ISCT ANZ 2026 REGIONAL MEETING

PROGRAM

International Society
ISCT
Cell & Gene Therapy®
AUSTRALIA AND NEW ZEALAND REGION

JULY 20-22, 2026 | MELBOURNE | AUSTRALIA

MELBOURNE CONVENTION AND EXHIBITION CENTRE

WWW.ISCT-ANZ2026.COM

Welcome from the Co-Chairs

Dear Colleagues and Friends,

Welcome! Nau mai, haere mai ki tēnei hui. We are delighted to welcome you to Melbourne for the International Society for Cell and Gene Therapy (ISCT) Australia & New Zealand 2026 Regional Meeting.

Our theme, "From Breakthrough Science to Patient Impact: Defining the Future of Cell and Gene Therapy," reflects the remarkable progress and momentum across our field. We are excited to bring together global and regional experts to share the latest advances in science, technology, translation, and clinical application, and we warmly invite you to engage in discussions that span academia, industry, regulatory bodies, and the healthcare system.

ISCT was founded on a vision to translate innovative science into safe and effective therapies that improve patients' lives worldwide. This ANZ meeting highlights the strength of our region in advancing that mission, with a dynamic program encompassing gene editing, nextgeneration immunotherapies, cell therapy platforms, and realworld clinical implementation.

We are delighted to host leading scientists and clinicians from academia and industry, alongside representatives from the Therapeutic Goods Administration, Medsafe New Zealand, and other key stakeholders. Together, these perspectives will help shape discussions on accelerating research translation, ensuring safety and quality, and improving equitable patient access across our region.

Across the plenary sessions, multiple concurrent sessions, and interactive roundtables, we aim to deliver a program that is stimulating, insightful, and future focused. We also encourage you to continue conversations and build connections during our Welcome Reception, poster sessions, and networking breaks - opportunities that are central to the collaborative spirit of ISCT.

We extend our sincere thanks to our speakers, sponsors, organising committee, and the broader ISCT community for their invaluable contributions. Above all, we thank you for being part of this meeting and for your commitment to advancing cell and gene therapy.

On behalf of the organising committee, we warmly welcome you to Melbourne and wish you an inspiring and rewarding meeting.

With best wishes,
Siok Tey and Emily Blyth
ISCT ANZ 2026 Meeting Co-Chairs

Siok Tey, MBBS (Hons), PhD, FRACP, FRCPA,
ISCT ANZ Regional VP
QIMR Berghofer Medical Research Institute, Royal Brisbane Women's Hospital
Australia

Emily Blyth, B.Med (Hons), FRACP, FRCPA, PhD
ISCT ANZ Past Regional VP
Westmead Hospital
Australia

Table of Contents

Organizing Committee

Program Co-Chairs

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| MBBS (Hons), PhD, FRACP, FRCPA
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QIMR Berghofer Medical Research Institute, Royal Brisbane & Women's Hospital
Brisbane, Australia

Emily Blyth
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Sydney, Australia

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| BASc, PhD
University of Queensland
Brisbane, Australia

Gaurav Sutrave
| BSc (Med), MBBS, PhD, FRACP, FRCPA
ISCT ANZ ESP Subcommittee Co-Chair
Westmead Hospital
Sydney, Australia

Zlatibor Velickovic
| BSc (Hons), PhD
Royal Perth Hospital, University of Western Australia,
Perth, Australia

General Conference Information

Registration Desk Hours

Foyer

Monday, July 20	07:00 - 18:00
Tuesday, July 21	07:30 - 18:00
Wednesday, July 22	07:30 - 11:30

Exhibit Hours

Poster and Exhibit Hall

Monday, July 20	08:00 - 20:00
Tuesday July 21	08:00 - 19:00
Wednesday July 22	08:00 - 12:30

Speaker Services Center

Room 102

Monday, July 20	07:00 - 18:00
Tuesday July 21	07:30 - 18:00

Wi-Fi

Public WiFi available through "MCEC Free WiFi"

Access & Security

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

Social & Networking Events

Events below are included for all registered delegates

MONDAY JULY 20

17:30 – 18:00
Welcome Address
Room 105 – 106

18:00 – 20:00
Welcome Reception
Poster and Exhibit Hall
Sponsored by GILEAD | Kite

Poster Reception 1
Poster and Exhibit Hall

TUESDAY JULY 21

18:00 – 19:00
Poster Reception 2
Poster and Exhibit Hall

Social Media

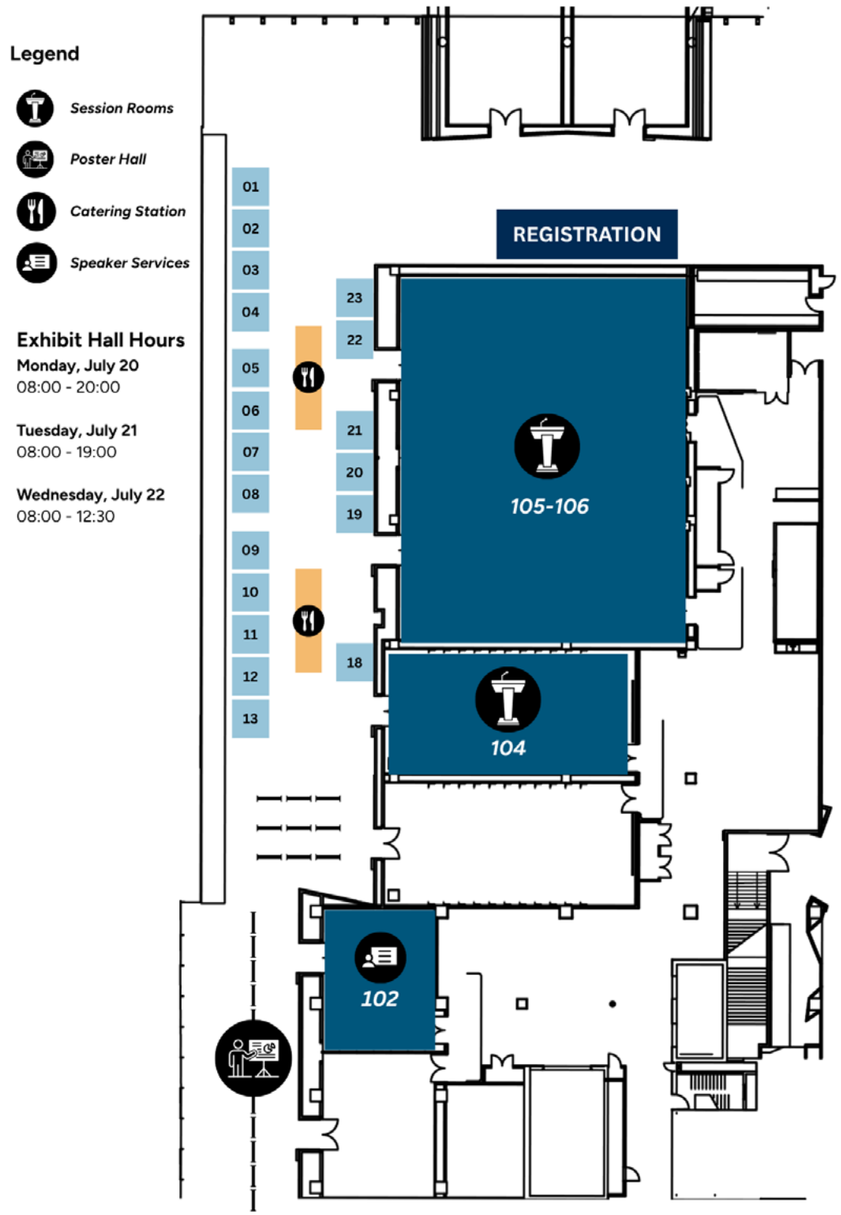
Join the conversation on LinkedIn, BlueSky, and X! #ISCTANZ2026

Questions?

Please stop by the Registration Desk Level 1 Foyer or email meetings@isctglobal.org for assistance.

Venue Map

MCEC Level One



Co-Chairs and Speakers

Simon Barry, *PhD, Adelaide University, Adelaide, Australia*

Paul Beavis, *PhD, Peter MacCallum Cancer Centre, Victoria, Australia*

Marie Bleakley, *BMBS, PhD, MMSc, Fred Hutchinson Cancer Centre, Seattle, United States*

Leon Brownrigg, *BSc, GDipSc, MMedSc, GDipEd, PhD, Cell and Tissue Therapies WA, Royal Perth Hospital, East Metropolitan Health Service, Perth, Australia*

Stuart Chambers, *PhD, University of Otago, Christchurch, New Zealand*

Colleen Delaney, *MD, MSc, Seattle Children's Research Institute, Seattle Children's Hospital, Seattle, United States*

Lachlan Dobson, *BBioMedSci, University of Sydney, Sydney, Australia*

Dennis Dowhan, *PhD, Therapeutic Goods Administration – Biological Science Section, Australia*

Boro Dropulić, *PhD, MBA, Caring Cross, Vector BioMed, Maryland, United States*

Vera Evtimov, *PhD, Cartherics Pty Ltd, Notting Hill, Australia*

Dominic Fernandez, *CCP, MS, MBA, Epworth Healthcare, Murdoch Children's Research Institute, Melbourne, Australia*

Vanessa Fitzgerald, *BASc, NSW Health, NSW, Australia*

Jess Frith, *PhD, Monash University, Melbourne, Australia*

Samantha Ginn, *PhD, Children's Medical Research Institute, Sydney, Australia*

Cibelly Goulart, *PhD, Australia Office of the Gene Technology Regulator, Australia*

Sarah Grandinette, *PhD, University of Pennsylvania School of Medicine, Philadephia, United States*

Simon Harrison, *MBBS, MRCP (UK), FRCPath (UK), FRACP, PhD, Peter MacCallum Cancer Centre, Melbourne, Australia*

Andras Heczey, *MD, Seattle Childrens Research Institute, Seattle, United States*

Andrea Henden, *BSc, MBBS (Hons), FRACP, FRCPA, PhD, Royal Brisbane & Women's Hospital, QIMR Berghofer, Herston, Australia*

Tracy Heng, *PhD, Monash University, Melbourne, Australia*

Matthew M. Hewitt, *BA, PhD, Charles River Laboratories, Wilmington, United States*

Misty Jenkins, *PhD, Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia*

Yazi Diana Ke, *PhD, Macquire Medical School, Sydney, Australia*

Glen Kennedy, *MBBS (Hons), FRACP, FRCPA, A/Prof, Queensland Department of Health, Royal Brisbane & Women's Hospital, Brisbane, Australia*

Kasey Kime, *MQS, MPhil, MBA, BioOra Limited, New Zealand*

Rebecca Lim, *PhD, INOVIQ Ltd, Melbourne, Australia*

Leszek Lisowski, *PhD, MBA, Viral Vector Manufacturing Facility, University of Sydney, Sydney, Australia*

Melissa Little, *AC, BSc (Hons I), PhD, GAICD, FAAHMS, FAAS, Murdoch Children's Research Institute, Novo Nordisk Foundation Centre for Stem Cell Medicine (reNEW), Melbourne, Australia*

Alyce Maksoud, *Therapeutic Goods Administration – Manufacturing Quality Branch, Australia*

Ali McCarron, *PhD, Adelaide University, Adelaide, Australia*

Colin McLean, *MSc, Cell Therapies Pty Ltd, Melbourne, Australia*

Alex McLellan, *PhD, Dept. Microbiology & Immunology, University of Otago, Dunedin, New Zealand*

Rebecca McQualter, *B.Med (Hons), PhD, Chimeric Therapeutics, Melbourne Australia*

Bev Menner, *PhD, Cell Therapies Pty Ltd, Melbourne, Australia*

Shalin Naik, *PhD, Walter and Eliza Hall Institute of Medical Research, Parkville, Australia*

Atefeh NamiPashaki, *PhD, University of Melbourne, Melbourne, Australia*

Geraldine O'Neill, *PhD, Children's Hospital Westmead, Westmead, Australia*

Jelena Rnjak-Kovacina, *PhD, University of New South Wales, Sydney, Australia*

Philipp C. Rommel, *Dr. rer. nat. , Garvan Institute of Medical Research, Sydney, Australia*

Ash Sargent, *PhD, University of Auckland, Auckland, New Zealand*

Penny Shakespeare, *LLB, Australian Department of Health, Canberra, Australia*

Sandeep Soni, *MD, Mammoth Biosciences, University of California, San Francisco, United States*

Tim Strabala, *PhD, Environmental Protection Authority, New Zealand*

Dario Stupar, *PhD, Q-Gen Cell Therapeutics (QIMR Berghofer), Brisbane, Australia*

Lachlan Thompson, *PhD, University of Sydney School of Medical Sciences, Sydney, Australia*

Stephen Thompson, *BEng (Hons) (Chem), Viral Vector Manufacturing Facility, Sydney, Australia*

Karin van Bart, *MBChB, Medsafe, New Zealand*

Dominic Wall, *PhD, FFScRCPA, Cell Therapies Pty Ltd, Peter MacCallum Cancer Centre, Melbourne, Australia*

Gordon Wallace, *PhD, Australian Institute for Innovative Materials, Intelligent Polymer Research Institute, University of Wollongong, Wollongong, Australia*

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

Kelly Wray, *BMedBiotech (Hons), Sydney Cell and Gene Therapy, Sydney, Australia*

Oral Abstract Presenters

Stephen Boyle, *MBChB, BSc (Hons), MRCP(UK), FRCPA, FRACP QIMR Berghofer Medical Research Institute, Australia*

Cheok Weng Chan, *BH-BMED, Peter MacCallum Cancer Centre, Australia*

Saeedeh Darzi, *PhD, Hudson Institute of Medical Research, Australia*

Deekshitha Dhulipati, *BMedSci (Hons), Westmead Institute for Medical Research, Australia*

