Separation efficiency
O1
O2


4(a)
Spent media
Portable in-house peristaltic pump
Clean media
Bioreactor
Spent media
Media exchange device
(b)
FITC
O1
Clean media
O2
(c)
(d)
FITC separation factor
In-house
Commercial
(e)
FITC concentration (µM)
Time elapsed (hrs)

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Process Development, and Manufacturing & Commercialization

RISK-BASED DESIGN OF ASEPTIC PROCESS SIMULATION FOR GMP OPEN-SYSTEM ATMP MANUFACTURING

C. Intasuk[1, 2], R. Singsathit[1, 2], P. Ruentip[1, 2], P. Lunka[1, 2], P. Jenkham[1, 2], N. Kittipongpisuth[1, 2], P. Jetinai[1, 2], C. Koaykul[1, 2], T. Bunaprasert[1, 2]

KEYWORDS: Aseptic process simulation (APS), Advanced Therapy Medicinal Products (ATMPs), Quality risk management (QRM).

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Background & Aim

Aseptic process simulation (APS), also known as media fill, is a core GMP requirement for demonstrating sterility assurance in the manufacture of advanced therapy medicinal products (ATMPs). PIC/S GMP Annex 1 (Sections 9.32–9.49) requires APS as part of the initial process validation. Annex 2A (Section 5.19) provides additional flexibility for infrequent ATMP production. However, applying conventional APS guidance, originally written for automated parenteral drug filling, directly to ATMP manufacturing is not straightforward. ATMPs typically involve ultra-small batch sizes, highly manual, open-system processes, multi-day aseptic operations without the option of terminal sterilization, and non-sterile or patient-derived starting materials that carry an intrinsic risk of contamination. These features make standard APS approaches difficult to implement without adaptation. This work presents a quality risk management (QRM)-guided framework for designing APS programs in a two-dimensional (2D) static culture, open-system ATMP manufacturing, aligned with PIC/S Annex 1 and Annex 2A, and informed by ATMP-specific industry guidance such as BioPhorum (2023).

Methods, Results & Conclusion

The framework covers six key areas: (1) microbial risk assessment to distinguish product-pathway from non-product-pathway interventions; (2) worst-case bracketing based on open-system duration, operator occupancy, and high-risk aseptic manipulations; (3) selection and validation of appropriate simulation media; (4) an operator qualification structure covering Grade A operators, Grade B support staff, and ancillary personnel; (5) a risk-based unit incubation strategy that prioritizes final drug product containers while appropriately managing intermediate process streams; and (6) process segmentation to keep multi-day APS programs operationally practical without reducing contamination control scope. This framework provides a practical, regulatory-aligned basis for designing APS programs that are achievable for ATMP processes, supporting both patient safety and GMP compliance in open-system cell and gene therapy manufacturing.

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Process Development, and Manufacturing & Commercialization

AUTOMATED HIGH-THROUGHPUT AMPLIFIED DSDNA PURIFICATION & DESALTING USING MONOLITH PLATE

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KEYWORDS: monolith chromatography, dsDNA purification & desalting, mRNA screening.

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Background & Aim

PCR amplification is a common method for high-throughput small scale DNA production. Before use as a template in IVT reactions for mRNA screening, PCR products must be purified. At therapeutic scales, anion exchange chromatography can be used to obtain highly pure linear pDNA, which is typically eluted at high salt concentrations. However, small scale desalting by ultrafiltration/diafiltration often suffers from low recovery due to membrane adsorption and dead volume. Here we utilize monolithic chromatography with CIM Swiper monolith plate for automated, high-throughput dsDNA purification with low salt elution.

Methods, Results & Conclusion

To address these challenges, we evaluated dsDNA recovery, integrity and overall processing time. The Swiper monolith leverages hydrogen bonding in combination with weak anion-exchange to enable high-recovery chromatographic purification of mRNA at neutral pH. In addition, 96-well 0.05mL monolithic plates support automated high-throughput screening at lab scale.
Taken these together, we started with utilizing CIM Swiper Monolithic 96-well plates for dsDNA desalting. We achieved 74% recovery rate for dsDNA desalting under IVT buffer condition. Then after buffer condition screening, we succeed in loading PCR products on Swiper plates and elution with IVT compatible buffer. We directly added the elution from Swiper into IVT reaction as template, without losing mRNA titer or integrity. Finally, with centrifuge

integrated in the automation platform, we achieved monolith-based fully automated high-throughput dsDNA purification and desalting solution at lab scales within 40 min.
In conclusion, these results demonstrate that Swiper monolith enables efficient dsDNA chromatographic purification and desalting at lab-scale, suitable for automated high-throughput screening. Moreover, the eluted product can be directly employed as the template for IVT reaction, thereby simplifying the workflow and facilitating scalable implementation.

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Process Development, and Manufacturing & Commercialization

SCALABLE, CLOSED-SYSTEM PRODUCTION OF IPSC-DERIVED NK CELLS INTEGRATING STIRRED-TANK BIOREACTOR DIFFERENTIATION AND COUNTERFLOW CENTRIFUGATION

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KEYWORDS: Cell Therapy Manufacturing, Automated Cell Processing, Regenerative Medicine.

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Background & Aim

iPSC-derived NK cells offer a scalable, donor-independent source for allogeneic cell therapy. However, clinical translation requires closed, GMP-compatible manufacturing processes that minimise manual handling and batch variability. Here we describe a proof-of-concept workflow integrating stirred-tank bioreactor differentiation with automated downstream processing towards a fully closed iPSC-to-NK manufacturing platform.

Methods, Results & Conclusion

Methods

Human iPSCs underwent two-stage directed differentiation: (i) iPSC-to-HSPC specification using an optimised in-house chemically defined medium, and (ii) HSPC-to-NK commitment and maturation. Both stages were conducted in BioBLU® single-use stirred-tank bioreactors at 100 mL working volume with continuous monitoring of dissolved oxygen, pH, temperature, and agitation. NK expansion and maturation utilised CTS™ NK-Xpander™ Medium, a defined, serum-free formulation compatible with GMP manufacturing. Downstream harvest, washing, and concentration were performed using the CTS™ Rotea™ Counterflow Centrifugation System, preserving closed-system integrity throughout.

Results

Proof-of-concept runs demonstrated feasibility of executing the full iPSC-to-NK differentiation sequence within a closed bioreactor environment. CTS™ Rotea™ system integration at harvest enabled automated concentration and buffer exchange without open manipulation.

Conclusion

This work establishes a closed-system framework for scalable iPSC-derived NK cell manufacturing. Combining stirred-tank bioreactor technology with automated counterflow centrifugation addresses a key bottleneck in allogeneic cell therapy production. Ongoing work targets quantitative yield, purity, and functional characterisation to support GMP translation.

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Process Development, and Manufacturing & Commercialization

A BULK FORMULATION STRATEGY IMPROVES FILL UNIFORMITY AND MANUFACTURING ROBUSTNESS OF KERAHEAL-ALLO, AN ALLOGENEIC KERATINOCYTE-BASED DRUG PRODUCT

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KEYWORDS: Manufacturing robustness, Bulk formulation.

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Background & Aim

Manufacturing robustness and fill-to-fill consistency are critical for cell-based drug products, especially when viscous excipients are combined with cell suspensions. Keraheal-Allo is an allogeneic keratinocyte-based drug product formulated with poloxamer in a prefilled syringe. The previous formulation/filling process required repeated syringe-by-syringe preparation, in which each cell suspension aliquot was mixed individually with poloxamer before filling. This workflow was operationally complex and potentially vulnerable to handling-related variability, including differential cell suspension loss during preparation. To improve process efficiency and product uniformity, the formulation/filling step was redesigned as a pooled bulk formulation followed by aliquoted filling into prefilled syringes.

Methods, Results & Conclusion

Methods

The formulation/filling process was revised by replacing repeated syringe-level formulation with pooled bulk formulation followed by aliquoted

filling into prefilled syringes. Comparability was assessed using historical pre-change data and representative post-change batches. Process performance was evaluated by in-process fill measurements and variability analysis, while product quality was assessed using predefined release and characterization assays, including content, identity, purity, residual impurities, and potency-associated functions.

Results

All evaluated quality attributes remained within predefined specifications after process implementation. The revised workflow reduced handling complexity and improved fill-to-fill consistency, with fill variability decreasing from 3.93% to 2.81% CV. Total cell count and total protein content remained comparable before and after the change (p=0.32 and p=0.78, respectively). Post-change lots met all predefined in-process and final product acceptance criteria, with no adverse trends in quality, identity, purity, residual impurities, or potency-associated assays.

Conclusion

Pooled bulk formulation followed by aliquoted filling simplified manufacturing operations and improved fill uniformity while maintaining product comparability. These results support the revised workflow as a practical process improvement strategy to enhance manufacturing robustness without compromising critical quality attributes of Keraheal-Allo.

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GMP PRODUCTION AND PRECLINICAL EVALUATION OF NASAL TURBINATE–DERIVED STEM CELLS FOR RHEUMATOID ARTHRITIS

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KEYWORDS: Human nasal turbinate-derived stem cells, Cell therapy, GMP manufacturing.

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Background & Aim

Human nasal turbinate-derived stem cells (hNTSCs) are tissue-derived adult stem cells that exhibit robust proliferative capacity and distinct immunomodulatory properties, offering therapeutic advantages for inflammatory diseases. Rheumatoid arthritis (RA) remains a chronic autoimmune disorder with incomplete responses to current biologics. While cell therapies are promising, clinical translation requires reproducible manufacturing and rigorous safety validation. In this study, we developed a clinical-grade injectable hNTSC product for RA treatment by integrating a GMP-equivalent manufacturing process, systematic quality control testing, and GLP-compliant nonclinical safety, biodistribution, and efficacy assessments. This integrated framework demonstrates the potential of hNTSCs as a distinct and translatable stem cell platform for RA therapy.

Methods, Results & Conclusion

Methods

Clinical-grade hNTSCs were manufactured via a GMP-equivalent process. Quality control included flow cytometry (FACS) for identity/purity, in vitro differentiation assays, and safety testing (viability, sterility, mycoplasma, endotoxin). Biodistribution was evaluated using a validated TaqMan-based quantitative PCR (qPCR) assay targeting human ALU sequences. GLP-compliant nonclinical studies evaluated single-dose biodistribution, repeated-dose toxicity, tumorigenicity, and efficacy in a collagen-induced arthritis (CIA) mouse model.

Results

The manufacturing process consistently produced reproducible hNTSC batches meeting all release criteria. FACS and differentiation assays confirmed satisfactory cell identity, purity, and biological characteristics. The qPCR assay sensitively detected hNTSC-derived DNA, showing predominant early localization in lungs followed by a time-dependent decline. Repeated-dose toxicity and tumorigenicity studies demonstrated no treatment-related mortality, systemic toxicity, or tumor formation. In the CIA model, hNTSCs significantly attenuated arthritis severity, joint destruction, and histopathological scores.

Conclusions

We successfully established a GMP-equivalent manufacturing process, comprehensive QC characterization (FACS and functional assays), and GLP-compliant nonclinical safety and efficacy profiles for hNTSC therapy. These findings support clinical translation of hNTSCs for rheumatoid arthritis treatment.

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Process Development, and Manufacturing & Commercialization

SIMPLE NOVEL BIOLUMINESCENT ASSAYS FOR DETECTING AAV NEUTRALIZING AND TOTAL ANTIBODIES IN SERUM SAMPLES

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KEYWORDS: AAV, Neutralizing Antibody, AAV Total Antibody.

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Background & Aim

Adeno-associated virus (AAV) is a promising tool for gene therapy. Unfortunately, pre-existing anti-AAV antibodies can severely limit therapeutic efficacy and available methods for detecting anti-AAV antibodies often require multi-day protocols, extensive hands-on time and specialized instrumentation.
Here we address these limitations with multiple novel assays for detecting anti-AAV Neutralizing Antibodies (NAbs) and Total Antibodies (TAbs) in serum samples.