Mark Dowling, *MD, PhD, Peter MacCallum Cancer Centre, Royal Melbourne Hospital, Australia*

Phoebe Dunbar, *BSc, Peter MacCallum Cancer Centre, Australia*

Sayali Gore, *BSc, The Kids Research Institute, Australia*

Yu-Kuan (Tony) Huang, *PhD, Peter MacCallum Cancer Centre, Australia*

Alexander Joechner, *MD, Biosceptre International Limited, Australia*

Sidra Khan, *MBBS, Centre of Cancer Biology, Australia*

Jingjing Li, *PhD, University of New South Wales, Australia*

Andy J. Y. Low, *PhD, Centre for Cancer Biology, Australia*

Patrick Marron, *BBioMedSc, University of Otago, New Zealand*

Isabelle Munoz, *PhD, Peter MacCallum Cancer Centre, Australia*

Mutsunori Murahashi, *MD, PhD, The Jikei University School of Medicine, Japan*

Eunwoo Nam, *MS, BS, Adelaide University, Australia*

Tim Oldham, *PhD, AdAlta Ltd, Australia*

Jane Tian, *BS, Westmead Institute for Medical Research, Australia*

Pei Tian, *BSc (Hons), Murdoch Children's Research Institute, Australia*

Program

DAY 1 - Monday July 20

07:00 - 18:00	**Registration Hours**
08:00 - 20:00	**Exhibit Hours**
08:00 - 09:00	**Beyond Blood Cancers: New Horizons for CAR Therapy** **Room: 105 - 106** **Co-Chairs:** Alicia Disbury, *PhD, The University of Auckland, New Zealand* Lachlan Dobson, *BBioMedSci, University of Syndey, Australia* **Speakers:** Boro Dropulić, *PhD, MBA, Caring Cross, Vector BioMed, United States* Misty Jenkins, *PhD, Walter and Eliza Hall Institute of Medical Research, Australia* Alex McLellan, *PhD, University of Otago, New Zealand*
	Oral Abstract Session **Room: 104** **Abstract Presenters:** **A Novel T-cell Receptor Therapeutic Product for the Treatment of WT1+ Malignancies** Sayali Gore, *BSc, The Kids Research Institute, Australia* **A Human iPSC-Derived Model for Studying Cell-State-Specific Responses to Mechanical and Hypoxic Regulation of Hemogenic Endothelial Development** Jingjing Li, *PhD, University of New South Wales, Australia* **Next-Generation CAR-T Cells Through Transcriptional Reprogramming** Isabelle Munoz, *PhD, Peter MacCallum Cancer Cantre, Australia* **Leveraging Endogenous Gene Regulation to Enable Tumor-Restricted Armoring of CAR T Cells with Enhanced Safety and Efficacy** Isabelle Munoz, *PhD, Peter MacCallum Cancer Cantre, Australia* **An East-to-West Business Model for Commercialising Solid Tumor CAR-T Therapies: Leveraging Cross-Border Partnerships, Adanced Manufacturing and Capital-Efficient Development** Tim Oldham, *PhD, AdAlta Ltd., Australia* **Ten Years in the Making: Australia's first GMP-Compliant Cord Blood-Derived iPSC Master Cell Bank for Translational and Clinical Research** Pei Tian, *Murdoch Children's Research Institute, Australia*

09:15 - 10:15	**Bioengineering - Engineering Cell Niches: Designing Microenvironments for Potent Therapies** **Room: 105 – 106** **Co-Chairs:** Robert Nordon, *MBBS, PhD, University of New South Wales, Australia* Sharon Sagnella, *PhD, Royal Prince Alfred Hospital, Australia* **Speakers:** Gordon Wallace, *PhD, Australian Institute for Innovative Materials, Intelligent Polymer Research Institute, University of Wollongong, Australia* Jess Frith, *PhD, Monash University, Australia* Jelena Rnjak-Kovacina, *PhD, University of New South Wales, Australia*
	Gilead Kite Corporate Session **Real-World Outcomes of Immunotherapy: From Trials to Clinical Practice** GILEAD | Kite **Room: 104** **Speakers:** Mark Dowling, *MBBS, PhD, Clinical Haematologist, Peter MacCallum Cancer Centre, Melbourne, Australia* Robert Weinkove, *MBBS, PhD, Clinical Director, Malaghan Institute of Medical Research, New Zealand* Gemma Reynolds, *MBBS, MPH, Infectious Diseases Physician, Austin Health, Australia*
10:15 – 10:45	**Coffee Break** **Poster and Exhibit Hall**
	Sartorius Company Presentation **Perfusion-Enabled CAR-T Manufacturing In Stirred-Tank Bioreactors Achieving 100+ Doses Per Batch** SARTORIUS **Room: 104** **Speaker:** Rukmini Ladi, *Segment Technology Manager, Cell Therapy, Sartorius*
10:45 – 12:15	**Plenary Session: Emerging Cell and Gene Therapy Strategies for Pulmonary Disease** **Room: 105 – 106** **Co-Chairs:** Emily Blyth, *B.Med(Hons), FRACP, FRCPA, PhD, Westmead Hospital, Australia* Siok Tey, *MBBS(Hons), PhD, FRACP, FRCPA, QIMR Berghofer Medical Research Institute, Royal Brisbane & Women's Hospital, Australia* **Speakers:** Daniel J. Weiss, *MD, PhD, University of Vermont, United States* Tracy Heng, *PhD, Monash University, Australia* Ali McCarron, *PhD, Adelaide University, Australia*
12:15 – 13:45	**Lunch** **Poster and Exhibit Hall**
13:45 – 14:45	**Engineering Next-Generation Therapies: From iPSC Cell Engineering to In Vivo Gene Editing** **Room: 105 – 106** **Co-Chairs:** Jingjing Li, *PhD, University of New South Wales, Australia* Zlatibor Velickovic, *BSc (Hons), PhD, Royal Perth Hospital, University of Western Australia, Australia* **Speakers:** Lachlan Thompson, *PhD, University of Sydney School of Medical Sciences, Australia* Stuart Chambers, *PhD, University of Otago, New Zealand* Sandeep Soni, *MD, Mammoth Biosciences, University of California, United States*

Validated Assays for Clinical Manufacture

Room: 105 – 106

Co-Chairs:

Heather Donaghy, *PhD, Therapeutic Innovation Australia, Australia*
Cheryl Hutchins, *PhD, Royal Brisbane & Women's Hospital, Australia*

Speakers:

Matthew M. Hewitt, *BA, PhD, Charles River Laboratories, United States*
Kelly Wray, *BMedBiotech (Hons), Sydney Cell and Gene Therapy, Australia*
Dario Stupar, *PhD, Q-Gen Cell Therapeutics (QIMR Berghofer), Australia*

15:00 – 16:00

Elevator Pitch Session

Room: 104

Co-Chairs:

Atefeh NamiPashaki, *PhD, University of Melbourne, Australia*
Ash Sargent, *PhD, University of Auckland, New Zealand*

Abstract Presenters:

Leveraging DC Activation to Overcome Tumor Heterogeneity in CAR T Cell Therapy
Cheok Weng Chan, *BH-BMED, Peter MacCallum Cancer Centre, Australia*

Targeted Integration of a Fungus-Specific Transgenic T Cell Receptor into Human T Cell Receptor Alpha Constant Locus
Deekshitha Dhulipati, *BMedSci (Hons), Westmead Institute for Medical Research, Australia*

Antigen-Heterogeneous Solid Tumour Targeting with Tumour-Localised T Cell Engager-Expressing T Cells
Yu-Kuan (Tony) Huang, *PhD, Peter MacCallum Cancer Centre, Australia*

Development of T Cell-Targeted Lentiviral Vectors for In Vivo Delivery of the BRiDGE Adaptor CAR System
Alexander Joechner, *MD, Biosceptre International Limited, Australia*

Developing Single or Multi-Targeting CAR-T Cell Therapy in the Treatment of Paediatric Brain Tumours
Andy J. Y. Low, *MSc, Centre for Cancer Biology, Australia*

Cooperative CAR T and CAR NK Cell Therapy for Durable Tumour Control
Patrick Marron, *BBioMedSc, University of Otago, New Zealand*

Armouring GD2 Chimeric Antigen Receptor (CAR)-T Cells with Chemokine Receptors and INTERLEUKIN (IL)-15 to Treat Glioblastoma
Eunwoo Nam, *MS, BS, Adelaide University, Australia*

Predicting Epitope-Binding TCR for T Cell-Based Therapies in Acute Myeloid Leukemia
Jane Tian, *BS, Westmead Institute for Medical Research, Australia*

16:00 – 16:30

Coffee Break

Poster and Exhibit Hall

GenScript Biotech Australia Company Presentation

Harnessing the synergic power of new tLNP formulation and CAR expression modality for in vivo CAR-T development

Room: 104 | 16:00 - 16:15

Speaker:

Lumeng Ye, *Head of Business Development, ANZ, GenScript Biotech Australia Pty. Ltd., Australia*

Ideagen Company Presentation

From Q-Pulse to Ideagen Quality Management: supporting Australia's cell and gene therapy community, today and what's next

Room: 104 | 16:15 - 16:30

Speaker:

Kevin McSharry, *VP Practice Lead, Quality, Ideagen, Australia*

16:30 – 17:30

Geoff Symonds Oration

Kidney Regeneration: a Long and Winding Road

Room: 105 – 106

Co-Chairs:

Emily Blyth, *B.Med(Hons), FRACP, FRCPA, PhD, Westmead Hospital, Australia*
Siok Tey, *MBBS(Hons), PhD, FRACP, FRCPA, QIMR Berghofer Medical Research Institute, Royal Brisbane & Women's Hospital, Australia*

Speaker:

Melissa Little, *AC, BSc (Hons I), PhD, GAICD, FAAHMS, FAAS, Novo Nordisk Foundation Centre for Stem Cell Medicine (reNEW), Murdoch Children's Research Institute, Australia*

17:30 – 18:00

Welcome Address

Room: 105 – 106

18:00 – 20:00

Welcome Reception and Poster Reception 1

Poster and Exhibit Hall

Sponsored by: GILEAD | Kite

DAY 2 - Tuesday July 21

07:30 - 18:00	**Registration Hours**
08:00 - 19:00	**Exhibit Hours**
08:00 - 09:00	**The Regulatory Pulse: Updates Shaping Cell and Gene Therapy in Australia and New Zealand** Room: 105 – 106 **Co-Chairs:** Dominic Wall, *PhD, FFScRCPA, Cell Therapies Pty Ltd, Peter MacCallum Cancer Centre, Australia* Kasey Kime, *MQS, MPhil, MBA, BioOra Limited, New Zealand* **Speakers:** Dennis Dowhan, *PhD, Therapeutic Goods Administration – Biological Science Section, Australia* Karin van Bart, *MBChB, New Zealand Medsafe, New Zealand* Cibelly Goulart, *PhD, Australia Office of the Gene Technology Regulator (OGTR), Australia* Tim Strabala, *PhD, Environmental Protection Authority, New Zealand* Alyce Maksoud, *Therapeutic Goods Administration – Manufacturing Quality Branch, Australia*
09:15 - 10:15	**Grill the Regulator** Room: 105 – 106 **Co-Chairs:** Dominic Wall, *PhD, FFScRCPA, Cell Therapies Pty Ltd, Peter MacCallum Cancer Centre, Australia* Kasey Kime, *MQS, MPhil, MBA, BioOra Limited, New Zealand* **Speakers:** Dennis Dowhan, *PhD, Therapeutic Goods Administration – Biological Science Section, Australia* Karin van Bart, *MBChB, New Zealand Medsafe, New Zealand* Cibelly Goulart, *PhD, Australia Office of the Gene Technology Regulator (OGTR), Australia* Tim Strabala, *PhD, Environmental Protection Authority, New Zealand* Alyce Maksoud, *Therapeutic Goods Administration – Manufacturing Quality Branch, Australia*
10:15 – 10:45	**Coffee Break Sponsored by:** GILEAD | Kite Poster and Exhibit Hall *Cytiva Company Presentation* **Integrated Closed-System Platforms for Scalable Cell Therapy Manufacturing: From T Cells to MSC/iPSC Expansion** Room: 104 **Speaker:** Andrea Zhao, *PhD, Application Specialist - Cell Therapy & Nanomedicine, Cytiva, Sydney, Australia*
10:45 – 12:15	**Plenary Session: Gene Editing: From Precision Design to Clinical Reality** Room: 105 – 106 **Co-Chairs:** Tessa Gargett, *BSc (Hons), PhD, SA Health, Australia* Jessica Li, *PhD, Peter MacCallum Cancer Centre, Australia* **Speakers:** Sarah Grandinette, *PhD, University of Pennsylvania School of Medicine, United States* Shalin Naik, *PhD, Walter and Eliza Hall Institute of Medical Research, Australia* Paul Beavis, *PhD, Peter MacCallum Cancer Centre, Australia*
12:15 – 13:45	**Lunch** Poster and Exhibit Hall
13:45 – 14:45	**Roundtable: National Strategy and Policy: Health Technology Assessment, Funding, and Future Access Pathways for Advanced Therapies** Room: 105 – 106 **Co-Chairs:** Emily Blyth, *B.Med(Hons), FRACP, FRCPA, PhD, Westmead Hospital, Australia* Dominic Fernandez, *CCP, MS, MBA, Epworth Healthcare, Murdoch Children's Research Institute, Australia* **Panelists:** Vanessa Fitzgerald, *BASc, NSW Health, Australia* Glen Kennedy, *MBBS (Hons), FRACP, FRCPA, A/Prof, Queensland Health, Royal Brisbane & Women's Hospital, Australia*

14:00 - 14:30	***Cell Signaling Technology Company Presentation*** **GMP-Grade Recombinant Monoclonal Antibody Conjugates for Cell Therapy Manufacturing & QC** **Room: 104 | 14:00 – 14:15** **Speaker:** Ryan Tay, *PhD, Commercial Lead APAC, Cell Signaling Technology*
	Neuroscientific Company Presentation **StemSmart™ MSC: A Next Generation Stem Cell Solution for Immune-Mediate Inflammatory Disorders** **Room: 104 | 14:15 - 14:30** **Speaker:** Catherine Cole, *MBBS FRACP FRCPA, Chief Medical Officer, NeuroScientific Biopharmaceuticals Ltd, Australia*
15:00 - 16:30	**Plenary Session: Off-the-Shelf Cell Therapies for Transplant and Immunotherapy** **Room: 105 – 106** **Chair:** Ngaire Elwood, *BSc(Hons), PhD, Murdoch Children's Research Institute, Australia* **Speakers:** Colleen Delaney, *MD, MSc, Seattle Children's Research Institute, Seattle Children's Hospital, United States* Rebecca Lim, *PhD, INOVIQ Ltd, Australia* Vera Evtimov, *PhD, Cartherics Pty Ltd, Australia*
16:30 – 16:45	**Coffee Break - Sponsored by:** **Poster and Exhibit Hall**
	Thermo Fisher Company Presentation **Modular Automated Processing, Formulation, and Fill-Finish for Diverse CAR-Engineered Cell Therapies** **Room: 104** **Speaker:** Poh Loong Soong, *PhD, Field Application Scientist, Cell and Gene Advanced Therapy, Asia Pacific and Japan, Thermo Fisher Scientific*

16:45 – 17:45	**Commercial Workstream – Capital Raising to FIH to path to Commercialisation** **Room: 105 – 106** **Chair:** Dominic Fernandez, *CCP, MS, MBA, Epworth Healthcare, Murdoch Children's Research Institute, Australia* **Speakers:** Leszek Lisowki, *PhD, MBA, Viral Vector Manufacturing Facility, University of Sydney, Australia* Colin McLean, *MSc, Cell Therapies Pty Ltd, Australia* Rebecca McQualter, *B.Med(Hons), PhD, Chimeric Therapeutics, Australia* **Panelists:** Stephen Thompson, *BEng (Hons) (Chem), Viral Vector Manufacturing Facility, Australia* Bev Menner, *PhD, Cell Therapies Pty Ltd, Australia*
	Oral Abstract Session **Room: 104** **Abstract Presenters:** **Investigating the Role of BCMA Mutations in CAR-T Resistance with Established and Novel CAR-T Constructs** Stephen Boyle, *MBChB, BSc (Hons), MRCP(UK), FRCPA, FRACP, QIMR Berghofer Medical Research Institute, Australia* **Bioengineered PLCL-MSC Vaginal Implants Promote Tissue Regeneration in an Ovine Model of Pelvic Organ Prolapse** Saeedeh Darzi, *PhD, Hudson Institute of Medical Research, Australia* **Time to First Fever is Strongly Associated with Subsequent Severe ICANS in R/R LBCL Treated with AXI-CEL** Mark Dowling, *MD, PhD, Peter MacCallum Cancer Centre, Royal Melbourne Hospital, Australia* **Generating CRISPR/CAS9 Armoured CAR- and TCR-T Cells for the Treatment of Solid Tumours** Phoebe Dunbar, *BSc, Peter MacCallum Cancer Centre, Australia* **Development of Anti-CAR Antibody Responses in CAR-T Therapy: Preliminary Data from Phase 1 Clinical Trials in Adult and Pediatric Brain Tumors** Sidra Khan, *MBBS, Centre of Cancer Biology, Australia* **A MicroRNA-Regulated Coxsackievirus B3 Platform Enables Safe and Effective Oncolytic Therapy in Pancreatic Cancer with Translational Readiness for First-in-Human Studies** Mutsunori Murahashi, *MD, PhD, The Jikei University School of Medicine, Japan*
18:00 – 19:00	**Poster Reception 2** **Poster and Exhibit Hall**

PROGRAM

DAY 3 - Wednesday July 22

07:30 - 11:30	**Registration Hours**
08:00 - 12:30	**Exhibit Hours**
08:00 - 09:00	**The Translational Pathway: Designing and Delivering Phase I Cell and Gene Therapy Trials** Room: 105 – 106 **Co-Chairs:** Tessa Gargett, *PhD, SA Health, Australia* Alicia Disbury, *PhD, The University of Auckland, New Zealand* **Speakers:** Simon Barry, *PhD, Adelaide University, Australia* Geraldine O'Neill, *PhD, Children's Hospital Westmead, Australia* Leon Brownrigg, *BSc, GDipSc, MMedSc, GDipEd, PhD, Cell and Tissue Therapies WA, Royal Perth Hospital, East Metropolitan Health Service, Australia*
09:15 - 10:45	**Plenary Session: Advancing T-Cell Therapies in Transplant and Malignancy** Room: 105 – 106 **Co-Chairs:** Zlatibor Velickovic, *BSc (Hons), PhD, Royal Perth Hospital, University of Western Australia, Australia* Francisco Chung, *PhD, New Zealand Blood Service, New Zealand* **Speakers:** Marie Bleakley, *BMBS, PhD, MMSc, Fred Hutchinson Cancer Center, United States* Andras Heczey, *MD, Seattle's Children's Research Institute, United States* Philipp C. Rommel, *Dr. rer.nat., Garvan Institute of Medical Research, Australia*
10:45 – 11:15	**Coffee Break** Poster and Exhibit Hall
11:30 – 12:30	**Gene Therapy in Human Studies: Signals, Safety and Promise** Room: 105 – 106 **Co-Chairs:** Mark Dowling, *BA, BSc (Hons), PhD, MBBS, FRACP, Peter MacCallum Cancer Centre, Royal Melbourne Hospital, Australia* Andrea Henden, *BSc, MBBS (Hons), FRACP, FRCPA, PhD, Royal Brisbane Women's Hospital, QIMR Berghofer, Australia* **Speakers:** Simon Harrison, *MBBS, MRCP (uk), FRCPath (uk), FRACP, PhD, Peter MacCallum Cancer Centre, Australia* Yazi Diana Ke, *PhD, Macquarie Medical School, Australia* Samantha Ginn, *PhD, Children's Medical Research Institute, Australia*
	Roundtable: Career Pathways Along the Translational Pipeline Room: 104 **Co-Chairs:** Gaurav Sutrave, *BSc (Med), MBBS, PhD, FRACP, FRCPA, Westmead Hospital, Australia* Gemma Moir-Meyer, *PhD, University of Otago, New Zealand* **Panelists:** Marie Bleakley, *BMBS, PhD, MMSc, Fred Hutchinson Cancer Center, United States* Simon Barry, *PhD, Adelaide University, Australia* Colleen Delaney, *MD, MSc, Seattle Children's Research Institute, Seattle Children's Hospital, United States* Dominic Fernandez, *CCP, MS, MBA, Epworth Healthcare, Murdoch Children's Research Institute, Australia*

Plenary Sessions

Emerging Cell and Gene Therapy Strategies for Pulmonary Disease

Monday, July 20 | 10:45 – 12:15

Room: 105 - 106
Co-Chairs: Emily Blyth, Siok Tey

MSCs in Pulmonary Diseases and Critical Illnesses: Current Applications and Future Directions
Daniel J. Weiss

Dying Cells, Living Signals: How Mesenchymal Stromal Cell Apoptosis Drives Therapeutic Responses in Lung Disease
Tracy Heng

Developing Effective Airway Gene Therapies for Cystic Fibrosis Lung Disease
Ali McCarron

Session Objectives:
1. Examine how advances in MSC biology and immune interactions inform therapeutic mechanisms in lung disease
2. Understand how microenvironmental and intrinsic cellular factors influence MSC potency, consistency, and clinical outcomes
3. Evaluate current progress in manufacturing and gene delivery strategies that support scalable, effective therapies for pulmonary indications

Gene Editing: From Precision Design to Clinical Reality

Tuesday, July 21 | 10:45 – 12:15

Room: 105 - 106
Co-Chairs: Jessica Li, Tessa Gargett

Developing Bespoke Gene Editing Therapies for Patients with Urea Cycle Disorders
Sarah Grandinette

CAR-DC1 for Solid Cancers, and Stem-FIX for Monogenic Blood and Immune Disorders
Shalin Naik

CRISPR/HDR Cytokine-Armoured CAR T Cells
Paul Beavis

Session Objectives:
1. Understand how synthetic biology and gene editing are being used to design next-generation cellular and antibody-based therapies
2. Explore innovative gene-editing strategies to rewire CAR T cells for improved specificity, function, and tumour-restricted activity
3. Evaluate emerging in vivo gene-editing approaches, including rapid, patient-specific therapies for rare genetic disorders, and their implications for future clinical translation

Off-the-Shelf Cell Therapies for Transplant and Immunotherapy

Tuesday, July 21 | 15:00 – 16:30

Room: 105 - 106
Co-Chairs: Ngaire Elwood, Gaurav Sutrave

Breaking the Accessibility Barrier: Off-the-Shelf Cellular Immunotherapies from Pooled Donor CD34+ Cord Blood Cells
Colleen Delaney

Surfing the new wave of EV therapeutics by leveraging existing and emerging technologies
Rebecca Lim

Pioneering cellular medicines for women's health
Vera Evtimov

Session Objectives:
1. Explore how cord blood–derived and other allogeneic platforms are enabling off-the-shelf cell therapies for transplantation and cancer treatment.
2. Examine innovative approaches such as exosome-based immunotherapies and engineered cell products to improve tumour targeting, safety, and cost-effectiveness.
3. Understand how expanded and engineered cell platforms can enhance engraftment, immune recovery, and anti-tumour responses.

Advancing T-Cell Therapies in Transplant and Malignancy

Wednesday, July 22 | 09:15 – 10:45

Room: 105 - 106
Co-Chairs: Zlatibor Velickovic, Francisco Chung

TCR-T for Blood Cancers
Marie Bleakley

Reverse Translation of Armoured GPC3-CAR T Cells in Patients
Andras Heczey

From Cells to Circuits: Engineering Next-Generation CAR T Cells to Outsmart Cancer
Philipp C. Rommel

Session Objectives:
1. Understand how next-generation T-cell engineering is being designed to overcome current limitations in safety, persistence, and tumour targeting.
2. Explore emerging strategies to extend immunotherapy effectiveness in solid tumours and resistant cancers.
3. Examine how transplant engineering approaches, including modified donor T-cell therapies, are improving outcomes and shaping the future integration of immunotherapy and haematopoietic cell transplantation.

Concurrent Sessions

Beyond Blood Cancers: New Horizons for CAR Therapy

Monday, July 20 | 08:00 – 09:00

Room: 105 - 106
Co-Chairs: Alicia Didsbury, Lachlan Dobson

Enabling Affordable Access of CAR-T and other Cellular Gene Therapies
Boro Dropulić

CAR T Cell Approaches for Brain Cancer
Misty Jenkins

Teamwork for the Cure: Combination CAR T and NK Cell Therapy for Blood and Solid Cancers
Alex McLellan

Session Objectives:
1. Despite major advances in haematological malignancies, the application of CAR-based therapies beyond blood cancers remains challenging due to barriers such as antigen heterogeneity, poor immune cell trafficking, immunosuppressive microenvironments, and persistence of chronic viral reservoirs.
2. To highlight advances in tumour immunology, virology, and cell engineering that are enabling improved targeting, persistence, and efficacy of CAR-T and CAR-NK therapies in solid tumours and chronic viral diseases such as HIV.
3. To showcase translational strategies and early clinical successes in CAR-based therapies, with a focus on overcoming current barriers to clinical implementation.

Bioengineering – Engineering Cell Niches: Designing Microenvironments for Potent Therapies

Monday, July 20 | 09:15 – 10:15

Room: 105 - 106
Co-Chairs: Sharon Sagnella, Robert Nordon

Driving Deployment of Bioengineered Products – The Journey so far
Gordon Wallace

Shaping the Mesenchymal Stromal Cell Microenvironment: Bioengineering Strategies for Improved Regenerative Outcomes
Jess Frith

Form Informs Function: Building Biomaterials Inspired by Living Systems
Jelena Rnjak-Kovacina

Session Objectives:
1. Describe how microenvironment cues influence stem cell function.
2. Present biofabrication methods such as melt electrowriting for building controlled scaffolds.
3. Show how biofabrication supports clinical needs in orthopaedics.
4. Explain how material systems and fabrication strategies can support future clinical translation.