Methods, Results & Conclusion

The first assay is a cell-based transduction inhibition (TI) assay designed to detect NAbs and inhibiting factors in serum. The assay utilizes NanoLuc® luciferase, which was found to be over 700-fold brighter than firefly luciferase, significantly enhancing assay sensitivity. Optimized for AAV2, AAV8, and AAV9 serotypes, the assay operates effectively at low multiplicities of infection (MOI ≥100) and minimal serum dilutions (MRD 1:3), enabling detection of low-titer antibodies. At higher MOIs (1,000–10,000), the assay's runtime can be reduced to as little as six hours, facilitating same-day results. Validated thaw-and-use cells further streamline the workflow and improve robustness.
The second approach involves both a solid-phase and a solution-phase immunoassay employing split NanoLuc technology for TAb detection. The solution phase method employs a completely homogeneous, no wash protocol that can be completed in as little as two hours. Ongoing studies aim to further characterize and validate its performance.
These assays provide sensitive, rapid, and user-friendly methods for detecting anti-AAV antibodies, addressing key limitations of existing technologies. Future studies will focus on expanding the assays to additional AAV serotypes and validating their utility in diverse settings.

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ASSESSING THE POTENTIAL OF CONJUGATED OLIGOELECTROLYTES (COES) IN REAL-TIME CELL BINDING ASSAYS FOR FC-MEDIATED MONOCYTE-TUMOUR CELL ENGAGEMENT

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KEYWORDS: Fc-mediated cell engagement, Real-time cell binding assay, Therapeutic antibody screening.

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Background & Aim

Fc receptor (FcR)-mediated recruitment of monocytes to antibody-opsonised tumour cells is a key mechanism underlying the efficacy of many immune-engaging therapeutics. However, most current assays provide only static or population-level measurements, offering limited insight into the dynamics of cell–cell interactions. We investigated the use of conjugated oligoelectrolytes (COEs), commercialised as AcoerelaTM dyes, combined with real-time cell binding assays (RT-CBA) to generate kinetic profiles of Fc-dependent monocyte–tumour interactions using J774A.1 and U937 cell models.

Methods, Results & Conclusion

Methods

J774A.1 and U937 monocytes were labelled with COEs under optimised conditions that maintained cell viability. Adherent target cell lines expressing an undisclosed antigen were opsonised with mouse monoclonal antibodies and seeded into LigandTracer compatible plates. The interactions of labelled monocytes with opsonised target cells were monitored in real time using LigandTracer Green technology. Association and dissociation kinetics, binding intensity, residence time, and temporal interaction patterns were analysed.

Results

Preliminary results suggest that COEs provided bright and stable cell labelling compatible with continuous LigandTracer detection. This compatibility of COEs with RT-CBA enables the measurement of association and dissociation kinetics, residence times, and analysis of complex patterns of cell engagement that are difficult to monitor using conventional endpoint assays. Differences between J774A.1 and U937 cells were also observed, suggesting that Fc receptor

expression and cellular phenotype contribute to variations in binding behaviour.

Conclusion

Combining COEs fluorescent labelling with LigandTracer RT-CBA establishes a scalable platform for the real-time analysis of Fc-mediated monocyte–tumour interactions. This approach may support preclinical evaluation and ranking of therapeutic antibodies, bispecific molecules, and engineered effector cells by providing kinetic insights that are relevant to their expected functional activity.

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Process Development, and Manufacturing & Commercialization

LONG-TERM STORABLE PLATELETS FOR CLINICAL APPLICATIONS: AUTO-PRP AND ASCL-PLC, ALLO-MANUFACTURING PLATELETS FROM ADIPOSE-TISSUES

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KEYWORDS: Platelets, Mesenchymal stem cell, regenerative medicine.

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Background & Aim

Platelets have not only a hemostatic effect but also a tissue repair effect. For tissue repair, platelet-rich plasma (PRP), which is a platelet fraction extracted from autologous blood, is used for various clinical field. Because PRP is autologous blood, it is thought to have a relatively low threshold for use as a regenerative therapy. However, it is difficult to obtain consensus on effectiveness in numerous clinical studies, and the discrepancies might be associated with the inter-individual variations in platelet count and function and the various methods for PRP preparation. In addition, platelets are known to have a short shelf life (PRP is several hours, platelets for transfusion are several days). To contribute to solving these problems, we have developed two kinds of platelets, auto PRP, which is profiled for platelet count and cytokine/growth factor levels, and ASCL-PLC, which is manufactured from mesenchymal stem cell line (2019 Blood, Matsubara et al). GMP-grade ASCL-PLC can be standardized, and a clinical study showed the effect in non-healing wound. Based on a development of platelets for clinical applications, we have developed a method to preserve platelet function and store it for a long time. In this study, we focused on the cryopreservation stability (-80 degree) of PRP and ASCL-PLC.

Methods, Results & Conclusion

PRP was prepared with centrifuge, and then the preservative reagent was added to PRP sample. ASCL-PLC was manufactured from ASCL with culture media for platelet differentiation for 14 days. Since platelets are anucleate, cell life and death and function were examined based on responses to stimuli. We measured growth factor levels in the presence and absence of stimulation in PRP and ASCL-PLC after storage. As a result, (1) cell number during storage was not significant different between PRP (n=3) and ASCL-PLC(n=3) , (2) the growth factor (basic-FGF) level measured by ELISA was 55.4 pg/mL in the plasma for PRP stored for 6 months, and 34.8 pg/mL was released from platelets upon stimulation. In ASCL-PLC stored for 12 months, 466.2 pg/mL was released from cells upon stimulation. Although basic-FGF levels in PRP was lower than that in ASCL-PLC, PRP stored by our method kept function for a long-term storage. We are continuing to accumulate data on cytokine/growth factor levels of PRP and ASCL-PLC under long-term storage.

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LINKING CRITICAL MATERIAL ATTRIBUTES (CMAS) TO CRITICAL QUALITY ATTRIBUTES (CQAS): AN FMEA-BASED RAW MATERIAL CRITICALITY ASSESSMENT FOR GMP MANUFACTURING OF AUTOLOGOUS ADIPOSE-DERIVED MESENCHYMAL STROMAL CELLS (MSCS)

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KEYWORDS: Critical Material Attributes, Quality Risk Management, Mesenchymal Stromal Cells.

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Background & Aim

Autologous adipose-derived mesenchymal stromal cell (MSC) products depend critically on the quality of their starting materials, human tissue (lipoaspirate) and ancillary raw materials, key determinants of manufacturing consistency and product quality. Aligned with PDA Technical Report No. 81 (TR-81), ICH Q8 and Q9 guidelines, and a GMP PIC/S quality

system, this study established a risk-based control strategy linking Critical Material Attributes (CMAs) of input materials to the product's Critical Quality Attributes (CQAs).

Methods, Results & Conclusion

Raw materials were mapped across the manufacturing workflow, covering lipoaspirate starting material and ancillary materials (i.e., culture media, reagents and enzymes, single-use consumables, and carbon dioxide gas). For each material, CMAs were identified and their potential impact on product CQAs (identity, viability, purity, potency, sterility, safety, and viable cell number) were assessed to classify materials as critical, potentially critical, or noncritical. Failure Mode and Effects Analysis (FMEA) was conducted per PDA TR-81, with each failure mode scored for Severity, Occurrence, and Detectability. Risk-reduction controls were applied following the control hierarchy, and residual risk was reassessed to verify effectiveness. The assessment produced a structured CMA-to-CQA traceability map and a raw material criticality classification clarifying which inputs most strongly influence product quality. Starting tissue and biological reagents emerged as the most influential materials, while several ancillary materials posed limited risk. Detectability of material failures, rather than severity alone, was decisive in prioritizing controls. After targeted controls such as supplier qualification, incoming testing, environmental monitoring, and chain-of-identity procedures, residual material-related risks were reduced to acceptable levels. A CMA-to-CQA, FMEA-based control strategy aligned with PDA TR-81 provides a structured, auditable approach to raw material control. The framework is transferable across cell therapy products and supports GMP compliance, regulatory submission (CMC document), and consistent product quality.

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Process Development, and Manufacturing & Commercialization

BIOLUMINESCENT METABOLITE PROFILING AS AN IN PROCESS TOOL TO TUNE T CELL ACTIVATION FOR CELL THERAPY MANUFACTURING

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KEYWORDS: Cell Therapy Manufacturing, in-process tool, Metabolite.

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Background & Aim

Ex vivo T cell activation initiates rapid metabolic remodeling that shapes early expansion dynamics and downstream cell state during cell therapy manufacturing. Because metabolic adaptation integrates stimulation signals with nutrient availability, the ability to control metabolic programming during ex vivo expansion is central to improving the potency and durability of transferred immune cells. However, information on how culture conditions shape these metabolic outcomes remains limited.
Here, we employed a modular, highly sensitive bioluminescent assay platform compatible with miniaturization and automation to profile metabolic adaptation during T cell activation and early expansion. The assay panel measures intracellular bioenergetic and redox state, including ATP, NAD+, NAD(P)H, and reducing capacity, together with extracellular nutrient flux, such as glucose consumption, lactate release, and malate accumulation. When integrated with homogeneous granzyme B and Lumit based cytokine secretion assays, these measurements provide a cohesive view of T cell transition from naïve to activated states.

Methods, Results & Conclusion

Using this platform, we profiled metabolic responses across commonly used activation conditions by varying culture medium, activation reagent strength, and cytokine supplementation, and identified distinct media- and activation-specific metabolic states that emerged upon T cell activation and persisted through early expansion. Targeted metabolic perturbations further demonstrated that pathway sensitivities are context dependent, indicating that metabolic dependencies are jointly shaped by stimulation parameters and the culture environment.
Together, we show that early metabolic profiling during T cell activation provides quantitative insight into how culture conditions define bioenergetic state and influence downstream expansion outcomes. In collaborative CAR T manufacturing

studies, we found that reduced early glycolytic output and balanced redox state were associated with enrichment of memory-like subsets and improved persistence, further highlighting the value of early metabolic assessment during activation.

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Process Development, and Manufacturing & Commercialization

INTEGRATED BIOMANUFACTURING HUBS IN INDIA: A SCALABLE MODEL FOR ACCELERATING ADVANCED THERAPY TRANSLATION, COMMERCIALIZATION, AND ACCESS IN LMICS

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KEYWORDS: Biomanufacturing, Clinical Acceleration , Cost effective .

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Background & Aim

Despite major advances in cell and gene therapies, clinical translation remains limited by fragmented development pathways, inadequate manufacturing infrastructure, regulatory complexity, high costs, and limited commercialization support. These challenges are particularly acute in LMICs, where dependence on imported technologies and constrained GMP manufacturing capacity restrict patient access. To address these gaps, the Department of Biotechnology, Government of India, through the BioE3 Policy,is establishing Integrated Biomanufacturing Hubs to accelerate advanced therapy development and commercialization. As part of this initiative, ACTREC -TMC, is establishing an Integrated Cell Therapy Biomanufacturing Hub as a national platform for advanced cellular therapies.

Methods, Results & Conclusion

The BioE3 framework establishes a nationally coordinated hub-and-spoke biomanufacturing ecosystem that integrates discovery research, proof-of-concept validation, process and analytical development, vector engineering, GMP manufacturing, quality systems, regulatory science, clinical trials, intellectual property management, technology transfer, manufacturing scale-up, and commercialization within a single translational pathway. Through shared infrastructure and fee-for-service, contract development, co-development, and translational partnership models, centralized hubs provide GMP manufacturing, vector production, quality testing, regulatory support, and clinical translation capabilities, while academic institutions, hospitals, start-ups, SMEs, and industry partners contribute innovative technologies, novel targets, disease expertise, and clinical cohorts. This model is expected to bridge the translational "valley of death" by enabling seamless progression from proof-of-concept and IND-enabling studies to clinical manufacturing, multicentric clinical trials, licensing, and commercialization, thereby reducing barriers to entry and accelerating product development. By supporting diverse CGT modalities, these hubs can facilitate indigenous innovation, manufacturing scale-up, and commercialization readiness while minimizing duplication of costly infrastructure. Leveraging centralized expertise, platform manufacturing approaches, workforce development, regulatory capacity building, and economies of scale, the model has the potential to reduce development costs, enhance affordability, strengthen domestic biomanufacturing capabilities, and expand patient access to advanced therapies in LMIC settings.

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AUTOMATED CLOSED-SYSTEM PROCESSING OF LEUKAPHERESIS SAMPLES USING THE SEPAX C-PRO TO FACILITATE CAR-T CELL MANUFACTURING

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KEYWORDS: CAR-T cells, Automation.

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Background & Aim

Robust isolation of peripheral blood mononuclear cells (PBMCs) from autologous leukapheresis is a critical first step in CAR-T cell manufacturing, particularly where T cells are transduced directly from the PBMC fraction without upfront T-cell enrichment — as in academic programmes. Manual Ficoll density-gradient processing is labour-intensive, operator-dependent, and entails numerous open manipulations. To improve consistency and aseptic assurance, we transitioned to the Sepax C-Pro, an automated, functionally closed platform, and benchmarked key operational and quality parameters against the manual method.

Methods, Results & Conclusion

Methods

Two PBMC isolation workflows were compared for autologous leukapheresis products prior to cryopreservation. In the manual arm, samples underwent open processing in a Biospherix isolator with Ficoll density-gradient centrifugation. In the automated arm, reagents were prepared in

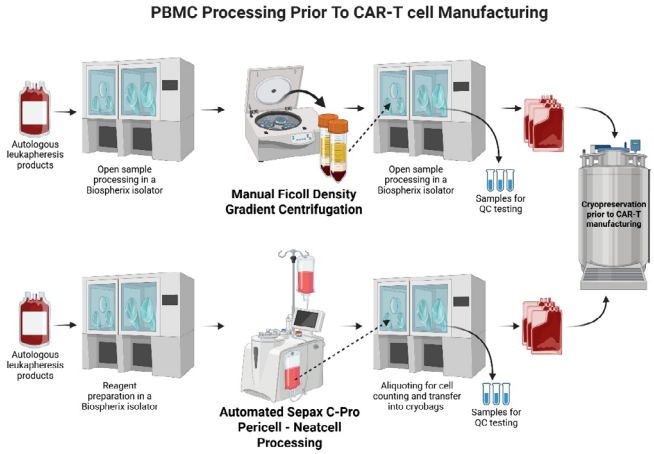
a Biospherix isolator and PBMCs were isolated on the Sepax C-Pro (PeriCell and NeatCell protocols). Processed samples were then counted and aliquoted prior to cryopreservation. All procedures were performed by a team of cell engineers in a GMP-certified, Grade D cleanroom. Anonymised data were analysed retrospectively from facility manufacturing records.

Results

Twenty-six samples were processed between January 2025 and June 2026 via the Sepax C-Pro (n=16; January 2025 – June 2026) or manual processing (n=10; January 2023 - July 2025). Open-manipulation steps decreased from 103 to 55. Cell recovery was significantly higher with Sepax (68.4% ± 12.4% vs 44.0% ± 11.8%; $p < 0.01$); post-processing viability was comparable (99.3% ± 1.0% vs 98.5% ± 1.7%; p = NS). Processing time decreased from 389.5 ± 46.5 to 302.5 ± 51.9 minutes; $p < 0.01$. Manpower utilisation also decreased from 12.98 ± 1.55 to 10.08 ± 1.73 man-hours per procedure; $p < 0.01$. Sterility was maintained in all completed runs. From the 16 Sepax-processed samples, 9 CAR-T products were manufactured (CD19=5, CD7=3, CD22=1), all meeting release criteria.

Conclusion

The Sepax C-Pro significantly reduced processing time and manpower utilization versus our manual method, while improving cell recovery and maintaining comparable viability and product quality. This automated, functionally closed workflow offers a safer, more reproducible, and scalable starting point for clinical-grade CAR-T cell manufacturing.



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DEVELOPMENT OF A GMP-COMPLIANT LENTIVIRAL VECTOR MANUFACTURING PROCESS FOR EX VIVO GENE THERAPY

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KEYWORDS: Lentiviral Vector, Gene Therapy, GMP

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Background & Aim

Although ex vivo gene therapy has demonstrated its profound efficacy and is attracting considerable attention, there remain major challenges of supplying investigational products especially for early phase clinical trials. Our institution was established as a core academic facility for manufacturing investigational products for cell and gene therapying in accordance with GMP. As part of this effort, we report the ongoing development of a manufacturing process for lentiviral vectors (LVVs) intended for novel ex vivo CAR-T cell therapies.

Methods, Results & Conclusion

In the upstream process, host cells and transfection reagents were optimized, and plasmid ratios were further optimized using Design of Experiments (DoE) with viral titer as the response variable. As a result, optimal conditions for LVV production using suspension-adapted HEK293 cells and a third-generation self-inactivating (SIN) vector system were established, enabling the production of high-titer LVVs. In the downstream process, purification and concentration steps, including depth filtration, anion exchange chromatography, and ultrafiltration/diafiltration (UF/DF), were performed. Consequently, >95% clearance of residual host cell-derived DNA and proteins was achieved while maintaining a biological titer of ≥1 × 10^7 TU/mL.
Furthermore, we established an integrated manufacturing platform encompassing LVV production and subsequent CAR-T cell manufacturing. These findings demonstrate the feasibility of GMP-compliant academic manufacturing of LVVs for ex vivo gene therapy applications and provide a foundation for future scale-up and adaptation of LVV manufacturing processes for in vivo gene therapy applications.

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CHALLENGE TO ESTABLISH AN ACADEMIC INFRASTRUCTURE FOR MANUFACTURING AND PROVISION OF VIRAL VECTOR TO ACCELERATE THE PRACTICAL APPLICATION OF GENE AND CELL THERAPY

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KEYWORDS: viral vector, cell therapy, CDMO GMP.

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Background & Aim

Currently, clinical research and development of gene therapy, along with regenerative medicine, is rapidly accelerating worldwide, and groundbreaking results in safety and efficacy have been revealed, and attracting considerable attention as a next-generation, innovative medical treatment.

Methods, Results & Conclusion

There are various challenges to overcome in order to translate excellent basic research into practical applications of gene therapy, and development efforts to overcome these challenges are intensifying around the world. In particular, in the field of gene therapy, the establishing manufacturing infrastructure become a major challenge. The challenge of technology transfer, i.e., how to transfer the results of basic research into the development of a scaled-up GMP-compliant manufacturing process and supply of investigational drugs, is the most important step toward conducting early clinical trials. To overcome these challenges, we have launched a national project to establish a manufacturing and development infrastructure like CDMO (contractive development and manufacturing organization) in academia and to manufacture and provide a wide variety of viral vectors in small quantities for a wide range of modalities covering in vivo and ex vivo gene therapy. Here we will report on the outline and results of this project. Furthermore, we will collaborate with comprehensive support systems that promote practical applications, including pharmaceutical affairs, project management, and intellectual property management, and will widely outreach efforts to pool our collective strengths to strongly promote practical application. In addition of the challenges of human resource development, we will focus on the aspects of manufacturing and development infrastructure, introduce sustainable challenges in academia, and hold a wide-ranging discussion, including recommendations for companies.

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LIPID NANOPARTICLE-MEDIATED CELL TRANSFECTION IN BIOREACTORS ACROSS DIVERSE CELL THERAPY WORKFLOWS

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KEYWORDS: LNP, Bioreactor, Cell Therapy.

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Background & Aim

Lipid nanoparticles (LNPs) have emerged as a promising solution for gene modification of immune cells due to their favorable manufacturing costs, low cytotoxicity and simplified cell culture process. To date, most LNP demonstrations in *ex vivo* cell therapy applications have been small-scale, preclinical studies. Here, we present data demonstrating LNPs in scalable workflows across larger manufacturing platforms, enabling gene modification in T cells, natural killer (NK) cells, and hematopoietic stem cells (HSCs) in different bioreactor systems.

Methods, Results & Conclusion

T cells, NK cells and HSCs were isolated from leukopaks using magnetic bead separation. LNPs encapsulating either GFP mRNA, or Cas9 mRNA plus TCR-targeted guide RNA (sgRNA) were manufactured using NxGen™ mixers on the NanoAssemblr™ Ignite instrument. LNP-mediated transfection was performed in four different systems: static (GRex™), stir-tank reactor (DASBox™), Xuri™ cell expansion system and a closed manufacturing system Sefia™ expansion system.
LNPs effectively transfected T cells in GRex, DASBox and the Xuri cell expansion system, while maintaining cell viability at the same level as controls and demonstrating over 99% transfection. LNPs were also well supported within the closed and automated Sefia™ Expansion system, again confirming compatibility with clinical workflows. NP-mediated NK transfection was tested in GRex, stir tank and rocking bioreactors, again demonstrating a high level of transfection efficiency with no associated impact on cell viability. Similarly, in HSCs, LNPs showed effective modification with no observed toxicity or growth impairment in GRex, stir tank and Xuri cell expansion system.
In conclusion, we have demonstrated that LNPs are well-suited for a range of larger scale cell culture workflows. We have also shown that LNPs are able

to effectively modify a range of hard-to-transfect cells including T cells, HSC and NK cells. The simple one-step LNP transfection process produces highly transfected cells with no detrimental effect on viability. This simplified and scalable process for gene modification has the potential to reduce manufacturing costs, supporting the utility of LNPs in next-generation cell therapy manufacturing.

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END-TO-END AUTOMATED SAMPLE PREPARATION FOR STANDARDIZED CELL AND GENE THERAPY CHARACTERIZATION: OPERATOR INDEPENDENCE, STAINING REPRODUCIBILITY, AND INTERLABORATORY CONCORDANCE

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KEYWORDS: Automated sample preparation, Interlaboratory standardization, Cell and gene therapy.

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Background & Aim

Reproducible sample preparation is a critical but under addressed source of variability in high-parameter flow cytometry for cell and gene therapy characterization. Antibody cocktailing and cell washing remain largely manual, introducing operator-dependent inconsistency that undermines cross-site comparability. We evaluated end-to-end automated sample preparation — using the Pluto Antibody Cocktailing Wizard (ACW) and C-FREE™ centrifuge-free washing — for staining reproducibility, operator independence, and concordance with manual methods across multiple sample types and sites.

Methods, Results & Conclusion

ACW operator independence was assessed using a 9-color TBNKM panel with cryopreserved PBMCs processed by 3 independent operators versus 1 experienced manual operator. Staining quality was evaluated across 10- and 24-color panels (n=5 donors) versus manual cocktail preparation. End-to-end automation (ACW + C-FREE™ washing) was validated using NIST ILS-2 reference material (activated PBMCs; CAR-T cells), comparing Pluto automated versus manual SOP sample preparation across replicate vials and independent sites.
ACW eliminated inter-operator variability in cocktail preparation: 5 of 6 markers achieved %CV ≤5% across 3 independent operators, with hands-on time reduced from 6:26 to 3:18–4:34 min. Stain index was consistent between automated and manual cocktail preparation across 10- and 24-color panels and 5 donors. In the NIST ILS-2 study, Pluto automated sample prep demonstrated high concordance with manual SOP (Pearson r=0.997) across immune populations and sample types, with equal or lower %CV in all populations. Vial-to-vial consistency was markedly improved: %CV 0.4% (Pluto) versus 1.9% (manual). End-to-end automated sample preparation on the Pluto platform — integrating ACW cocktailing and C-FREE™ centrifuge-free washing — delivers operator-independent, reproducible results comparable to manual SOP across panel sizes, sample types, and sites. Elimination of vial-to-vial drift and reduction in hands-on time support its application in standardized CGT characterization and interlaboratory workflows.