Engineering Next-Generation Therapies: From iPSC Cell Engineering to In Vivo Gene Editing

Monday, July 20 | 13:45 – 14:45

Room: 105 - 106
Co-Chairs: Jane Li, Zlatibor Velickovic

Stem Cell Therapy for Parkinson's Disease: Past, Present and Future
Lachlan Thompson

Image Based-Machine Learning for Pluripotent Stem Cell Derived Therapeutics
Stuart Chambers

In-Vivo Gene Editing: New Era of One-Time CRISPR Treatments for Non-Malignant Disorders
Sandeep Soni

Session Objectives:

1. Highlight/showcase recent advances in next-generation cell and gene engineering technologies.
2. Assess how these approaches improve precision, scalability, and therapeutic effectiveness for complex diseases.
3. Identify key opportunities and challenges in translating next-generation cell and gene therapies into clinical applications

Validated Assays for Clinical Manufacture

Monday, July 20 | 15:00 – 16:00

Room: 105 - 106
Co-Chairs: Cheryl Hutchins, Heather Donaghy

Employing Analytical Methodology to Enable a Measure Once, Report Once Framework: The Evolving ATMP Testing Landscape
Matthew M. Hewitt

Validation of Flow Cytometry Assays for Enumeration and Composition of T Cell Products
Kelly Wray

QC Assay and Process Validation for Clinical Manufacture
Dario Stupar

Session Objectives:

1. Delve into the quality control assays needed for clinical trial manufacture.
2. Understand what a regulator expects in a validated quality control assay.
3. Learn how different teams approach flow cytometry, PCR and potency assay design, verification and validation

The Regulatory Pulse: Updates Shaping Cell and Gene Therapy in Australia and New Zealand

Tuesday, July 21 | 08:00 – 09:00

Room: 105 - 106
Co-Chairs: Dominic Wall, Kasey Kime

Update from the Therapeutic Goods Administration (TGA)
Dennis Dowhan

Medsafe Regulatory Updates
Karin van Bart

OGTR Updates: Regulation of Human Clinical Trials with GMOs
Cibelly Goulart

Tim Strabala

ATMP and Regulation
Alyce Maksoud

Session Objectives:

1. Understand regulatory requirements and changes affecting cell and gene therapy products across Australia and New Zealand
2. Learn how to apply updated regulatory expectations
3. Strengthen regulator and regulated community understanding and engagement

"Grill" the Regulator

Tuesday, July 21 | 09:15 – 10:15

Room: 105 - 106
Co-Chairs: Dominic Wall, Kasey Kime

Panelists
Dennis Dowhan
Karin van Bart
Cibelly Goulart
Tim Strabala
Alyce Maksoud

Session Objectives:

Understand how regulators in Australia and New Zealand would approach new developments in cell and gene therapy in the areas of

1. Clinical trials, research and product development
2. Gene technology and the environment
3. Regulatory advances

Commercial Workstream – Capital Raising to FIH to Path to Commercialisation

Tuesday, July 21 | 16:45 – 17:45

Room: 105 - 106
Chair: Dominic Fernandez

From Bench to Bath Down Under: Balancing Sustainability, Pricing, and Access in a "Small" Market – A CDMO Perspective on Commercial Reality for Australian Gene Therapies
Leszek Lisowki

CDMO Strategy: A Critical Driver of Commercial Success
Colin McLean

The Journey of Chimeric Therapeutics
Rebecca McQualter

Panelists
Bev Menner
Stephen Thompson

Session Objectives:

1. Clarify the pathway from translation to investability. Define the clinical, regulatory, and manufacturing thresholds required for early stage assets to become commercially viable and attract capital.
2. Examine CDMO strategy as a determinant of commercial success. Explore how facilities like Viral Vector Manufacturing Facility (VVMF)/Cell Therapies Pty Ltd balance sustainability, pricing competitiveness, and capacity in a constrained but growing market.
3. Interrogate IP strategy and asset positioning. Identify how emerging entities should structure IP, licensing, and data ownership to maximise long term value and partnering potential.
4. Deconstruct regulatory planning as a strategic lever. Assess how early regulatory pathway decisions influence development timelines, risk profiles, and downstream valuation.
5. Establish a capital strategy framework for advanced therapies. Outline how to sequence funding sources from early development through to commercial scale to avoid the common translational and financing gaps seen in Australia.

The Translational Pathway: Designing and Delivering Phase I Cell and Gene Therapy Trials

Wednesday, July 22 | 08:00 – 09:00

Room: 105 – 106
Co-Chairs: Tessa Gargett, Alicia Didsbury

Taking a CAR T for Solid Cancer from R&D to FDA Approved Clinical Trials
Simon Barry

Simple in Principle, Complex in Practice: Building a Phase 1 CAR T Cell Trial with local Vector and Place-of-Care Manufacture
Geraldine O'Neill

Place of Care Manufacturing: TIL Therapy for Melanoma
Leon Brownrigg

Session Objectives:

1. Highlight the current landscape and unique challenges of cell therapy clinical trials in Australia and New Zealand.
2. Share practical insights from leading investigators on translating cell therapies from bench to early-phase trials.
3. Examine key considerations in trial design for cell therapies, including patient selection, endpoints, and manufacturing constraints.
4. Discuss regulatory pathways and approval processes specific to ANZ
5. Identify challenges in trial execution (e.g., process validation, site readiness, logistics, apheresis, vein-to-vein time) and strategies to address them

CONCURRENT SESSIONS

Gene Therapy in Human Studies: Signals, Safety, and Promise

Wednesday, July 22 | 11:30 – 12:30

Room: 105 – 106
Co-Chairs: Mark Dowling, Andrea Henden

Phase 1 Clinical Trials of In Vivo CAR T Therapy for Multiple Myeloma
Simon Harrison

Disease-Modifying Genetic Medicine for Motor Neuron Disease
Yazi Diana Ke

Gene Therapy for Inherited Liver Diseases
Samantha Ginn

Session Objectives:

1. Provide an overview of how gene therapies are being tested in current clinical trials across different disease areas.
2. Explore what early clinical signals, such as biological changes or safety patterns, can reveal about future potential.
3. Discuss how gene therapy approaches may evolve as trial data grows and more patient groups are included.

Roundtable Sessions

National Strategy and Policy: Health Technology Assessment, Funding, and Future Access Pathways for Advanced Therapies

Tuesday, July 21 | 13:45 – 14:45

Room: 105 - 106
Moderators: Emily Blyth, Dominic Fernandez

Panelists:
Penny Shakespeare
Vanessa Fitzgerald
Glen Kennedy

Session Objectives:

1. Provide a clear understanding of how national HTA processes intersect with state-level delivery of advanced therapies, including funding pathways and operational models.
2. Compare how different jurisdictions organise, resource, and govern access to CAR T and related therapies, and how these differences influence patient access.
3. Examine how not for profit and/or decentralised and point of care manufacturing may alter assessment, funding, and reimbursement frameworks for hospital based production.
4. Identify key policy considerations for future national and state collaboration to support sustainable, equitable access to advanced therapies across Australia and Aotearoa New Zealand.

Career Pathways Along the Translational Pipeline

Wednesday, July 22 | 11:30 – 12:30

Room: 104
Moderators: Gaurav Sutrav, Gemma Moir-Meyer

Panelists:
Marie Bleakley
Simon Barry
Colleen Delaney
Dominic Fernandez

Session Objectives:

1. Explore career trajectories and the decisions that shaped them across academia, industry and clinical care.
2. Engage with panelists to discuss the essential skills for a success in a cross-functional CGT ecosystem.

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Gilead Kite Company Presentation

Monday, July 20, 2026 | 09:15 – 10:15

Room 104

Real-World Outcomes of Immunotherapy: From Trials to Clinical Practice

Speakers:
Dr. Mark Dowling, Clinical Haematologist, Peter MacCallum Cancer Centre, Melbourne, Australia
Honorary Professor Robert Weinkove, Clinical Director, Malaghan Institute of Medical Research, Wellington, NZ
Dr. Gemma Reynolds, Infectious Diseases Physician, Austin Health, Melbourne, Australia

This session will examine how immunotherapies are performing in real world clinical settings, with insights from registry data, national consortia, and clinical experience. Speakers will explore effectiveness, safety, patient selection, and health system challenges to understand how outcomes in practice compare with clinical trial expectations.

Session Objectives:

1. Analyse real-world data on immunotherapy outcomes, including effectiveness, durability, and safety across diverse patient populations.
2. Understand how registry and consortium data are informing clinical decision-making and health policy.
3. Identify key factors influencing real-world outcomes, including patient selection, toxicity management, and service delivery models.
4. Discuss strategies to optimise access, equity, and long-term outcomes for immunotherapy in routine clinical practice.

Sartorius Company Presentation

Monday, July 20, 2026 | 10:15 – 10:45

Room 104

Perfusion-Enabled CAR-T Manufacturing In Stirred-Tank Bioreactors Achieving 100+ Doses Per Batch

Speaker:
Rukmini Ladi, Segment Technology Manager, Cell Therapy, Sartorius

To realize the potential of CAR-T therapies for broader patient accessibility, current manufacturing limitations of approved autologous CAR-T products must be addressed. To this end, we evaluated a perfusion-based autologous CAR-T expansion process in both 250 mL and 2L stirred-tank bioreactors, coupled with an automated system for harvest, wash, and concentration. Healthy donor-derived anti-CD19 CAR-T cells were cultured in serum-free medium for seven days, achieving ~125-fold expansion and consistent yields of ~50 billion viable cells with preserved phenotype and functionality. Comparability was observed between both production scales, and automated harvesting recovered >90% of cells while maintaining quality. These findings demonstrate a robust, scalable platform for multi-liter CAR-T manufacturing, ideally suited for mass production of future allogeneic therapies.

CORPORATE PROGRAM

GenScript Company Presentation

Monday, July 20, 2026 | 16:00 – 16:15

Room 104

Harnessing the synergic power of new tLNP formulation and CAR expression modality for in vivo CAR-T development

Speaker:
Dr. Lumeng Ye, Head of Business Development, ANZ, GenScript Biotech Australia Pty. Ltd., Australia

In the past two years, in vivo CAR-T therapy moved fast from conceptual and NHP data to 100% ORR human clinical data. More and more practical understanding on the design of targeted delivery approach and CAR molecule format, reported with proven clinical data. Currently, both viral vector and LNP delivery were reported with promising targeted and efficient delivery, with the right antibody decoration. In this 15 minutes presentation, we will take the non-viral LNP approach as example, elucidate the best practice on CAR design, LNP formulation, choices of antibody for target delivery, to maximize the treatment effect of in vivo CAR-T therapy in systematic manner.

Session Objectives:

1. Choices on the payload design and format for targeted and long expression of CAR modality
2. Best combination of LNP formulation and antibody conjugation for targeted delivery to spleen and T cell
3. Considerations on CMC of tLNP-RNA/DNA solution for in vivo CAR-T development
4. Total solution from GenScript for in vivo CAR-T therapy development

Ideagen Company Presentation

Monday, July 20, 2026 | 16:15 – 16:30

Room 104

From Q-Pulse to Ideagen Quality Management: supporting Australia's cell and gene therapy community, today and what's next

Speaker:
Kevin McSharry, VP Practice Lead, Quality, Ideagen, Australia

If you've worked with Ideagen's quality platform before, you'll know it as Q-Pulse. In this session, Kevin McSharry, who leads Ideagen's Quality practice, shares what's changed, what hasn't, and what's coming next for cell and gene therapy manufacturers, laboratories and clinical trial sponsors across Australia.

Ideagen remains deeply invested in supporting ANZ organisations navigating ISO 13485, NATA accreditation and TGA compliance, with a local team who understand the regulatory landscape you work in.

Kevin will also demonstrate how Ideagen's AI capabilities are already cutting the manual effort out of quality management, from drafting investigations to tracking corrective actions to closure.

Whether you're a long-time customer or exploring a new QMS, this is a chance to see what's next and talk directly with the team building it.

Session Objectives:

1. *Understand what's changed (and what hasn't) since Q-Pulse became Ideagen Quality Management, and what local support looks like today*
2. *See how peer organisations across Australia's cell and gene therapy sector are managing ISO 13485, NATA accreditation and TGA compliance*
3. *Learn how AI is being used to cut manual effort out of quality processes, from investigations to corrective action tracking*

CORPORATE PROGRAM

Cytiva Company Presentation

Tuesday, July 21, 2026 | 10:15 – 10:45

Room 104

Integrated Closed-System Platforms for Scalable Cell Therapy Manufacturing: From T Cells to MSC/iPSC Expansion

Speaker:
Andrea Zhao, PhD, Application Specialist - Cell Therapy & Nanomedicine, Cytiva, Sydney, Australia

This presentation outlines Cytiva's integrated platforms for end-to-end cell therapy manufacturing, spanning from PBMC isolation and T cell enrichment, activation, expansion, and downstream harvesting, formulation, and cryopreservation. We will describe industry-validated suspension culture systems widely deployed in CAR T and other immunotherapy workflows, emphasizing closed processing, process control, and scalability in bioreactor-based expansion. In addition, we will introduce the Sefia™ platform, including Sefia Select for automated cell enrichment and Sefia Expansion for controlled, scalable proliferation within a closed architecture. In parallel, we will showcase non-viral cell engineering approaches using Cytiva lipid nanoparticle (LNP) technologies, with data demonstrating efficient delivery and compatibility with closed, modular manufacturing workflows.

The second part focuses on a scalable, fully closed and automated adherent cell manufacturing workflow integrating Cytiva platforms with CellFiber™ scaffold technology for MSC and iPSC expansion. This system enables high-density 3D culture under controlled conditions while maintaining critical quality attributes. A key innovation is the harvest mechanism, where controlled dissolution of the scaffold replaces enzymatic detachment, eliminating open handling steps. This approach improves cell recovery, preserves viability, and enhances process consistency and scalability, supporting robust, GMP-aligned manufacturing across adherent cell therapy applications.

Session Objectives:

1. End-to-End, Modular, and Closed Manufacturing Platform from research to translation and commercial manufacturing.
2. Next-Generation Processing with Sefia™ and Non-Viral LNP Technologies.
3. Scalable, Fully Closed Adherent Cell Manufacturing with CellFiber™ Integration.

Cell Signaling Company Presentation

Tuesday, July 21, 2026 | 14:00 – 14:15

Room: 104

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

Speaker:
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.

NeuroScientific Company Presentation

Tuesday, July 21, 2026 | 14:15 – 14:30

Room 104

NeuroScientific

StemSmart™ MSC: A Next Generation Stem Cell Solution for Immune-Mediate Inflammatory Disorders

Speaker:
Professor Catherine Cole, MBBS FRACP FRCPA, Chief Medical Officer, NeuroScientific Biopharmaceuticals Ltd, Australia

NeuroScientific Biopharmaceuticals Ltd (ASX:NSB) is developing the StemSmart™ mesenchymal stem cell technology platform derived from a patented manufacturing process resulting in activated MSCs. StemSmart™ has significant early-stage clinical trial and Special Access Scheme data in humans that demonstrates its significant impact on immune-mediated inflammation. NSB is progressing towards Phase 2 clinical trials in Crohn's disease off the strength of this data, with plans to initiate by the end of 2026.