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SIMPLIFICATION OF AN IN-HOUSE CRYOPRESERVATION MEDIUM WITHOUT COMPROMISING HUCB-MSC QUALITY OR 36-MONTH CRYOPRESERVATION STABILITY

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KEYWORDS: Cryopreservation medium, process development, Mesenchymal stem cells.

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Background & Aim

Cryopreservation medium formulation is a critical factor in maintaining the post-thaw quality and manufacturing consistency of cell therapy products. Although antioxidants are commonly incorporated into cryopreservation media to minimize cellular damage during freezing and thawing, certain antioxidant components may have limited chemical stability during storage, thereby increasing formulation complexity and creating additional challenges for quality control. This study aimed to evaluate whether removal of an antioxidant component with limited chemical stability from an in-house cryopreservation medium could simplify the formulation without compromising the quality attributes or long-term cryopreservation stability of human umbilical cord blood-derived mesenchymal stem cells (hUCB-MSCs).

Methods, Results & Conclusion

hUCB-MSCs were cryopreserved using either the original cryopreservation medium containing the antioxidant component or a modified formulation from which the component was removed. Long-term cryopreservation stability was evaluated for up to 36 months by assessing post-thaw cell viability. Cellular

comparability between the two formulations was further evaluated through identity and purity testing, post-thaw proliferative capacity, and anti-inflammatory potency.
Post-thaw cell viability remained stable for up to 36 months in both formulations, with no significant differences observed between the antioxidant-containing and antioxidant-free conditions. In addition, removal of the antioxidant component did not affect post-thaw proliferative capacity up to Passage 10 or anti-inflammatory potency, indicating that key cellular and functional quality attributes were maintained after long-term cryopreservation.
Collectively, these results demonstrate that removal of the antioxidant component did not compromise the post-thaw quality, cellular characteristics, or functional properties of hUCB-MSCs under the evaluated conditions. These findings support the feasibility of simplifying the cryopreservation medium while maintaining key hUCB-MSC quality attributes and cryopreservation stability for up to 36 months. By eliminating a component with limited chemical stability, this formulation strategy may reduce formulation complexity, streamline quality control, and improve manufacturing consistency, thereby contributing to a more robust and reproducible cryopreservation process for hUCB-MSC-based cell therapy products.

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BRIDGING PROCESS DEVELOPMENT AND GMP MANUFACTURING: ESCO ASTER'S INTEGRATED CDMO FRAMEWORK FOR ACCELERATING CELL AND GENE THERAPY TRANSLATION IN ASIA

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KEYWORDS: GMP, Process Development, Technology Transfer.

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Background & Aim

The rapid growth of cell and gene therapies (CGTs) has increased demand for scalable manufacturing solutions supporting products from early development through clinical implementation. Many CGT developers — particularly emerging biotechs and academic groups transitioning to clinical translation — encounter significant barriers at the process development-to-GMP interface, including process complexity, technology transfer risk, evolving regulatory expectations, and limited access to integrated manufacturing infrastructure. In the Asia-Pacific region, where the CGT landscape is expanding rapidly, end-to-end CDMO capabilities are critical to advancing locally developed therapies toward clinical realisation.

Methods, Results & Conclusion

Esco Aster, a Singapore-based GMP CDMO specialising in cell and gene therapy and extracellular vesicle (EV) manufacturing, developed an integrated framework spanning process development (PD), analytical development (AD), technology transfer, GMP facility qualification, raw material management, and quality oversight. Co-localising PD and AD functions reduces inter-organisational handoff risk, accelerates CMC readiness, and enables iterative optimisation. Risk-based workflows were implemented to maintain flexibility across autologous and allogeneic cell therapies, gene-modified products, and EV-based biologics.

The framework has supported CGT programs across multiple modalities and regulatory jurisdictions. Notably, Esco Aster manufactured clinical-grade EV therapeutics under GMP to support an FDA-accepted IND for a Phase 1 clinical trial — demonstrating capability to meet rigorous technical, analytical, and documentation standards required by major regulatory agencies. Key outcomes include early identification of process and analytical gaps, successful GMP technology transfer with reduced cycle times, and robust quality systems aligned with PIC/S GMP standards and ICH guidelines.
Successful CGT translation requires more than GMP

infrastructure — it demands integrated process knowledge, analytical capability, and quality systems within a single organisation. Esco Aster's end-to-end CDMO framework demonstrates how co-located PD, AD, and GMP capabilities reduce development bottlenecks and accelerate clinical advancement. As the Asia-Pacific CGT ecosystem matures, purpose-built regional CDMO infrastructure will be essential in bridging scientific innovation and clinical delivery.

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RISK-BASED IDENTIFICATION OF CRITICAL PROCESS PARAMETERS FOR GMP MANUFACTURING OF AUTOLOGOUS ADIPOSE-DERIVED MESENCHYMAL STROMAL CELLS

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KEYWORDS: Advanced Therapy Medicinal Products (ATMPs), Critical Process Parameters (CPPs), Critical Quality Attributes (CQAs).

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Background & Aim

The manufacturing of autologous adipose-derived mesenchymal stromal cells (MSCs) involves multiple processing steps in which variations in operating conditions may affect product quality and consistency. This work aimed to identify and prioritize Critical Process Parameters (CPPs) using a risk-based approach to establish a robust control strategy in accordance with PDA Technical Report No. 81, ICH Q9 guideline, and GMP PIC/S principles.

Methods, Results & Conclusion

The Input–Process–Output (IPO) model was constructed to map process conditions across eight manufacturing operations, including tissue collection, collagenase digestion, cell culture expansion, cryopreservation, post-thaw recovery, harvest, formulation, and final preparation. Process parameters were evaluated for their potential impact on Critical Quality Attributes (CQAs), including safety, identity, purity, potency, and viable cell number. Failure Mode and Effects Analysis (FMEA) was then applied to assess severity, occurrence, and detectability, allowing parameters to be prioritized based on Risk Priority Number (RPN). The assessment identified enzymatic digestion, cell culture expansion, and cryopreservation as the operations containing the most critical parameters. Variables related to collagenase exposure, culture conditions, and freezing processes showed the highest risk of affecting cell viability and biological function, while routine transfer and resuspension steps had comparatively low impact. Detectability emerged as a key contributor to overall risk, highlighting the importance of effective in-process monitoring. A structured CPP identification framework based on IPO mapping and FMEA provides an auditable and risk-based control strategy that enhances GMP readiness, supports regulatory expectations, and improves batch-to-batch consistency in autologous MSC manufacturing. To our knowledge, this represents one of the first systematic applications of IPO mapping combined with FMEA for CPP identification in autologous adipose-derived MSC manufacturing under GMP PIC/S compliance.

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VALIDATION OF THE INTERFERON-GAMMA ELISA ASSAY TO ASSESS POTENCY OF TUMOUR-INFILTRATING LYMPHOCYTES

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KEYWORDS: Potency, T-Cell, IFN.

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Background & Aim

Manufactured tumour-infiltrating lymphocytes (TIL) require identity characterisation (e.g. surface expression of CD45, CD3, CD4, and CD8), and potency may be assessed by cytokine production (e.g. IFNγ). Functional-potency analysis can be achieved by culturing the TILs with a defined stimulation (PMA + ionomycin) to secrete IFN-γ (a key cytokine for anti-tumor activity). Harvested culture supernatants can then be measured for IFNγ levels using a quantitative immunoassay (ELISA). IFN-γ secreted into culture supernatant is quantified against the kit calibrators, which are traceable to the WHO International Standard. We have prepared a validation protocol to validate an IFNγ ELISA kit ensuring compliance with the Good Manufacturing Practice (GMP) principles. The validation was also designed to comply with ICH Q2(R2) and WHO Annex 2 standards as outlined in Table 7.

Methods, Results & Conclusion

TILs were manufactured using the rapid expansion protocol (REP-TIL) with an anti-CD3 agonist,

irradiated feeder cells, and IL-2. Cryopreserved retention vials were thawed and stimulated by PMA and ionomycin to activate the TILs to produce IFNγ for 4 hours. Culture supernatants were then harvested and stored at -80°C. The IFN-γ ELISA Kit (KAC1231) from Thermo Fisher Scientific was selected for validation as it includes all the reagents needed to quantify IFN-γ with defined calibrators as per the WHO standard. In addition to the calibrated standard the kit includes the capture antibody-coated 96-well plates, wash and diluent buffers, detection antibody, secondary detection reagents, stabilised chromogen, stop solution, and plate covers. We have tested and validated the performance characteristics of this kit including: Specificity, Response, Range, Lower range limits, Accuracy and Precision. The validation comprises establishing a PMA/ionomycin-based stimulation culture system that induces detectable IFN-γ secretion and validating the ELISA kit and plate reader performance (the TECAN Sparks plate reader and its associated software).
Accurate quantification and characterisation of cell therapy products is fundamental to establishing well-defined acceptance criteria for quality testing. This study validates an ELISA assay to assess the potency of TIL products through IFNγ concentration. Critical process parameters and key variables have been established and will be further discussed in the context of the results.

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OPTIMIZED CELL THERAPY MANUFACTURE PROCESS WITH HYDROGEL-BASED CELLFIBER® ENCAPSULATION TECHNOLOGY

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KEYWORDS: Alginate Hydrogel, Encapsulation, Expansion Culture.

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Background & Aim

Regenerative medicine offers a powerful modality for treating cancer and tissue injury, yet its diverse indications and cell types introduce complex manufacturing challenges for clinical dosages. CellFiber is a encapsulation technology which is using alginate hydrogel to make a tubular shell for 3D cell culture (Figure 1). This structure provide the protective environment that shields cells from mechanical stress, engage cells for biomimetic conditions, and simplifies process manipulation.
In this study, we showcase the CellFiber intergrated cell culture plarform and summarized the adaptions on iPSC, MSC and T cells.

Methods, Results & Conclusion

Cryopreserved working cell bank of iPSC and MSC were thawed and statically cultured for 4~7 days in 2D culture vessels for gathering optimal cell numbers before encapsulation. CD3 T cell was enriched from frozen PBMC, followed by CD2/3/28 activation inside the CellFiber alginate shell.
All the three cell types are cultured in the cellbag bioreactor (Xuri™ W25 cell expansion system, Cytiva) after the encapsulation, enabling the real-time monitoring and conditioned media feeding strategy. The expanded cells were being collected by automated harvest systems right after the non-enzymatic hydrogel shell dissolution, and then followed by phenotype analysis (Figure 2). The fiber-cultured stem cells (iPSC and MSC) with optimal proliferation fold possess normal pluripotency, and potential improved differentiation ability on iPSC. Fiber-cultured CD3 T cells demonstrate promising yield with higher naïve $CD8^+$ and central memory $CD4^+$ populations comparing 2D non-fiber culture, and fiber culture significantly performs >50% lentiviral transduction efficiency by low viral vector (MOI=1) without transduction enhancer compared to 2D non-fiber culture (Table 1).
These results demonstrate CellFiber's capacity to

enhance production efficiency and clinical efficacy in cell manufacturing.

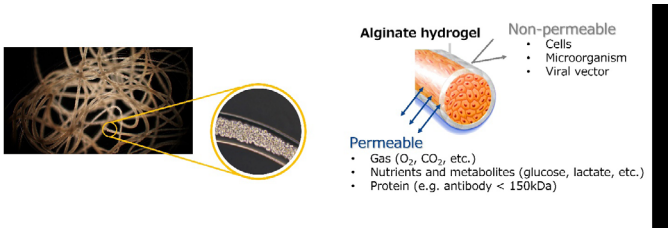


Figure 1. CellFiber® cell encapsulation technology

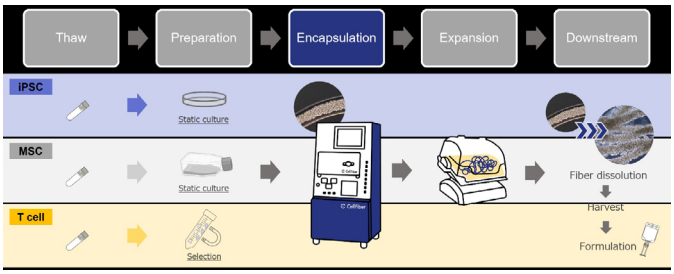


Figure 2. CellFiber integrated cell manufacturing platform

Table 1: Summarized results of CellFiber integrated expansion cultures

Cell type	MSC	iPSC	CD3+ T cells
Media scale (Litre)	5	1	1
Initial encapsulated number (cells)	1.56e7	2.00e8	3.12e7
Culture duration (days)	8	7	12
Expanded cell number (cells)	1.11e9	1.11e10	1.94e10
Expansion fold (-fold)	70.5	55.5	621.8
Phenotype characteristics compared to non-fiber 2D culture (method)	Comparable pluripotency (Flow Cytometry)	Higher trilineage differentiation ability (qRT-PCR)	Higher naïve cell populations and transduction efficiency (Flow Cytometry)

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MONOLITHIC CHROMATOGRAPHY AS A SCALABLE PLATFORM FOR EXOSOME PURIFICATION IN THERAPEUTIC EXTRACELLULAR VESICLE MANUFACTURING

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KEYWORDS: exosome, chromatography, purification.

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Background & Aim

Exosomes are under wide development for therapeutic and non-therapeutic applications, including gene transfection, parenteral treatment of human and animal diseases, topical treatment of dermatological disorders, and cosmetics. They are typically derived from human or animal cell cultures, with the conditioned culture fluid further processed to remove contaminants including extraneous proteins, carbohydrates, hormones, host cell proteins, host cell DNA, and other impurities.
A key challenge in exosome purification lies in the physical limitations of conventional bead-based chromatography, where dead-end pores rely on diffusion of molecules into and out of the solid phase — a mechanism that restricts separation of large biomolecules such as exosomes and viruses. Monolithic chromatography, characterised by a continuous macroporous structure and the absence of diffusion-dependent pores, allows large biomolecules to move freely through the stationary phase via convective flow, offering a structurally advantageous alternative for EV purification in cell and gene therapy manufacturing.

Methods, Results & Conclusion

METHODS

Exosomes were provided by Paracelsus Medical University in Salzburg Austria (confirm spelling), which also performed analytical testing to determine particle numbers and purity. Purification was performed on quaternary amine ion exchange chromatography AXISFLOW™ monoliths developed by BioChromatographix International (BCI) in Singapore. Purifications were developed and run on Cytiva Akta® and Bio-Rad NGC® FPLC instruments using HEPES and NaCl buffer at pH 7.2 with elution by increasing NaCl concentration.

RESULTS

Results show a clear increase in purity of exosomes following binding and elution on AXISFLOW® QA columns, as measured by the removal of contaminants introduced during the cell culture process. Host cell

protein, host cell DNA and endotoxin concentrations were reduced by significant levels.

CONCLUSIONS

AXISFLOW® monolithic chromatography columns have demonstrated the ability to remove cell culture related impurities from exosome-containing cell culture supernatant, thus reducing the risk associated with the use of exosomes in parenteral applications.

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EVALUATION OF A NOVEL POINT-OF-CARE CELL SELECTION INSTRUMENT FOR CELL PURIFICATION FROM WHOLE BLOOD

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KEYWORDS: Selection, T cell, Automation.

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Background & Aim

T cell therapeutics, such as chimeric antigen receptor (CAR) T cells, have revolutionized the treatment of hematological malignancies. However, current manufacturing processes are lengthy, expensive and complex. Standard workflows typically involve leukocyte collection by apheresis, cell washing, volume reduction, and CD4/CD8 positive selection. The resulting T cells are then modified with lentiviral vectors, expanded, and cryopreserved before infusion. Closed-system, point-of-care processing of whole blood provides an attractive alternative manufacturing pipeline, yet very few instruments are designed for GMP compliant selection directly from whole blood.

Methods, Results & Conclusion

This preliminary study evaluated a novel non-magnetic, automated selection device intended to streamline cell therapy production through T cell isolation from whole blood. Paired optimization runs were performed to assess purity and potency of the new device. Purity was assessed by Sysmex hematology analyzer and flow cytometry phenotyping.
Selections were effective, yielding excellent purity and viability across all runs, with efficient T cell recovery. Potency was confirmed by bead activation, resulting in robust proliferation, 49-fold expansion, after 7 days in culture. T cell functionality was assessed by flow cytometry with significantly increased expression of CD25, HLA-DR, Granzyme B, and surface CD107a in activated $CD4^+$ and $CD8^+$ T cells.
These findings demonstrate the feasibility and efficacy of automated whole blood isolation solutions. By enabling faster and more efficient T-cell isolation without compromising quality, this approach has the potential to transform point of care cell manufacturing and expand access to advanced cellular therapies.

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SUPERIORITY OF STABLE PRODUCER CELL LINES FOR MANUFACTURING IN VIVO CAR-T LENTIVIRAL VECTORS: ENHANCED PROCESS STABILITY, PRODUCT QUALITY, AND PRECLINICAL SAFETY

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KEYWORDS: in-vivo, CAR-T, Lentiviral vector.

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Background & Aim

Lentiviral vector (LVV) production for in vivo CAR-T applications has traditionally relied on multi-plasmid transient transfection. While scalable, this method faces challenges in lot-to-lot consistency, product quality, and safety profile. Stable producer cell lines (SPCLs) offer a promising alternative by integrating all necessary viral components into the host genome, enabling constitutive and stable vector production.

Methods, Results & Conclusion

Methods

Multiple single-clone stable producer cell lines (SPCLs) were generated in 293T cells by integrating inducible/constitutive gag-pol, rev, a multidomain fusion protein, cocal-pseudotyped envelope, and an anti-CD19 CAR-IRES-EGFP transfer vector. Clones were screened by functional titer in Jurkat cells, T-cell transduction efficiency, and growth profiles. Upstream process development in shake flasks (4×500mL) compared SPCL and transient transfection across various seeding densities, induction timing, and feeding strategies. Downstream purification (2L scale) utilized chromatography, evaluated by recovery rate, quality attributes, and impurities (HCD/HCP). Primary human T cells assessed in vitro transduction, activation, and expansion, while a human PBMC assay evaluated cytokine release profiles.

Results

SPCL clones showed stable, passage-resilient LVV production with consistent genomic integration. In upstream processes, SPCLs demonstrated a broad operational cell density (8E6–1.5E7 cells/mL) and low

batch-to-batch variability (CV < 20%) vs. transient systems. Purified SPCL-LVVs exhibited superior lot consistency in quality attributes and lower impurities. Notably, SPCL-derived vectors achieved comparable transduction efficiency in primary T cells but induced significantly lower release of CRS-associated cytokines than transiently produced vectors at identical doses.

Conclusion

The SPCL platform offers a robust, scalable, and consistent alternative for in vivo CAR-T applications with enhanced process stability and superior product safety profiles, supporting its clinical development potential.

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MARS GOFAST RAPID MANUFACTURING WITH SYNECTA™ T1 ACTIVATION INCREASES THE FREQUENCY OF MULTIFUNCTIONAL "HERO" CAR-T CELLS

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KEYWORDS: GoFast, Activation, single-cell.

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Background & Aim

Background

Rapid autologous CAR-T manufacturing is increasingly important as cell therapy expands into autoimmune disease and solid tumors, where treatment urgency, starting-material variability, and product fitness remain major barriers. These applications require CAR-T products with rapid availability, preserved functional fitness, sustained target engagement, proliferation, and durability. We evaluated whether Synecta T1 cell-derived nanoparticles (CDNPs), a physiological T-cell activation platform, combined with MARS GoFast, a streamlined column-free workflow, could enrich multifunctional CAR-T phenotypes in an ultra-rapid 24-hour process.

Methods, Results & Conclusion

Methods

CAR-T products were generated across three variables:
Activation : Synecta T1 CNDPs versus standard polymeric nanomatrix beads
Manufacturing workflow: MARS GoFast versus standard 7-day manufacturing
Isolation method: MARS column-free magnetic isolation vs column-based isolation
Functional heterogeneity was evaluated using the Celldom CloneXplorer high-density nanowell platform. Bulk products were assessed by CCR7/CD45RA flow cytometry, and single CAR-T cells were co-cultured with target tumor cells and tracked for 5 days using AI-enabled video analytics to quantify target engagement, IFN-γ secretion, cytotoxic kinetics, serial killing, expansion, and persistence.

Results

Celldom analysis showed that CAR-T cells manufactured by combining Synecta T1 CDNPs activation with MARS GoFast manufacturing started IFN-γ secretion earlier with less heterogeneity compared to CAR-T cells made in the 7-day process. GoFast CAR-T cells also demonstrated more effective killing between 20-40 hours. Celldom analysis identified a higher proportion of multifunctional "hero" CAR-T cells, defined by coordinated target-cell engagement and killing, IFN-γ secretion, continued proliferation, and persistence over time in the combined approach. Together, these single-cell data indicate sustained functional output in an ultra-rapid manufacturing process.

Conclusion

These preliminary findings support further evaluation of the integrated Synecta T1/MARS GoFast workflow as a rapid manufacturing approach for next-generation CAR-T applications, with studies ongoing across additional donors. This integrated workflow has potential to address key barriers to next-generation CAR-T applications: rapid immune-depletion strategies for autoimmune disease and durable, multifunctional potency for solid tumors.

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CTS™DETACHABLE DYNABEADS™CD4 AND CD8 ENABLE HIGH-PURITY ISOLATION OF T CELLS FROM WHOLE BLOOD

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KEYWORDS: T cell isolation, whole blood, convenience.

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Background & Aim

T cell manufacturing has become a critical focus in recent years to support the production of powerful immunotherapeutic treatments, particularly, chimeric antigen receptor T cell (CAR-T) therapies. As the development of these treatments accelerates, there is an increasing demand for a reliable source of T cells. Commonly, T cells are sourced from specially prepared blood products including buffy coats, leukocyte reduction system chambers, or leukopaks, which contain various concentrations and purities of the target cells. The high concentration of PBMCs in leukopaks offers a stable source of T cells for isolation, manipulation, and expansion in the manufacture of T cell-based therapeutics. The production of leukopaks through apheresis requires expensive specialized equipment, which may not be readily available at many treatment centers, especially those with limited resources. Additionally, the process requires patients to be attached to the machine for several hours, potentially causing discomfort. These challenges highlight the need for alternative T cell sources. To address these issues, the isolation and expansion of T cells directly from whole blood has been evaluated.

Methods, Results & Conclusion

Whole blood packs are a low-cost, readily accessible source of T cells that can be obtained from patients in a typical clinic within approximately 15 minutes, without the need for specialized equipment. UsingGMP-compliantCTS™DetachableDynabeads™CD4andCD8 along with the Gibco™ CTS™ DynaCellect™ Magnetic Separation System, ahighlypurepopulationofCD3+Tcellscanbe isolated directly from whole blood, eliminating the need for additional pre-processing and lysing steps. This method offers a practical alternative starting material for T cell manufacturing, potentially broadening the availability of CAR-T therapies to patients with limited access to leukapheresis.

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ENHANCING CAR T MANUFACTURING: INNOVATIVE GIBCO SOLUBLE DYNACTIVATOR CD3/CD28 PROTOTYPE

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KEYWORDS: T cell activation, flexibility.