Session Objectives:

1. Overview of MSC technology and what differentiates StemSmart™ from the rest of the product class
2. Why StemSmart™ MSCs are an effective in Crohn's disease and other immune-mediate inflammatory diseases
3. Overview of the upcoming clinical trials in Crohn's disease and the future of the StemSmart™ platform.

ThermoFisher Scientific Company Presentation

Tuesday, July 21, 2026 | 16:30 – 16:45

Room 104

ThermoFisher SCIENTIFIC

Modular Automated Processing, Formulation, and Fill-Finish for Diverse CAR-Engineered Cell Therapies

Speaker:
Dr Poh Loong Soong, Field Application Scientist, Cell and Gene Advanced Therapy, Asia Pacific and Japan, Thermo Fisher Scientific

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.

Session Objectives:

1. Learn how automated cell concentration, washing, formulation, and fill-finish operations can be integrated into a seamless end-to-end workflow.
2. Explore strategies for maintaining critical quality attributes, including cell recovery, viability, and phenotype, throughout downstream processing.
3. Review performance data demonstrating accurate and consistent dispensing across a wide range of fill volumes and product configurations.
4. Examine how automated fill-finish solutions can support multi-dose, multi-output, bag and vial formats while reducing process variability and contamination risk.

Exhibitor Directory

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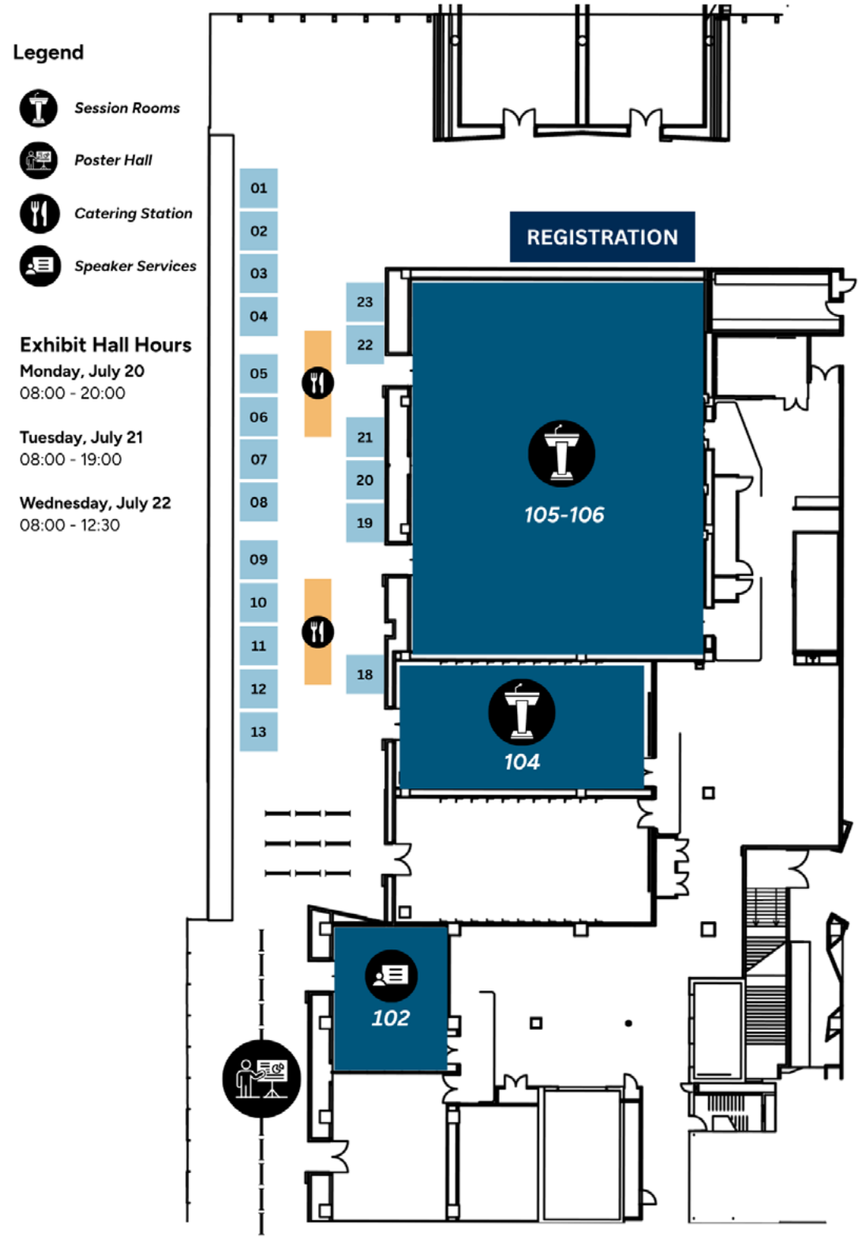
Venue Map (Exhibitors)



Exhibitors and Sponsors

Adjutor Group — Tabletop #7

Adjutor Group is an Australia-based healthcare consultancy focused on accelerating the development, registration, and commercialisation of innovative medicines and medical technologies across global markets. With a strong presence in Australia, New Zealand, and Hong Kong, and a trusted international partner network, Adjutor offers clients a single access point to key regions including Asia-Pacific, the EU/UK, and theericas.

Backed by over a decade of consulting experience, Adjutor combines expertise in regulatory, clinical, quality, and commercial domains. The team has supported the registration of hundreds of medicines and medical devices across all classes, helping clients navigate complex regulatory pathways while optimising timelines, cost, and risk.

Adjutor provides end-to-end consultancy services covering product development strategy, clinical development, regulatory affairs, quality systems, training, sponsorship, and lifecycle management. Regulatory services include dossier preparation, submission management, agency interactions, and ongoing compliance support. Through local legal entities, Adjutor can also act as product sponsor in selected markets, facilitating efficient submissions and commercial supply.

Clinical CRO services are delivered across multiple regions, spanning early strategy and feasibility to trial management and study reporting. Complementary quality and training services support the development of compliant systems aligned with global standards.

Positioned at the intersection of clinical development, regulatory strategy, and market entry, Adjutor operates as a strategic partner to innovators, biotech companies, and investors, enabling seamless progression from concept to patient impact.

Beckman Coulter Life Sciences — Tabletop #6

With a legacy dating back to 1935, we continue our ongoing mission to help a diverse variety of experts discover answers to some of life's most important questions. Wherever people need answers that matter, you can find reliable technologies from Beckman Coulter Life Sciences.

Biomérieux — Tabletop #4

A world leader in industrial microbiology testing, for more than 30 years, bioMérieux is present in 46 countries and serves more than 160 countries through a large network of distributors. bioMérieux provides contamination detection solutions (systems, reagents, software and services) to clients of the pharmaceutical industries. These solutions enable product quality control at all steps of the manufacturing process in order to protect patients' and consumers' safety. Our automated solutions and services answer laboratories' challenges and help maximize their operational efficiency.

Bluecord — Tabletop #19

Bluecord is an electronic quality management system (eQMS) and manufacturing operations platform purpose-built for cell and gene therapy organizations. Bluecord helps academic medical centers, biotech companies, and GMP manufacturing facilities streamline quality, manufacturing, training, inventory, and regulatory workflows within a single validated cloud platform. Trusted by leading cell therapy programs globally, Bluecord supports compliant operations from early development through commercial manufacturing. The platform is designed specifically for the unique operational and regulatory needs of advanced therapies, enabling organizations to improve efficiency, maintain data integrity, and accelerate the delivery of life-saving treatments.

Cell Signaling Technology — Tabletop #20

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.

Charles River — Tabletop #18

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.

Learn more at www.criver.com.

Cytiva

Tabletop #5

Cytiva is a global life sciences leader dedicated to helping customers discover and commercialize the next generation of therapeutics. With a rich heritage dating back hundreds of years, Cytiva brings a wealth of technical expertise and talent, a broad and deep portfolio, and exceptional service help researchers and biopharma advance therapeutics at every stage from discovery to delivery. We supply the tools and support our customers need to work better, faster, and safer, leading to the delivery of transformative medicines to patients. Our combined portfolio includes well-recognized names such as Allegro™, Supor™, iCELLis™, and Kleenpak™, in addition to ÄKTA™,ersham™, Biacore™, FlexFactory™, HyClone™, MabSelect™, Sefia™, Whatman™, and Xcellerex™. Visit cytiva.com to learn more.

Eurofins Biopharma Product Testing

Tabletop #13

Eurofins Scientific through it's subsidiaries is the world leader in Food, Environment, Pharmaceutical and Cosmetic Products testing and in Agroscience CRO services. It is also one of the global independent market leaders in testing and laboratory services for genomics, discovery pharmacology, forensics, advanced material sciences and for supporting clinical studies.

GenScript Biotech Australia Pty Ltd

Tabletop #8

Founded in 2002 in New Jersey, GenScript Biotech Corporation accelerates innovation in biotech and healthcare by providing researchers and companies with the building blocks needed to develop groundbreaking treatments and products. Guided by its mission to Make People and Nature Healthier Through Biotechnology, and its role as a well-recognized biotechnology company, GenScript has a team of approximately 6,165 employees and has served more than 200,000 customers across over 100 countries and regions.

Gilead Kite

Kite, a Gilead Company, is a global biopharmaceutical company based in Santa Monica, California, focused on achieving cures with cell therapy. As the global cell therapy leader, Kite has treated more patients with CAR T-cell therapy than any other company. Kite has the largest in-house cell therapy manufacturing network in the world, spanning process development, vector manufacturing, clinical trial supply and commercial product manufacturing. For more information on Kite, please visit www.kitepharma.com.

Ideagen

Tabletop #11

Ideagen is a global leader in governance, risk and compliance (GRC) software, helping more than 16,000 customers worldwide manage risk, ensure compliance and operate safely in highly regulated industries. Ideagen Quality Management (IQM, previously known as Q-Pulse) supports life sciences and healthcare organisations, including pathology, radiology, pharmaceutical and medical device providers, to streamline document control, training, audits, non-conformances and CAPA management within a single connected system.

Built for organisations operating under strict regulatory frameworks such as ISO 13485, ISO 17025 and NATA accreditation, IQM gives quality and compliance teams real-time visibility over risk and performance, reducing manual administration and supporting continuous improvement and accreditation readiness.

Across the ANZ region, Ideagen partners with cell and gene therapy providers, tissue banks and laboratories to help maintain the rigorous quality standards required to protect patient safety and product integrity. By bringing quality management processes into one platform, Ideagen helps organisations reduce risk, simplify compliance and free up time for the work that matters most: delivering safe, effective care.

Invetech

Tabletop #10

Invetech works with Diagnostics and Cell and Gene Invetech is a health technology design, engineering and manufacturing company helping life sciences, diagnostics and cell and gene therapy innovators bring life-changing products to market.
For 39 years, we have turned complex science into scalable reality, supporting clients from early feasibility through product development, regulatory-ready design, scale manufacturing and lifecycle support.

Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity. Learn more at https://www.jnj.com/ About Johnson & Johnson
At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity. Learn more at https://www.jnj.com/

EXHIBITORS

Miltenyi Biotec

Tabletop #21

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 over 5,000 employees across 27 countries.

NeuroScientific Biopharmaceuticals Ltd

NeuroScientific Biopharmaceuticals Limited (ASX: NSB) is a biotechnology company focused on the development of novel therapeutics targeting immune-mediated inflammatory disorders. The Company's research is centred on modulating pathological immune responses involved in chronic and degenerative conditions, particularly where current therapeutic options demonstrate limited efficacy or durability. NSB applies advanced preclinical and translational strategies to support the development of first-in-class or best-in-class biologics addressing significant unmet clinical need.

Following the acquisition of Isopogen WA Ltd, NSB is prioritizing the application of its proprietary StemSmart technology through a SAS program targeting fistulising Crohn's disease—a severe and treatment-resistant form of the condition. Favourable outcomes will support the Company's progression to a Phase 2 clinical trial to further evaluate safety and preliminary efficacy in refractory and/or fistulising Crohn's disease. This initiative aligns with NSB's broader strategy to obtain regulatory and reimbursement approval for its MSC therapy both in Australia and internationally, with the goal of making the treatment available to patients with fistulising and refractory Crohn's disease, for whom current therapies remain inadequate.

Sartorius

Tabletop #12

Sartorius is a leading international partner to the biopharmaceutical research and manufacturing industries. The Lab Products & Services Division focuses on innovative laboratory instruments and consumables for research and quality assurance laboratories in pharmaceutical and biopharmaceutical companies as well as academic research institutions. The Bioprocess Solutions Division supports customers with a broad product portfolio focused on single-use solutions for the safer, faster, and more sustainable production of biotech drugs, vaccines, and cell and gene therapies. With around 60 production and sales locations worldwide, the Göttingen-based company has a strong global presence. Sartorius regularly supplements its portfolio with acquisitions of complementary technologies. In 2025 the company generated sales revenue of around 3.5 billion euros. More than 14,000 employees serve customers around the globe.

Scientifix

Tabletop #9

Scientifix is a well-established Australian-owned life science product provider. Specialising in workflow solutions for cell biology including gene therapy stem cells, gene therapy MSCs, iPSCs and Exosomes, molecular biology, protein research and cryopreservation. Our tools for gene-editing reprogramming, stem-cell/iPSC culture, engineering, differentiation, and NGS analysis will remove technical hurdles to push experiments forward.

Stemcell Technologies

Tabletop #3

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.

Thermo Fisher Scientific

Tabletop #22 and 23

Thermo Fisher Scientific is the world leader in serving science. Our Mission is to enable our customers to make the world healthier, cleaner and safer.

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Exosomes/EVs

RESTORING HUVEC PROLIFERATION AND VIABILITY: DMSC-DERIVED EXTRACELLULAR VESICLES COUNTERACT VEGF INHIBITOR-INDUCED ENDOTHELIAL DAMAGE

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KEYWORDS: Extracellular Vesicles , VEGF inhibitors, Endothelial dysfunction.

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2. Department of Maternal-Fetal Medicine, Royal Women's Hospital, Melbourne, VIC, Australia.

Background & Aim:

Vascular endothelial growth factor (VEGF) inhibitors such as sunitinib are effective anticancer therapies but frequently induce vascular toxicity and endothelial dysfunction. Although sunitinib impairs human umbilical vein endothelial cell (HUVEC) proliferation, the mechanisms underlying this injury remain elusive, and protective strategies are lacking. Given prior evidence that extracellular vesicles (EVs) derived from decidual mesenchymal stem/stromal cells (DMSCs) mitigate preeclampsia serum induced endothelial injury, we hypothesized that these EVs may preserve endothelial integrity during anti-angiogenic stress. This study investigated whether DMSC-EVs can mitigate sunitinib-induced damage and restore HUVEC growth.

Methods, Results & Conclusion:

EVs were isolated from DMSCs and characterized using standard techniques. HUVECs were treated with increasing concentrations of sunitinib (2-20 µM), and proliferation was monitored using the xCELLigence real-time cell analysis system over 96 h. Sunitinib 10 µM was used as the half-maximal inhibitory concentration (IC50) for subsequent experiments. Cell morphology and viability were evaluated by live-cell imaging over 48 h. To determine whether EVs could mitigate sunitinib-induced injury, HUVECs were co-treated with sunitinib (10 µM) and EVs (6.25, 12.5, 25, 50, and 100 µg/mL) for 48 h. Conditioned media were collected at 48 h for quantification of angiogenic and inflammatory mediators using multiplex flow cytometry.

Sunitinib increased early HUVEC attachment at 2 h (~2-fold vs control; $P<0.05$), but reduced proliferation by ~50% across 24–96 h. This was accompanied by ~50% cell death at 48 h, as shown by live-cell imaging. Co-treatment with EVs at 6.25 µg/mL, but not higher doses, significantly increased proliferation compared with sunitinib alone. The cell index for sunitinib-treated cells was 1.64 ± 0.1 at 24 h and 2.43 ± 0.1 at 48 h, whereas co-treatment with EVs increased these values to 2.74 ± 0.1 and 3.28 ± 0.1, respectively (n=7–8; $P < 0.05$).

These findings show that sunitinib impairs HUVEC proliferation and that DMSC-EVs partially mitigate this effect and enhance endothelial cell growth. Collectively, EV-based therapies may represent a promising strategy to mitigate VEGF inhibitor–induced vascular toxicity and promote endothelial repair during anti-angiogenic treatment.

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Hematopoietic Stem/Progenitor Cells and Engineering

IMPLEMENTING A STABILITY-BASED EXPIRY STRATEGY FOR CRYOPRESERVED HEMATOPOIETIC PROGENITOR CELLS: REAL-WORLD EXPERIENCE FROM AN INDIAN TRANSPLANT CENTER

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KEYWORDS: Stability studies, Indian transplant center, Expiry dates.

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3. Laboratory Hematology, Tata Medical Center, Kolkata, West Bengal, India.

Background & Aim:

Hematopoietic Progenitor cells (HPC) cryopreservation is essential for autologous transplants especially in lymphomas, where the conditioning last for 5-7 days and it also allows logistic flexibility in allogeneic transplants. However, cryopreservation and thawing procedures have potential risk of loss in cell viability and potency. Since there is no uniformity between centers in cryopreservation procedures, each step from collection to infusion may impact the intended therapeutic function of HPC. Hence, well-controlled and validated processes are essential to maintain optimal target cell recovery and functional potency. Accreditation bodies (like FACT, AABB, ISCT) recommended initiation of a stability program to periodically evaluate key manufacturing steps to ensure graft quality and validated product shelf-life.

Aim

To develop a stability program for cryopreserved HPC products at our transplant centre

To establish a method to predict stability/expiry and safety of cryopreserved HPC products

Methods, Results & Conclusion:

HPC product cryopreservations (with 10% DMSO) were performed by controlled-rate freezing as per Institution's standard operating procedure. Parallel to the management of products for clinical use, the stability program was initiated on 1st January'2023 and it included product bags or segments of Cryopreserved HPC products stored in vapor phase nitrogen at -196C from 1st January 2016 to 31st May 2025. Annually, 10% of cryopreserved products samples were thawed at 37C and tested for stability from one-week upto ten years after cryopreservation and compared with pre-freeze baseline data. Stability was defined as CD34+ cell recovery and 7-AAD viability of 70% or higher and negative sterility results at 5 days.

Result

Stability testing was performed on 20 thawed Cryopreserved HPC samples. The acceptable CD34+ recovery rate & 7-AAD viability (>70%) was achieved in all the samples(16) stored for <5 years. 3 out of 4 samples which were older than 5years reported 50% decline in Median CD34+ cell recovery and 5.2% reduced post-thaw(7-AAD) viability (see table-1). All samples were negative on Microbiological culture & all recipients had successfully engrafted.

Conclusion

The stability program of cryopreserved HPC products is useful to monitor and analyse the quality, safety and efficacy of cryopreserved HPC products. It helps the transplant program to objectively interpret testing results and modify the product expiry, while working towards standardization in the field

Table 1 (Abstract 102): Stability Test results of cryopreserved products with respect to storage period

Storage Time period	<1 year	1-2 years	2-3 years	3-5 years	>5 years
	Median (Range)	Median (Range)	Median (Range)	Median (Range)	Median (Range)
No of samples tested	8	3	3	2	4
CD 34+ Recovery %	97.5 (86.2 - 120.4)	97.8 (88.4 - 120.4)	83.7 (81.4 - 97.8)	107.6 (97.8 - 117.3)	49.54 (46 - 103.58)
CD 34+ Viability% (7-AAD)	98.34 (97.54 - 98.67)	98.17 (97.25 - 98.96)	97.38 (96.7 - 98.34)	98.17 (97.38 - 98.16)	94.8 (90 - 98.1)
Trypan Blue Viability%	65 (60 - 75)	72.5 (60-85)	58 (55 - 85)	72.5 (60 - 85)	37.5 (30 - 65)
CD45+ Recovery%	72.1 (68.3 - 101.8)	73.2 (68.4 - 84.5)	75.3 (70.6 - 82.2)	73.8 (68.4 - 79.1)	22.3 (21.3 - 71)
TNCC Recovery%	96.3 (84 - 114.2)	92.6 (88.7 - 99.4)	92.4 (79.5 - 92.6)	58.9 (25.3 - 92.6)	101.2 (94.9 – 118)
Microbial Culture	Negative	Negative	Negative	Negative	Negative

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Hematopoietic Stem/Progenitor Cells and Engineering

RELOCATION OF CRYOPRESERVED INVENTORY AND REGULATORY COMPLIANCE DURING A MAJOR FACILITY UPGRADE

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KEYWORDS: HPC, Cryopreserved, Validation.

1. RPA Haematology, New South Wales Health Pathology, Sydney, NSW, Australia.

Background & Aim:

The RPA transplant program has held a TGA manufacturing licence for collection, processing, testing, storage and release of hematopoietic stem cells since 2008 and performs approximately 170 MNC(A) and HPC(A), collections each year (auto, allo and registry). A 2023 FACT inspection noted risks to patient confidentiality and product process flow concerns due to limited space. While NSQHS Standards do not specify minimum space requirements, an institutional review agreed that improvement was required and in 2025 expansion and refurbishment was funded.

Methods, Results & Conclusion:

A campus wide search for space to temporarily house services was performed considering WHS, security, engineering and operational requirements. Advice was sought from vendors, cryogenic experts and transplant colleagues who had undertaken inventory relocation projects both locally and internationally. A risk assessment determined we could not move tanks with inventory, and options for relocation of services were limited with extensive redevelopment across the hospital.

Work was carried out in 2 stages and all operations had to be relocated for a minimum period of 5 months to maintain the Cell Therapy collection and BMT service. Stage 1 involved demolition and construction of a material store, file storage and workspace for supporting staff, while Stage 2 involves completely rebuilding Apheresis and Laboratory.

A detailed plan for inventory relocation, off-site storage and costing was developed with Cryosite; CryoCart to move product through the hospital, Jumbo Shipper at the dock, and for transfer to Cryosite tanks. Master service and quality agreements were executed considering TGA requirements and operational needs. The movement of inventory required co-ordination, communication and documentation; moving LN2 and tanks through clinical areas, out of hours staff, dock access, lift lock outs (Table 1).

Over 7 days, inventory from main and back up tanks was relocated to Cryosite. Quarantine tank inventory was moved into a requalified tank in a new location and inventory required within 6 months was moved to a new qualified LN2 tank. Empty tanks were dried out and are in local storage pending requalification in the new facility.

Traceability of inventory movement was managed using paper-based mapping. Cryosite's electronic inventory management is mapped to electronic inventory in CERNER. Product release for infusion remains the responsibility of the RPA team with the ability to request product from Cryosite if required.

Table 1 (Abstract 103): Summary of inventory Movement and Logistic Requirements

Day	Tank/Inventory origin	Tank/Inventory Destination	Dock Access Required	Lift Lock Out Required	CryoCart	Jumbo Shipper	Hours
Prior	Main and back up Inventory	Disposal	No	No	No	No	-
Wed	Back up Inventory	Cryosite	Yes	Yes	Yes	Yes	5
Thurs	Main Inventory	CryoSite	Yes	Yes	Yes	Yes	4
Thurs/Fri	Quarantine Inventory	Back up Tank	No	No	No	No	5
Fri	Back up Tank, Quarantine Inventory	B65, L6	No	No (managed locally)	No	No	1
Mon	Main Inventory	B89, L2 (new tank)	No	Yes	Yes	No	2
Mon	Quarantine Inventory	B65, L6 Quarantine Tank	No	Yes	Yes	No	2

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Gene Editing/Gene Therapies

GENERATING CRISPR/CAS9 ARMOURED CAR- AND TCR-T CELLS FOR THE TREATMENT OF SOLID TUMOURS

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KEYWORDS: CRISPR/Cas9, Adoptive Cell Therapies.

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3. Peter MacCallum Cancer Centre, Melbourne, VIC, Australia.

Background & Aim:

CAR-T cell therapy has exhibited remarkable clinical success in the treatment of haematological malignancies, however, their efficacy in solid tumours is limited by antigen heterogeneity and immunosuppression imposed by the tumour microenvironment. To overcome these barriers, 'armoured' CAR-T cells which secrete pro-inflammatory cytokines have been developed. However, toxicities related to the unrestricted expression of the armouring transgene has limited the application of these CAR-T cells in the clinic. Our lab has developed a novel CRISPR/Cas9-mediated homology directed repair (HDR) strategy, whereby we engaged endogenous gene regulatory mechanisms to drive transgene expression in a tumour-localised manner (Chen & Yap et al., Nature 2025). Genome-wide RNA-sequencing was used to identify genes in CAR-T cells with tumour-specific expression resulting in the promotor NR4A2 to be identified as a key candidate due to its inhibitory role in T cells. This novel CRISPR HDR strategy was employed to knock in (KI) proinflammatory cytokine, IL-12, under the control of the NR4A2 promoter. This supported tumour localised delivery of IL-12, reducing peripheral toxicities and leading to enhanced anti-tumour efficacy and long-term survival of mice in both syngeneic and xenogeneic models. Although we have developed a novel technology that tightly restricts expression of pro-inflammatory cytokines to T cell activation, we have sought to even further refine the safety profile of this technology through the application of neoantigen specific TCR-T cells and the use of an alternative CRISPR KI strategy.

Methods, Results & Conclusion:

We have generated T cells expressing an engineered TCR targeting the tumour neoantigen KRAS G12D which we further engineered to express an NR4A2/IL-12 KI, eliciting improved anti-tumour efficacy and safety in xenographic mouse models. We further generated CAR- and TCR-T cells to express an armouring transgene upon the tumour-specific induction of the NR4A2 promotor whilst maintaining endogenous NR4A2 gene function, resulting in reduced transgene expression. We validated that this reduced expression system displays a matched therapeutic benefit to our current KI technology in both xenographic and syngeneic mouse models whilst eliciting an enhanced safety profile compared to our current CRISPR KI technology.These findings allow for tumour-specific delivery of IL-12 across a range of CAR- and TCR-T cell systems whist eliciting an even further refined safety profile.

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Gene Editing/Gene Therapies

A MICRORNA-REGULATED COXSACKIEVIRUS B3 PLATFORM ENABLES SAFE AND EFFECTIVE ONCOLYTIC THERAPY IN PANCREATIC CANCER WITH TRANSLATIONAL READINESS FOR FIRST-IN-HUMAN STUDIES

M. Murahashi[1], S. Miyamoto[1], S. Ito[1], Y. Momoda[1], Y. Kobayashi[1], Y. Sakashita[1], K. Sato[1], Y. Kamata[1], K. Tani[2]

KEYWORDS: Oncolytic Virotherapy, Pancreatic Cancer, Translational Medicine.

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2. NPT Corporation, Tokyo, Japan.