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Background & Aim

The Gibco Soluble DynActivator CD3/CD28 Prototype represents a significant advancement in the field of cell therapy manufacturing. This soluble activation technology is designed to enable the activation and expansion of T cells, a critical component in the development of effective immunotherapies. Traditional methods of T cell activation often face challenges such as inconsistent activation, limited scalability, and high costs. Gibco Soluble DynActivator CD3/CD28 Prototype addresses these issues by providing a soluble, easy-to-use activator that enable robust and cost effective T cell activation.

Methods, Results & Conclusion

In this study, we demonstrate the efficacy of Gibco Soluble DynActivator CD3/CD28 Prototype in various cell therapy manufacturing processes. Our results show that Gibco Soluble DynActivator CD3/CD28 Prototype enables gentle activation, robust proliferation rates of T cells and maintains their functionality and viability over extended culture periods. Additionally, the soluble nature of DynActivator simplifies the manufacturing workflow, reducing the need for complex and labor intensive procedures.

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Regulatory Affairs, Quality Systems, Policy, Ethics, and Patient Access

THE CHALLENGES OF VALIDATING AND IMPLEMENTING AN ALL-ENCOMPASSING ELECTRONIC QUALITY MANAGEMENT SYSTEM FOR ADVANCED THERAPIES

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KEYWORDS: Computer System Validation, Electronic Quality Management System, System Implementation.

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Background & Aim

The implementation of an electronic quality management system for advanced therapies involves more than just the validation and use of the system. CTTWA identified the need to implement a fit-for-purpose integrated electronic quality management system (eQMS) to improve operational efficiencies across quality and manufacturing. The system also must to be compliant with the numerous regulations applicable to CTTWA's licences and accreditations, including Therapeutic Goods Administration Code of Good Manufacturing Practice (GMP) for Medicines and Biologicals, PIC/S Annex 11, ISO15189:2022, and Foundation for Accreditation of Cellular Therapy Cell Therapy Standards, and Food and Drug Administration Code of Federal Regulations Title 21 Part 11.
Bluecord, a US-company, cloud-based system was selected due to its purpose-built configurations and integration across quality assurance, inventory, quality control and environmental monitoring trending and manufacturing modules (including electronic batch records) – and was able to meet compliance with defined operational, regulatory, and Western Australian Health requirements.
During the system selection, validation planning, validation, and implementation stages of Bluecord there have been multiple challenges that may not be realised prior to undertaking a large-scale eQMS implementation project.

Methods, Results & Conclusion

Challenges included:
- Defining clear user requirement specifications both operationally and to incorporate regulatory requirements
- Undergoing multiple WA Health cloud-based system cyber security reviews, privacy impact assessment, and risk assessments in addition to CTTWA GMP risk assessment processes
- Designing a validation approach and implementation plan for a complex, integrated system for a gradual workflow roll-out to replace the current QMS that would be accepted by system users, and by regulatory bodies (see Figure 1)
- Documentation requirements to develop clear, detailed validation test cases in validation protocols and to outline results in outcome reports
- Devising a training program for the implementation of modules with the added challenge of moving the team from paper-based to an electronic system.
Each challenge has been met and overcome during the Bluecord validation and implementation project, with this presentation detailing the outcomes and lessons learned to enable collaborative improvements for computerised system implementation across the advanced therapy manufacturing field.

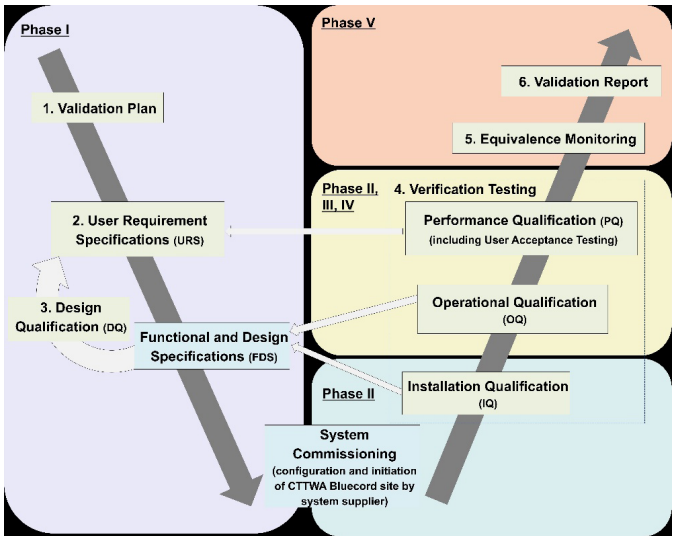


Figure 1: Showing the phased validation approach based on the GAMP 5 Guidance and PIC/S Guidance (PI 011-3, version 17).

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LEVERAGING TRUTITER™ TECHNOLOGY TO OVERCOME THERMAL STABILITY CHALLENGES IN THE DETERMINATION OF ENGINEERED AAV GENOME TITER

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KEYWORDS: AAV Titer, DNase, Genome Titer.

1. Promega Corporation, Madison, WI, United States.

Background & Aim

Current methods of AAV Titer rely on a combination of mammalian infectivity assays and digital PCR coupled with DNase pre-treatment. These approaches are often cumbersome and lack the precision needed for accurate determination of viral titer. The workflow described below uses a novel molecule (TruTiter™ Reagent) pre-treatment approach to estimate the functional AAV titer. The TruTiter™ Reagent, owing to its small size, has enhanced accessibility to exposed nucleic acids from damaged viral or non-viral sources. Furthermore, use of this reagent suppresses the PCR signal more consistently from such exposed nucleic acids, allowing for a more precise determination of functional AAV titer. This new platform, enables users to quantify AAV preparations in a more robust and accurate manner.
Engineered AAV capsid variants are often used in gene therapy approaches to escape immune system detection and degradation. The thermal stability of the AAV variants can differ from that of wild type AAV, resulting in different sentivities to DNase treatment conditions, therefore, inconsisent and/or inaccurate genome titer.

Methods, Results & Conclusion

In this study, we used TruTiter™ technology to quantitatively titer four AAV2 engineered capsid variants. For all four variants, the TruTiter™ workflow resulted in higher titers compared to a traditional DNase-pretreatment workflow. Using digital PCR, TruTiter™ treated samples exhibited two to four-fold higher gene titers compared to the same variant treated with DNase, resulting in a quantitative measure that was closer to the expected value. We hypothesized that the decreased titer observed with DNase-treated samples was due to the potential reduced thermal stability of the engineered AAV2 capsid variants. To test this, SYPRO Orange dye was used to perform differential scanning fluorimetry (DSF), which can differentiate general capsid stability between AAV variants. Using DSF, clear differences were observed between WT and engineered AAV2 capsids.

Overall, this data suggests that the TruTiter™ workflow can better address the challenges associated with the accurate titering of AAV capsid variants compared to traditional workflows.

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Regulatory Affairs, Quality Systems, Policy, Ethics, and Patient Access

NEW BIOLUMINESCENCE METHODS FOR MOA-BASED CAR-T POTENCY TESTING

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KEYWORDS: CAR-T, Potency Assays, Target Cell Killing.

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Background & Aim

The development and optimization of CAR-T cell therapies require robust and accurate methods for potency testing. This poster highlights some simple mechanism of action (MOA)-based potency assays for CAR-T development.

Methods, Results & Conclusion

1. HiBiT Technology for Monitoring Target Cell Killing (TCK): The HiBiT Target Cell Killing Assay (HiBiT TCK Assay) is a streamlined, sensitive method for selectively quantifying target cell lysis in coculture experiments with effector cells. HiBiT is an 11AA peptide that binds with high affinity to LgBiT, forming a bright, luminescent enzyme. For HiBiT TCK, target cells are engineered or transiently transfected to express a HiBiT-tagged protein, and release of this protein by dead/dying cells leads to complementation with the cell impermeable LgBiT. This gain-of-signal approach enables precise measurements of target cell killing induced by various effectors, including CAR-T cells.
2. Lumit® Immunoassays for Cytokine Detection: Homogeneous Lumit® immunoassays are simple, fast, and sensitive, requiring no washing steps. We have developed a suite Lumit® immunoassays for the measurement of cytokine secretion by CAR-T cells. This suite of methods offers a robust framework for MOA-based potency testing of CAR-T cell therapies, aiming to enhance their development and clinical application.

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ASEPTIC PROCESS VALIDATION - A COMPREHENSIVE RISK-BASED APPROACH

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KEYWORDS: Quality, Risk Assessment, Aseptic.

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Background & Aim

This presentation will discuss a risk-based approach to the design and implementation of cGMP-compliant aseptic process validation studies.
With the worldwide adoption of version 17 of the PIC/S Guide to GMP for Medicinal Products, the importance of a comprehensive contamination control strategy has become prevalent due to the major overhaul of Annex I. Aseptic Process Validation (APV), also known as media fill, is a key component of a comprehensive contamination control strategy. The purpose of APV is to demonstrate the aseptic integrity of a manufacturing process, and to verify that controls used to maintain the integrity of a process are robust enough to prevent the ingress of contaminants. Interventions are challenges to the aseptic process that are aimed to demonstrate the robustness of contamination controls employed during the manufacturing process. It is a regulatory expectation that known interventions to the manufacturing process are incorporated into the aseptic process validation for that process. For existing processes with historical data this is relatively simple, as instances of interventions to the aseptic process may be reviewed and incorporated into APV procedures. However, for novel or new manufacturing processes for which limited data beyond engineering and development work is available, a different approach is required.

Methods, Results & Conclusion

The manufacturing process used to product tumour-infiltrating lymphocytes (TILs) for treatment of melanoma was analysed using a risk-based approach. Potential interventions were determined for each step of the manufacturing process based on those that had occurred during process development. The potential interventions at each stage of the process are then assessed using a modified FMEA approach. Each intervention was subject to scoring against the following factors to determine the overall risk associated with each:
Frequency – The number of times an intervention is expected to occur.
Proximity – How close to the critical processing site the expected intervention occurs.
Duration – How complex an intervention is and how long it is expected to occur for.
Each category is scored from 1 (lowest risk) to 5 (highest risk), with the overall risk score obtained by multiplication. The overall risk is then used to determine the frequency at which interventions should be performed during aseptic process validation, and the frequency at which they should be repeated during routine aseptic process simulation.