Background & Aim:

Pancreatic cancer is a prototypical "cold tumor" characterized by a dense stromal microenvironment, poor immune infiltration, and limited responsiveness to immune checkpoint inhibitors. Oncolytic virus-based therapy attractive for this disease because it can lyse tumor cells while promoting immunogenic cell death (ICD), a mechanism associated with calreticulin exposure and ATP release that may help convert cold tumors into responsive ones. Coxsackievirus B3 (CVB3) has potent oncolytic activity; however, its clinical application has been limited by toxicity in normal pancreatic and hepatic tissues. To address this limitation, we developed a microRNA-regulated CVB3 platform, CVB3-BHP, designed to suppress viral replication in normal tissues while preserving antitumor efficacy.

Methods, Results & Conclusion:

CVB3-BHP demonstrated significantly reduced hepatic and pancreatic toxicity compared to wild-type CVB3 in vivo, while maintaining comparable antitumor efficacy. In vitro studies using pancreatic cancer patient-derived

cell lines (PDCLs) confirmed robust cytotoxic activity, supporting its relevance to clinically representative pancreatic cancer models. Furthermore, in vivo xenograft models established from pancreatic cancer PDCLs showed clear tumor growth inhibition following intratumoral administration of CVB3-BHP, providing preclinical proof-of-concept for local oncolytic virus therapy in pancreatic cancer.

To support clinical translation, we have advanced process development and manufacturing readiness at the JIKEI Cell Processing Facility. Preclinical proof-of-concept studies, process development, non-GMP manufacturing runs, and safety studies have been completed. The current focus is GMP manufacturing, scale-up, and technology transfer. The workflow incorporates ultrafiltration and chromatography-based purification and is designed to enable scalable, high-titer viral production under a GMP-oriented framework. These activities position the program for engineering lot production and subsequent GMP technology transfer as part of a regulatory-aligned development pathway.

Together, these findings indicate that CVB3-BHP combines safety-by-design, preserved oncolytic efficacy, activity against pancreatic cancer PDCLs, in vivo antitumor efficacy, and GMP-oriented manufacturing readiness. CVB3-BHP therefore provides a translational foundation for advancing toward first-in-human clinical evaluation of oncolytic virotherapy for pancreatic cancer.

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Gene Editing/Gene Therapies

LIPID NANOPARTICLES ENABLE HIGH EFFICIENCY CRISPR HDR MEDIATED GENE INSERTIONS IN PRIMARY HUMAN T CELLS

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KEYWORDS: LNP, CRISPR, Gene Editing.

1. Cytiva, Lane Cove West, NSW, Australia.

Background & Aim:

Stable, site specific insertion of large genetic cargos is critical for next generation CAR T therapies, enabling safer and more accessible treatments. Current approaches rely on viral vectors, which pose challenges in cost, manufacturing complexity, and insertional risk, or electroporation (EP), which can reduce cell yield and induce cellular stress (1). Lipid nanoparticles (LNPs) represent a promising non viral, fully synthetic, and scalable delivery platform that is typically gentler than EP (2,3) and suitable for large-scale deployment. However, efficient homology-directed repair (HDR) in primary human T cells remains difficult due to competition with error-prone repair pathways, cell-cycle constraints (G2/S phase dependence), immune recognition of donor DNA, and the requirement for donor presence at the cut site. Here, we systematically map key variables impacting LNP-mediated HDR in primary human T cells. Using Cas9 mRNA, sgRNA, and HDR donor templates, we evaluate both small insertions (HA tag) and large insertions (TRAC-targeted CD19 CAR). Variables assessed include basal media, dose and RNA:DNA ratios, donor timing, transient NHEJ inhibition, donor format (dsDNA vs cssDNA), as well as functional cytotoxicity and scalability in large scale manufacturing workflows.

Methods, Results & Conclusion:

Methodology

Cas9 mRNA, a chemically synthesized guide RNA (sgRNA) and a □100 nt single-stranded donor oligonucleotide (ssODN) were produced using a novel LNP composition and scalable production platform. A haemagglutinin (HA) epitope tag was knocked in at the CD5 locus as an easily quantifiable read-out for CPP optimization. CD3+ primary T cells from healthy donors were cultured in well-plates and the CRISPR LNPs added to the media in a one-step process, without further cell manipulation.

Results

Various parameters were identified and systematically varied, including (and not limited to) the length of cell activation, cell density, nucleic acid dose and the RNA/DNA molar ratios. Through multiple rounds of optimizations, LNPs achieved on average 31 ±7% HDR in n=5 T cell donors, detected through dual CD5/HA flow cytometry 4-days post-LNP administration. Viability of the cells remained high at 96 ± 5% at the time of HDR detection, relative to untreated controls. The aforementioned results reflect no added enhancers; however, when we tested various small molecules, such as NHEJ inhibitors, HDR rates further improved to over 50% in primary T cells. Finally, we compared the optimized LNP protocol to EP which resulted in similar HA+ frequencies in the cell population. However, most notably, the yield of viable edited cells by LNP was an order of magnitude higher than EP owing to improved cell viability and proliferation.

Conclusion

All together, this data demonstrates how LNPs can achieve clinically relevant knock in frequences and showcases the benefits of LNPs as a non-viral alternative for gene insertion. The CPP evaluation offers a ready-to-implement framework applicable to a diverse set of therapeutic loci, providing for a foundational dataset for the rapid application of LNPs to enable the next generation of T cell therapies.

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

ACHIEVING HIGH CAR T CELL TRANSDUCTION USING THE AUTOMATED END TO END SEFIA™ CELL THERAPY PLATFORM

J. Bryce[1]

KEYWORDS: CAR-T, Automated, Manufacturing.

1. Cytiva, Lane Cove West, NSW, Australia.

Background & Aim:

Hematologic malignancies areong the most common cancers worldwide, with incidence continuing to rise. Although autologous chimeric antigen receptor (CAR) T cell therapies have demonstrated significant clinical potential, complex and costly manufacturing remains a major barrier to broad patient access. Automating workflows and reducing operator dependence offers a path to lower costs, improved reproducibility, and increased productivity. However, existing all in one automated manufacturing platforms often lack the flexibility needed to meet evolving CAR T market demands.

Methods, Results & Conclusion:

The Sefia™ cell therapy platform is an automated, functionally closed, modular system designed to enable simultaneous CAR T expansion and increased throughput. When integrated with Chronicle™ automation and electronic batch record software, the platform supports streamlined process execution and monitoring. To assess biological performance under GMP aligned conditions, end to end manufacturing runs were conducted using three healthy donors, followed by post thaw evaluation of CAR T phenotype, cytotoxicity, and IFNγ production.

The Sefia cell therapy platform demonstrated strong potential for end to end CAR T cell therapy manufacturing.

Cell selection achieved high purity and reliable recovery, supporting parallel seeding across multiple systems.

Expansion was highly consistent across donors, maintaining ~ 60% CAR positivity over 12 days of culture.

Harvest and formulation preserved cell viability and recovery.

Final CAR T products exhibited a predominantly central memory phenotype with robust cytotoxicity and IFNγ production.

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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

J. Bryce[1]

KEYWORDS: NK Cells, Semi Automated.

1. Cytiva, Lane Cove West, NSW, Australia.

Background & Aim:

Natural killer (NK) cells are a powerful immunotherapy modality with the potential to enable scalable allogeneic cell therapies and expand patient access. NK cells can target tumor cells without major histocompatibility complex (MHC) presentation, reducing the risk of graft versus host disease. Preclinical and clinical studies have reported favorable safety and encouraging efficacy in multiple malignancies, including solid tumors. However, current NK manufacturing approaches rely heavily on manual processing and feeder cells, driving high costs, safety risk, scale limitations, and regulatory complexity. Feeder free, closed, and automated manufacturing strategies offer a scalable path forward by simplifying raw material control, reducing contamination risk, and accelerating regulatory acceptance. In this study, we demonstrate steps toward a scalable, feederfree workflow using semi automated, GMP friendly systems, achieving >15 billion NK cells with >99% purity, post process viability of 92 ± 0.3%, and post thaw viability of 88 ± 2%.

Methods, Results & Conclusion:

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 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 with IL2 and IL15, and gently rocked (2 rpm, 2° angle). Cultures were sampled starting 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 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% 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

Our data demonstrates the successful manufacturing of NK cell at scales relevant for allogeneic NK cell production, including:

- Feeder free activation and expansion utilizing the Xuri cell expansion system.
- Expansion reaching 16.7 to 26.6 billion cells between days 13 and 19, with > 99% NK cell purity.
- Automated wash, formulation, freeze, and thaw using the Sefia S2000, VIA Freeze, and VIA Thaw systems.

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

ACCELERATING AUTOLOGOUS CAR T CELL EXPANSION WITH THE AUTOMATED, END TO END SEFIA CELL THERAPY PLATFORM

J. Bryce[1]

KEYWORDS: CAR-T, Semi Automated, Manufacturing.

1. Cytiva, Lane Cove West, NSW, Australia.

Background & Aim:

Autologous chimeric antigen receptor (CAR) T cell therapies have transformed outcomes for patients with leukemia and B cell malignancies; however, durable responses in solid tumors and lymphomas remain challenging. Sustaining efficacy in these settings often requires multiple CAR T doses, placing added demands on ex vivo manufacturing. A central challenge is achieving high-fold T cell expansion without inducing exhaustion, while minimizing manufacturing time to enable rapid patient delivery. CAR T production is further complicated by multi step workflows that depend on highly trained operators and require extensive traceability and documentation to meet regulatory standards.
The Sefia cell therapy platform addresses these challenges as a modular, semi automated, functionally closed manufacturing solution. When integrated with Chronicle automation and electronic batch record software, it enables streamlined documentation and efficient process execution. Using frozen apheresis from healthy donors (n = 3), we evaluated an end to end CAR T workflow including T-cell isolation, CD19 CAR lentiviral transduction, expansion in serum free media with a singleuse silicone based kit, followed by washing, formulation, and cryopreservation. Post thaw CAR T phenotype, cytotoxicity, and IFNγ production were assessed.

Methods, Results & Conclusion:

Conclusion

Efficient, end to end CAR T manufacturing was achieved across three runs, delivering high yields within 8 to 9 days and supporting dose requirements for solid tumor lymphoma.

Robust isolation and expansion performance, with consistent T cell recovery and purity on Sefia Select and accelerated growth on the Sefia expansion system. High viability and recovery maintained through final washing and formulation on Sefia Select.

Functional, high quality CAR T cells were produced, exhibiting a predominantly central memory phenotype, effective cytotoxicity, and IFNγ production.

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

INVESTIGATING THE ROLE OF BCMA MUTATIONS IN CAR-T RESISTANCE WITH ESTABLISHED AND NOVEL CAR-T CONSTRUCTS

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KEYWORDS: BCMA , CAR-T, Myeloma.

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2. Royal Brisbane Hospital, Brisbane, QLD, Australia.

Background & Aim:

Resistance to BCMA-directed therapies in multiple myeloma can occur due to alterations in BCMA expression or structure. Three specific mutations - S30del, P34del and R27P - have been identified in patients relapsing on BCMA T-cell engaging therapies and been shown in vitro to potentially confer resistance. The most successful BCMA-directed treatment, ciltacabtagene autoleucel (cilta-cel) is a CAR-T therapy that utilises two single domain nanobodies targeting different epitopes on BCMA which may lead to improved tumour killing in the presence of such resistance mutations, but this has not to our knowledge been previously investigated. Rational design of new CAR-T constructs should also aim to generate binders that are active against these mutations if feasible.

Methods, Results & Conclusion:

Methods

K562 cells expressing wild type (WT) BCMA and the S30del, P34del and R27P variants were generated. Cytotoxicity assays were performed using CAR T cells comprising cilta-cel intact with both nanobodies, or with either nanobody 1 (VHH1), or 2 (VHH2) alone, as well as idecabtagene vicleucel (ide-cel) and a panel of 14 novel BCMA-targeting VHH binders derived from an alpaca immunization campaign.

Results

All constructs demonstrated potent killing of WT BCMA-expressing targets. VHH1 showed markedly impaired activity against S30del (~10-fold reduction versus WT BCMA), while maintaining activity against R27P and P34del. In contrast, VHH2, full cilta-cel and ide-cel retained robust killing of S30del targets.ong 14 novel BCMA-targeting VHH binders, most retained activity against WT BCMA but demonstrated substantially reduced cytotoxicity against S30del targets, with only VHH09 and VHH22 maintaining robust activity.

Conclusion

These findings suggest that S30del selectively disrupts a commonly targeted BCMA epitope and may represent a broader vulnerability across diverse BCMA-directed binders. Dual-epitope targeting and selection of binders resilient to structural variation may reduce susceptibility to antigen escape.

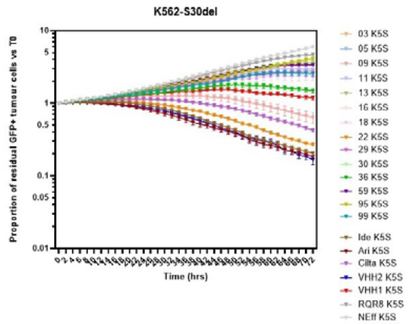

Figure 1 (Abstract 110). Shows poor target killing against K562 cells expressing the S30del variant of BCMA for novel constructs and VHH1 of cilta-cel.