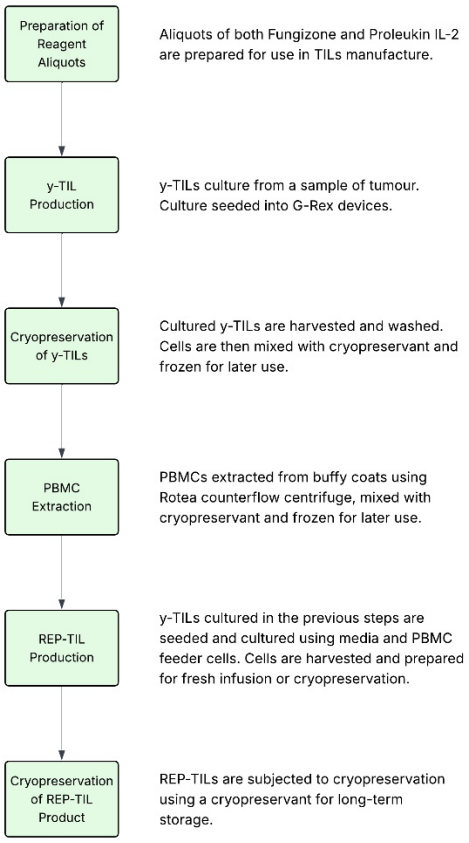


Figure 1. Process Overview - Manufacture of REP-TILs for Melanoma

Score	Justification
	Frequency
1	May be expected to occur at a frequency of once per calendar year or less.
2	May be expected to occur at a frequency of once per calendar month. Used if no historical data for frequency of occurrence is available.
3	Occurs approximately once per week.
4	Occurs every 2-3 shifts/processing sessions.
5	Occurs at least once per shift/processing session.
	Proximity
1	Occurs outside of the aseptic processing zone.
2	Occurs adjacent to the aseptic processing zone.
3	Occurs within the aseptic processing zone but does not impact the critical sterile site.
4	Occurs within the aseptic processing zone adjacent to the critical sterile site.
5	Occurs directly above the critical sterile site within the aseptic processing zone.
	Duration
1	Simple intervention - lasts for less than 30 seconds
2	Simple intervention - lasts for up to a minute
3	Simple intervention - lasts for up to 2 minutes
4	Complex intervention - lasts for up to 5 minutes
5	Complex intervention - lasts for greater than 5 minutes

Figure 2. Risk Scoring Factors - Aseptic Interventions

Step		Intervention	Frequency	Proximity	Duration	Score	Outcome
1	Proleukin rIL-2 & Fungizone Aliquot Preparation	A screwcap vial falls over during filling, leading to the vial requiring replacement by the operator	3	3	1	9	Low Risk Intervention - To be incorporated into each APS and Operator Qualification run - multiple screwcap vials to be replaced.
		The pipette combitip fouls on the external surface of a screwcap vial during filling.	3	4	1	12	Medium Risk Intervention - To be incorporated into each APS and Operator Qualification run - simulated fouling on screwcap vial.
		The needle of a syringe used to reconstitute the IL-2 or Fungizone requires replacement	2	2	2	8	Low Risk Intervention - To be incorporated into each APS and Operator Qualification run - forced replacement of IL-2 needle.
3	y-TIL RPMI CM batch preparation	The pipette tip fouls on the exterior of a container.	3	4	1	12	Medium Risk Intervention - Intervention captured above.
		The mixing cannula fouls on the edge of the media container	3	4	1	12	Medium Risk Intervention - To be incorporated into each APS run - simulated fouling on media container.
5	y-TIL culture setup in 5x G-Rex10M units	The cannula fouls on the exterior of the container and requires changing.	3	4	1	12	Intervention captured above.
7	Harvest y-TILs via filter, sample and cryopreserve	The mixing cannula fouls on the edge of the container	3	4	1	12	Intervention captured above.
		A sterile weld fails, requiring the operator to clamp the joint immediately and reweld to prevent loss of product.	2	5	4	40	High Risk Intervention - To be incorporated into initial and routine APS - simulate clamping and re-welding.
		A heat seal fails, requiring the operator to clamp the joint immediately and re-seal.	2	5	4	40	High Risk Intervention - To be incorporated into initial and routine APS - simulate clamping and re-sealing.
		A luer connection fails and requires replacement	2	2	3	12	Medium Risk Intervention - To be incorporated into each APS run - forced replacement of luer connection.
		The 3-way valve fails and requires replacement.	2	3	3	18	Medium Risk Intervention - To be incorporated into each APS run - forced replacement of luer connection.
11	Extract 3x PBMCs (with 1x Rotea kit; 3x Harvest Products)	The Needle perforates the septum tubing requiring a replacement bag to be transferred into the BSC	2	3	2	12	Medium Risk Intervention - To be incorporated into each APS run - forced replacement of luer connection.
12	Cryobank 3x PBMC feeder cellbags and QC vials	A heat seal fails, requiring the operator to clamp the joint immediately and re-seal.	2	5	4	40	High Risk Intervention - To be incorporated into APS during initial validation runs - simulate clamping and re-sealing.
		The 3-way valve fails and requires replacement.	2	3	2	12	Medium Risk Intervention - To be incorporated into each APS run - forced replacement of luer connection.
17	Thaw y-TIL, rest in CM at 37degC	The mixing cannula fouls on the edge of the container	3	4	1	12	Intervention captured above.
18	REP-TILs Harvest (Gatherex)	Luer failure on 5L waste bags requires the process to be stopped, the bag to be sealed and replaced.	2	3	4	24	Medium Risk Intervention - To be incorporated into each APS run.
35	REP-TIL Product and Retention Samples Cryopreservation	Maximum number of cryobags are filled	3	5	5	75	High Risk Intervention - To be incorporated into initial, routine APS and Operator Qualification - simulation of max batch size
N/A	N/A	A fatigued operator performs processing at the end of a shift	N/A	N/A	N/A	N/A	Inherently simulated - process occurs over extended periods of processing
N/A	N/A	Multiple operators are present in the room whilst processing occurs	N/A	N/A	N/A	N/A	Inherently simulated - multiple operators required for manufacturing process

Figure 3. Example Aseptic Intervention Risk Assessment

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TRANSCRIPTOMIC ANALYSIS OF HUMAN CORNEAL STROMAL CELLS DURING EX VIVO EXPANSION AND SUBSEQUENT FABRICATION OF STROMAL TISSUE

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KEYWORDS: Corneal stromal cells, Single cell RNA-Seq, Flow cytometry.

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Background & Aim

Cultivated human corneal stromal cells (HCSC) have the potential to generate bioengineered corneal stromal tissue constructs for treating corneal diseases. Nevertheless, therapies based upon use of HCSC are limited by a poor understanding of culture heterogeneity and markers for assessment of cell quality. We therefore explored changes in the transcriptomic profile at key stages of HCSC expansion and subsequent tissue manufacture.

Methods, Results & Conclusion

Primary HCSC derived from three independent donors were analysed immediately following isolation from cadaveric donor tissue (p0), then after expansion with 5% FBS (p2), and following conditioning with 1% FBS (p4), and finally after isolation from self-assembled stromal tissue (SAS; p5). Flow cytometry and single-cell RNA sequencing (scRNA-seq) were used to assess cell state transitions and monitor transcriptomic changes at each timepoint.
Flow cytometry revealed expected increases in stromal cell activation markers CD73, CD90 and CD105 during ex vivo expansion of HCSC, followed by a significant decline in CD90 and CD105 after conditioning and subsequent fabrication of SAS. Cluster analysis of scRNA-seq data revealed distinct transcriptomic profiles for each timepoint. p0 cells exhibited acute fibroblastic activation, characterised by intense inflammatory signalling and heightened sensitivity to external stimuli. Contaminating immune cells and epithelial cells present at p0 were absent by p2. A shift in the global transcriptomic profile was observed during progression from p0 to p5, with cells at p2 displaying an activated and inflammatory fibroblast signature, while cells at p4 and p5 had a profile that was consistent with transition from proliferation to extracellular matrix (ECM) remodelling. Pseudobulk time-series differential expression and functional enrichment analysis confirmed that genes upregulated over time were strongly enriched for structural maturation programs vital to stromal

homeostatic function, specifically extracellular matrix and structure organization (*TIMP3*, *COL6A1*), and cell adhesion (*PCDH7)*. Conversely, genes demonstrating a downward trajectory were related to cell cycling (*CDK18*) and myofibroblast formation (*LRRC15*). In summary, these findings highlight distinct changes in the transcriptomic profile of HCSC at different stages of ex vivo expansion and de novo tissue synthesis. Thus, providing insights on how to select optimal timepoints and culture conditions when growing HCSC for clinical applications.

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Tissue Engineering

ENGINEERING MACROPOROUS GELMA/TANNIC ACID CRYOGELS FOR ENHANCED ANGIO-OSTEOGENIC TISSUE REGENERATION

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KEYWORDS: Macroporous hydrogel, Angiogenesis, Osteogenesis.

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Background & Aim

Vascularization is essential for tissue survival and bone regeneration, particularly in traumatic bone defects where impaired blood supply limits tissue infiltration and osteogenesis. Gelatin methacryloyl (GelMA) cryogels provide cell-adhesive, interconnected macroporous structures, but their mechanical stability and intrinsic biological functions remain limited. Tannic acid (TA) can reinforce polymer networks through reversible interactions while providing antioxidant and antibacterial activity. This study aimed to engineer a dual-crosslinked GelMA/TA (TAG) cryogel as a multifunctional scaffold for angio-osteogenic regeneration.

Methods, Results & Conclusion

Methods

Macroporous GelMA cryogels were fabricated by freezing, photopolymerization, and lyophilization of GelMA/LAP precursor solutions. TA was introduced by post-immersion treatment to avoid premature precursor gelation while preserving macroporosity. Four groups were prepared: GM, TAG3, TAG6, and TAG10. Physicochemical properties were analyzed by SEM, swelling/pore quantification, compression, rheology, and enzymatic degradation. Biocompatibility was assessed by live/dead staining, metabolic activity, and hemolysis. Antibacterial, antioxidant, angiogenic, biomineralization, and osteogenic activities were evaluated using bacterial inhibition, ROS/ABTS assays, HUVEC migration/tube formation, SBF immersion, and hBMSC ALP/ARS/RT-qPCR analyses. In vivo tissue integration and vascularization were examined after 4-week subcutaneous implantation.

Results & Conclusion

Post-immersion TA treatment produced stable TAG cryogels that maintained interconnected macroporosity while improving structural stability. TA incorporation reduced swelling and pore size, increased compressive/viscoelastic stiffness, and slowed enzymatic degradation. TAG cryogels showed cytocompatibility and hemocompatibility, inhibited bacterial growth, and reduced oxidative stress. TAG-conditioned environments enhanced HUVEC migration, tube formation, and angiogenic marker expression. TAG cryogels promoted Ca/P-rich mineral deposition in SBF and enhanced hBMSC osteogenic differentiation, indicated by increased ALP activity, calcium deposition, and osteogenic marker expression. Subcutaneous implantation showed improved host cell infiltration and CD31-positive vascularization. These findings suggest that TAG cryogels provide a reinforced, antioxidant, antibacterial, and angio-osteogenic scaffold platform for vascularized bone tissue regeneration.

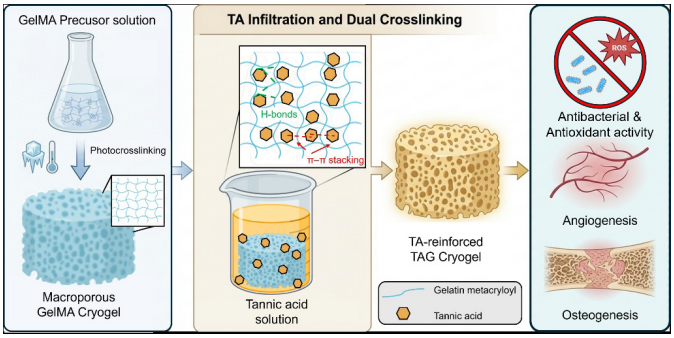


Figure 1. TA Infiltration and Dual Crosslinking

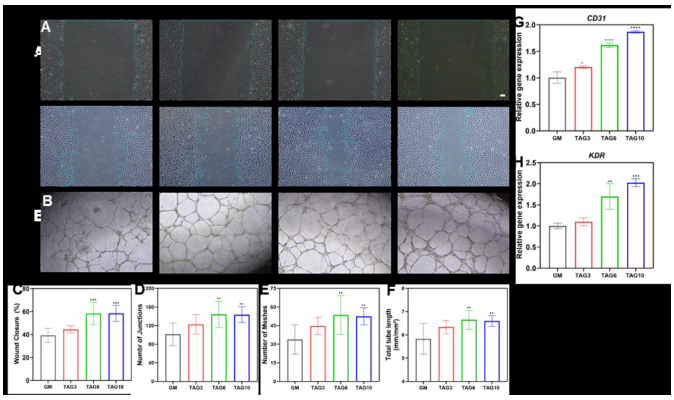


Figure 2. Angiogenesis

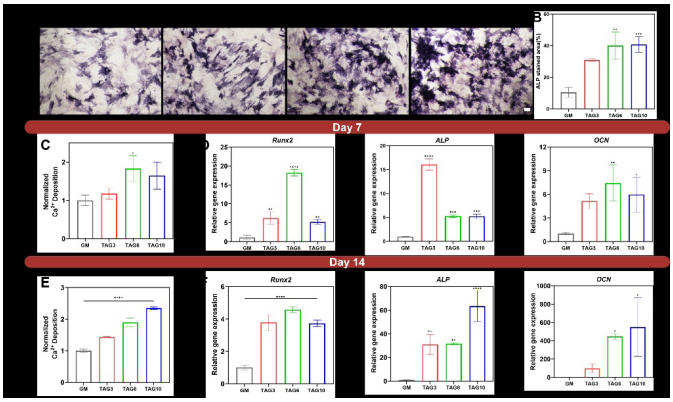


Figure 3. Osteogenesis

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Tissue Engineering

ASSEMBLED MODULAR MICROGEL CARRIERS: A VERSATILE CELL THERAPY PLATFORM FOR TAILORED BONE REGENERATION

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KEYWORDS: scaffold, assembly, tissue engineering.

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Background & Aim

Advanced additive manufacturing enables the creation of patient-specific implants; however, its widespread clinical adoption is severely hindered by high economic burdens and intensive labor. To resolve these challenges, we introduce HIVE: a modular, manually reconfigurable scaffold fabricated via digital light processing (DLP). This system empowers clinicians to easily assemble scaffolds of arbitrary geometries by hand at the point of care, ensuring an immediate, precise fit at the defect site. This study aims to evaluate the HIVE system as an advanced multi-channel delivery platform for growth factors, bioceramics, and living cells to achieve compartmentalized, site-specific tissue regeneration.

Methods, Results & Conclusion

Methods

Modular HIVE architectures were fabricated via DLP 3D printing and loaded with microcryogels (MCs) encapsulating distinct therapeutic agents. The system's capability was evaluated using growth factors (BMP-2 and VEGF), bioceramics, and co-cultures of human mesenchymal stem cells (hMSCs) and human umbilical vein endothelial cells (HUVECs). We performed comprehensive structural analyses, examined in vitro osteogenic/angiogenic differentiation and cell migration, and finally evaluated localized bone matrix and blood vessel regeneration via an in vivo rat subcutaneous model.

Results

HIVE provided controlled, sequential release of BMP-2 and VEGF, successfully stimulating osteogenic and angiogenic differentiation in hMSCs and HUVECs. Incorporating bioceramics significantly enhanced mineralization and bone-forming activity. When delivering HUVECs via the HIVE platform, we detected a robust upregulation of both angiogenic and osteogenic gene markers in co-cultured hMSCs. Systematically positioning various MC combinations triggered targeted, localized biological responses while maintaining unhindered cell migration throughout the interconnected structure. Notably, the in vivo subcutaneous rat study demonstrated accelerated localized bone matrix deposition and functional neovascularization.

Conclusion

The HIVE platform provides a highly versatile, cost-effective blueprint for personalized medicine through its limitless hand-assembly configurations. By bridging the gap between intraoperative customization and advanced cell/factor delivery, it shows great promise for next-generation, patient-specific bone tissue engineering.

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Tissue Engineering

TUNABLE IGF-1 RELEASE VIA DEXTRAN SULFATE FUNCTIONALIZED CRYOGELS FOR ACCELERATED BONE REGENERAION

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KEYWORDS: Cryogel, Controlled release, Growth factor delivery.

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Background & Aim

Large bone defects exceeding the critical size cannot heal spontaneously, and clinical autograft/allograft options remain limited by donor-site morbidity, restricted availability, and immune or infection risks. Growth factor-based therapies are promising but constrained by burst release, short half-life, and rapid loss of local bioactivity. This study aimed to develop a GelMA/dextran sulfate (DXS) cryogel as a tunable scaffold that regulates release of the cationic osteogenic factor IGF-1 through electrostatic interaction with anionic sulfate groups, while coordinating scaffold structure, bioactivity, and bone-regenerative performance.

Methods, Results & Conclusion

Methods

GelMA/DXS cryogels (GD 0–5; 0–5% DXS) were fabricated by APS/TEMED-initiated cryopolymerization at −20°C, lyophilized, and loaded with IGF-1. Pore morphology (SEM), interconnected porosity, swelling, enzymatic degradation, and mechanical/rheological properties were characterized. Mineralization (SBF immersion, ICP-QQQ), BSA adsorption, and FITC-BSA/IGF-1 release (ELISA) were assessed. Using hBMSCs, viability, F-actin spreading, ALP/ARS staining, and osteogenic gene expression (RT-qPCR) were evaluated. In vivo bone regeneration was tested in a 6 mm mouse calvarial defect model by micro-CT at 8 weeks.

Results & Conclusion

DXS modulated cryogel properties non-monotonically: intermediate DXS enlarged pores and lowered stiffness, whereas higher DXS densified the network and restored mechanical strength, while interconnected porosity (~54–58%) was preserved. GD 3 exhibited a balanced combination of porosity, structural stability, and cytocompatibility (>94%), with progressive IGF-1 release (73.7% by day 21) driven by sulfate-mediated electrostatic retention. GD 3 also enhanced mineralization, cell spreading (3.45-fold vs GD 0), ALP/ARS staining, and osteogenic marker expression. In vivo, DXS-containing cryogels improved bone regeneration, with the GD 3 + hBMSC group achieving the highest bone volume fraction (BV/TV 23.6% vs 5.58% in GD 0). These findings establish DXS concentration as a key design parameter for coordinating scaffold structure, controlled IGF-1 delivery, and bone regeneration in GelMA-based cryogels.

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Tissue Engineering

POLYROTAXANE-BASED CELL CULTURE SURFACES FOR PROMOTING MSC DIFFERENTIATION VIA MOLECULAR MOBILITY AND SURFACE FUNCTIONALIZATION

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KEYWORDS: MSC, Differentiation, Polymer.

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Background & Aim

Precise and reproducible control of cell behavior is crucial for cell therapies. Mesenchymal stromal cells (MSCs) are promising therapeutic candidates due to their multilineage differentiation and immunomodulatory properties. MSCs are typically cultured on tissue-culture polystyrene (TCPS) coated with adhesive proteins, such as collagen and fibronectin; however, these methods provide limited control over cell functions, particularly lineage-specific differentiation. Additionally, animal-derived components raise concerns regarding batch-to-batch variability and safety. Thus, we aimed to design surface-engineered substrates that accelerate MSC differentiation in a reproducible and well-defined manner.

Methods, Results & Conclusion

Polyrotaxanes (PRXs) are synthetic supramolecular polymers composed of poly(ethylene glycol) chains threaded through α-cyclodextrins (αCDs), exhibiting unique molecular mobility through the sliding motion of αCDs. This dynamic feature has been shown to facilitate interactions with biomolecules and modulate cytoskeleton-related signaling, leading to the regulation of cell morphology, proliferation, migration, and differentiation. In addition, PRXs with various functional groups have been examined to assess how surface properties affect MSC differentiation. Sulfonated PRXs were found to promote both osteogenic and adipogenic differentiation, presumably due to the synergistic effects of molecular mobility and strongly negative surface charge; however, their efficiency remained lower than on fibronectin-coated surfaces. Herein, we optimized the chemical composition of

sulfonated PRXs to outperform widely used fibronectin-coated surfaces by accelerating MSC differentiation. More than 20 PRX variants with varying αCD threading numbers and sulfonate modifications were synthesized and coated on TCPS. Human bone marrow MSCs were cultured, and osteogenic differentiation was assessed by alkaline phosphatase (ALP) and Alizarin Red S staining. As a result, we identified the optimized sulfonated PRXs that significantly improved osteogenic differentiation without cell detachment, showing stronger ALP staining at day 3 and mineralization at day 7 compared with TCPS and fibronectin-coated surfaces. These findings demonstrate that sulfonated PRX surfaces promote MSC differentiation compared with conventional ones. While further studies are required for clinical applications, this platform provides a promising approach for controlling cell culture systems.

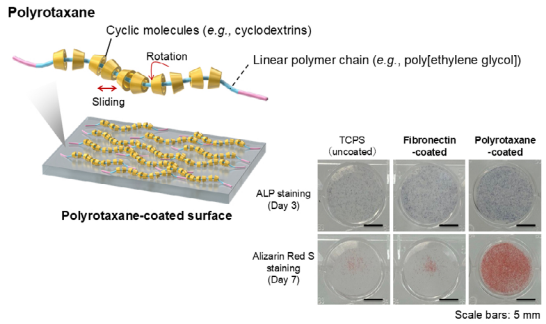


Figure 1. Accelerating osteogenic differentiation of MSCs on polyrotaxane-coated surfaces

Notes

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Thursday, September 3 | 04:30 p.m.
Adherent Cell Culture System on the CliniMACS Prodigy® Platform

Friday, September 4 | 10:15 a.m.
CAR T cell manufacturing workflow on the CliniMACS Prodigy Platform

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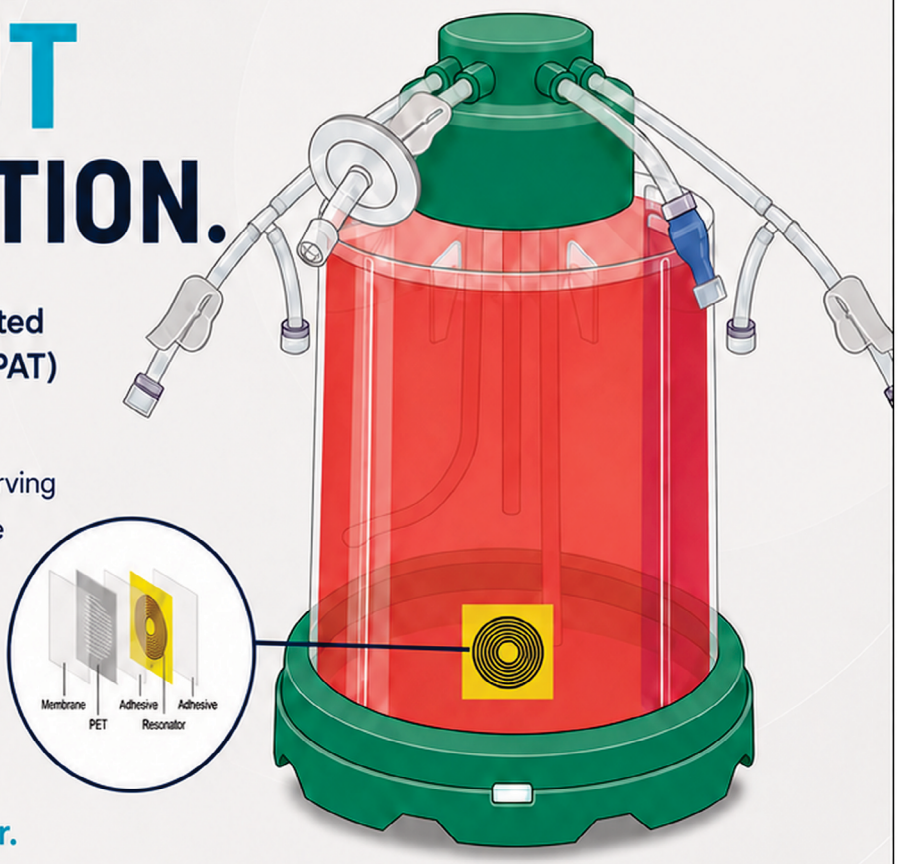
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G-REX®

SMART™ G-Rex® brings integrated Process Analytical Technology (PAT) to the G-Rex® platform.

It advances process insight while preserving the simplicity and scalability that define manufacturing with G-Rex®.



SMART™

= Secreted Metabolite Absorbing Resonant Transducer.

Eliminate Manual Sampling

Preserve Closed-System Integrity

Maintain Scalability

FEATURED PRESENTATION

Wednesday, September 2 | 12:00–13:00

Join us for an insightful session on how integrated PAT on the G-Rex® platform is shaping the future of process insight.

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Visit the ScaleReady booth to see SMART™ G-Rex® firsthand and speak with our team.

Learn more

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