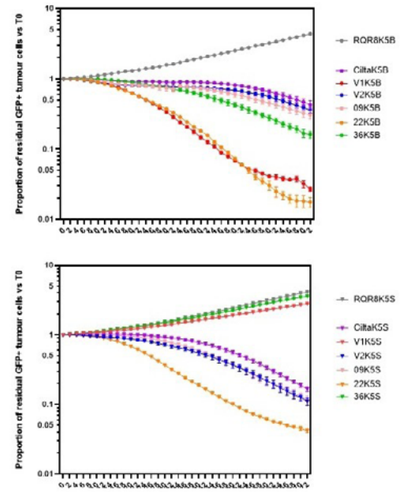

Figure 2 (Abstract 110). Demonstrates loss of killing with VHH1 against the S30del variant but shows this is preserved with the #22 novel binder

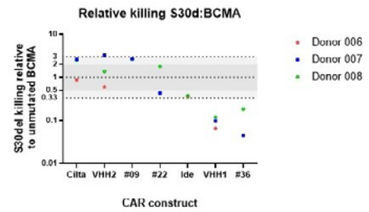

Figure 3 (Abstract 110). Shows repeats from 3 runs across separate donors, highlighting the loss of efficacy in VHH1 due to the S30del mutation, which also abrogates the killing of the novel #36 binder

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

LEVERAGING DC ACTIVATION TO OVERCOME TUMOR HETEROGENEITY IN CAR T CELL THERAPY

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KEYWORDS: Dendritic Cells, CAR T cell, Antitumor immunity.

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Background & Aim:

Adoptive cell transfer (ACT) therapy using patient-derived T cells genetically engineered to express a chimeric antigen receptor (CAR) is highly effective in B cell malignancies and is now FDA-approved. However, antigen heterogeneity remains a major challenge in treating solid tumors due to the relapse of tumors negative for CAR-targeted antigen. Previously we demonstrated that CAR T cells engineered to secrete dendritic cell (DC) growth factor Fms like tyrosine kinase 3 ligand (Flt3L) promote host antitumor immunity to effectively eradicate heterogeneous tumors by expanding intratumoral conventional type 1 dendritic cells (cDC1s) (DOI: 10.1038/s41590-020-0676-7). cDC1 is a critical mediator in activation of antitumor cytotoxic responses. A key aspect of this study was that despite the increased population of intratumoral cDC1s, cDC1s required a second activatory stimulus to elicit antitumor immunity. Here, we explored the possibility of leveraging the CD40 axis to promote cDC1 function and synergise with Flt3L-secreting ACT therapy.

Methods, Results & Conclusion:

Engagement of upregulated CD40 on antigen-experienced DC with its ligand CD40L, which is traditionally expressed on activated T cells, induces DC activation. Upon anti-CD40 and Flt3L treatment, upregulation of co-stimulatory molecules (CD80, CD86) on cDC1, indicative of DC maturation, as well as expansion of tumor-antigen specific T cells was observed. To incorporate the CD40 axis activation in adoptive cell therapy, successful engineering of CAR T cells was conducted using a novel construct to induce CD40L overexpression. Furthermore, as Type I interferon (IFN) potentiates DC activation in response to CD40 stimulation, CRISPR/Cas9-mediated homology directed repair was employed to induce tumor-localized secretion of IFNβ on CD40L-overexpressing CAR T cells, enhancing cDC1 activation. Co-culture of DCs with engineered T cells enhanced cDC1 maturation. Improved DC activation and CD8 T cell priming was observed upon adoptive transfer of IFNβ/CD40L-expressing T cells, correlated with improved antitumor efficacy. Based on our results of the synergistic effect between Flt3L and CD40 axis on cDC1, we are poised to further incorporate this with Flt3L-secreting CAR T cell to achieve cDC1 expansion and activation upon ACT. Our study has demonstrated an enhanced efficacy of CAR T cell treatment in solid cancers by harnessing the endogenous immune responses against tumors.

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

TARGETED INTEGRATION OF A FUNGUS-SPECIFIC TRANSGENIC T CELL RECEPTOR INTO HUMAN T CELL RECEPTOR ALPHA CONSTANT LOCUS

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KEYWORDS: TCR, Cell Therapies.

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3. Kids Research, Sydney, NSW, Australia.

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Background & Aim:

Invasive fungal infections (IFIs) remain a major issue following allogeneic stem cell transplantation. We have preliminary evidence that fungus-specific adoptive T cell therapy restores antifungal immunity and have generated fungus-specific transgenic T cell receptor (tgTCR) T cells. However, the persistence of endogenous T cell receptor (TCR) expression raises the risk of graft-versus-host disease (GvHD) and TCR mispairing. Here, we report a CRISPR/Cas9-mediated homology-directed repair (HDR) approach for precise knockin of a tgTCR into the human T cell receptor alpha constant (TRAC) locus.

Methods, Results & Conclusion:

We identified an Aspergillus–specific TCR recognizing fungal antigens presented by HLA-DR*01, whose variable regions were used to generate a tgTCR in a piggyBac transposon system. Three guide RNAs (sgRNAs) designed using CRISPick and CHOPCHOP were screened for knockout (KO) efficiency. A HDR template (HDRT) containing the tgTCR, 500 bp and 300 bp 5 and 3 homology arms, and a 5 Cas9 targeting sequence was generated. Human donor T cells were electroporated with the HDRT, Cas9, and sgRNA, and expanded for 15 days using irradiated artificial antigen-presenting cells and IL-15. Functional assays compared random tgTCR integration with or without endogenous TCR KO against TRAC locus targeted integration of tgTCR.

3 novel candidate sgRNAs were tested. All showed similarly reduced levels of endogenous TCR expression (range 24-28%) with preserved tgTCR (range 87-91%). We selected the sgRNA that demonstrated highest endogenous TCR KO. Optimization of HDRT molar ratio identified 6 µg as optimal dose based on tgTCR expression and cellular expansion. TgTCR T cells, regardless of integration strategy, showed TNFα response and enhanced antifungal activity. Significant difference in TNFα production between CD4+ tgTCR+ TCR- cells (2.77%) and CD4+ tgTCR+ TCR+ cells (0.78%, p=0.0226, 2-way ANOVA) generated using TRAC locus targeted integration was seen. TgTCR T cells without TRAC KO demonstrated significantly enhanced antifungal response against Aspergillus terreus compared to innate leukocyte effectors alone (1.45-fold; p=0.0178).

We generated tgTCR T cells with efficient TRAC locus targeted integration and showed that the cells retained fungal responsiveness. Currently we are evaluating alloreactivity and identifying potential off-target edits. Ultimately, our aim is to develop a bank of fungus-specific tgTCR T cells with reduced GvHD potential for use in immunocompromised patients.

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

TIME TO FIRST FEVER IS STRONGLY ASSOCIATED WITH SUBSEQUENT SEVERE ICANS IN R/R LBCL TREATED WITH AXI-CEL

S. Farina[1], N. O'Leary[1], J. Stewart[1], K. Purcell[1], B. Panozzo[1, 4], A. Edelkina[3], J. F. Seymour[1], P. A. Thompson[1, 2], M. Anderson[1], S. Harrison[1, 2, 3], M. Dickinson[1, 2, 3], M. Dowling[1, 2, 3]

KEYWORDS: ICANS, CRS, TIME.

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3. Centre of Excellence in Cellular Immunotherapy, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia.

4. Department of Malignant Haematology & Stem Cell Transplantation, The Alfred Hospital, Melbourne, VIC, Australia.

Background & Aim:

Axicabtagene ciloleucel (axi-cel) is now standard-of-care treatment for relapsed/refractory large B-cell lymphoma (r/r LBCL) in second line (2L) and beyond. However, immune effector cell associated neurotoxicity syndrome (ICANS) is a serious adverse event that can result in significant morbidity and mortality. Pre-infusion patient and disease characteristics were analysed to identify factors associated with time of onset of sequential grades of cytokine release syndrome (CRS) and ICANS and the temporal relationship between toxicity events.

Methods, Results & Conclusion:

Method:

Patients treated with axi-cel at a single Australian centre between 01/08/2021–31/12/2025 were included. Univariable and multivariable logistic regression was used for the occurrence of toxicity events, while Cox proportional hazards was performed for time to events.

Results:

222 patients were included. The median age was 65 (range 16–85) years; 46% were ECOG 1+; 24% received 2L axi-cel; histological subtypes included DLBCL (58%), transformed lymphoma (23%), high grade lymphoma (12%) and other (7%). Median time to onset of first fever ≥38.0° C (G≥1 CRS) was 29h (range 5–317h). On univariable analysis, only male sex (HR 1.43; 1.07–1.89) and 2L vs 3L+ therapy (hazard ratio (HR) 1.79; 1.30–2.44) were associated with earlier fever. Only ECOG ≥1 (odds ratio (OR) 2.09; 1.03–4.06) and disease bulk ≥10cm (OR 3.27; 1.38–7.74) pre-infusion were associated with G≥3 ICANS. Univariable spline analysis demonstrated a strong association between time to first fever and subsequent occurrence of G≥3 ICANS (Figure 1). Risk of G≥3 ICANS was 36% with first fever at <24 hours, 19% at 24-48 hours, 6% at 48-72 hours and 5% at >72 hours. On multivariable analysis, this relationship was independent of baseline variables (ECOG, bulk, bridging response and LDH).

Conclusion:

Early onset of fever is strongly associated with subsequent severe ICANS in axi-cel-treated patients with r/r LBCL and may warrant more intensive observation and/or earlier intervention.

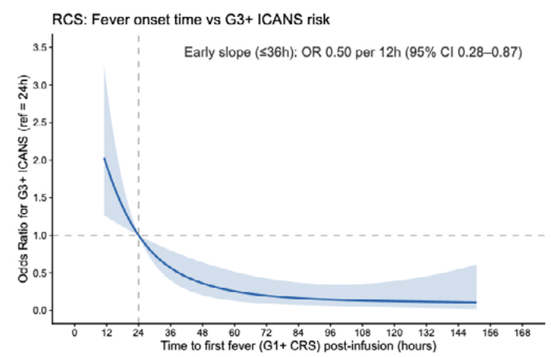

Figure 1 (Abstract 113). Relationship between time to first fever and OR for severe ICANS (with reference to 24h) in R/R LBCL patients treated with axi-cel.

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

INVESTIGATING THE DENDRITIC CELL - T CELL AXIS IN GLIOBLASTOMA TO EXPLORE NEW COMBINATION IMMUNOTHERAPY TREATMENT OPTIONS

B. Gardam[1, 2], T. Gargett[1, 2, 3], E. Nam[1, 2], S. Khan[2, 3], R. J. Ormsby[4], S. I. Poonoose[1, 4, 5], J. Bracken[2], A. Pasam[6], S. Lenin[2], B. Gliddon[2], M. Tea[2], C. L. Shard[2], S. Pitson[1, 2], G. A. Gomez[2], K. A. Pillman[2], S. Sandhu[6, 7], M. P. Brown[1, 2, 3], L. Ebert[1, 2]

KEYWORDS: CAR-T Cells, Dendritic Cells, Brain Tumours.

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5. Department of Neurosurgery, Flinders Medical Centre, Adelaide, SA, Australia.

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7. Sir Peter MacCallum Cancer Department of Oncology, University of Melbourne, Melbourne, VIC, Australia.

Background & Aim:

Background: Glioblastoma is an aggressive form of brain tumour with a median survival of only 15 months, with few advances in treatment for over 20 years. T cells have long been associated with anti-tumour responses but require professional antigen-presenting cells for effective priming and activation. Dendritic cells (DCs) are the most effective professional antigen-presenting cells for priming and activating this response. Others have reported reduced DCs in glioblastoma patients, although it is currently unclear which DC subsets are most affected. Here, we define the affected DC subsets, identify a suitable murine model, and investigate approaches to restore DCs and trial a combination immunotherapy.

Methods, Results & Conclusion:

Methods: High-parameter flow cytometry was used to analyse DC populations and functional markers in peripheral blood and tumour tissue from glioblastoma patients, patients with other cancers, healthy donors, and the immune populations in five orthotopic murine brain tumour models. The effects of FMS-like tyrosine kinase 3 ligand (FLT3L), granulocyte colony-stimulating factor (G-CSF), and granulocyte-macrophage colony-stimulating factor (GM-CSF) were evaluated in a preclinical mouse model. Combination therapy incorporating radiation, growth factors, and CAR-T cells was also investigated.

Results: Glioblastoma patients showed reduced circulating DCs, with altered expression of DC functional markers in blood and tumour tissue compared with healthy donors. Similar reductions were found in patients with other primary and metastatic brain tumours, but not in patients with tumours outside the brain, suggesting a relationship between tumour location and reduced DCs. In murine studies, immunocompetent orthotopic models showed significant differences in DC populations between tumour-bearing and tumour-free mice. Treatment with FLT3L, G-CSF, or GM-CSF restored DC populations in the syngeneic brain tumour models. While combination treatment with radiation, growth factors, and CAR-T cells altered the immune landscape in tumour-bearing mice, no significant improvement in overall survival was observed.

Conclusion: Brain tumours are associated with systemic reductions in dendritic cell populations and altered immune phenotypes. Growth factors can restore DC populations in murine brain tumour models. Although survival benefits were not achieved in our combination study, we show measurable immune changes that may guide future therapeutic optimisation for glioblastoma.

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

A NOVEL T-CELL RECEPTOR THERAPEUTIC PRODUCT FOR THE TREATMENT OF WT1+ MALIGNANCIES

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KEYWORDS: TCR, WT1,L.

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8. The Daffodil Centre, The University of Sydney and Cancer Council NSW, Sydney, NSW, Australia.

9. Sydney Medical School, Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia.

Background & Aim:

T cell receptor (TCR) therapies are an emerging adoptive cell therapy showing great promise for cancers such as acute myeloid leukaemia (AML) and solid tumours that express a wide range of intracellular antigens. TCRs have highly specific recognition of processed antigenic peptides (epitopes), presented via the human leukocyte antigen (HLA). T cells rewired to express antigen specific TCRs can thus act as effective therapeutic cells.

Wilms tumour 1 (WT1) is a promising target and an antigen found to be highly overexpressed in several cancers linked to poorer prognosis in patients and includes a highly immunogenic universal epitope, the VLD peptide (WT137-45). This study has generated a new WT1 specific TCR-T cell product with novel features that include a unique dimerising motif involving leucine zippers to ensure proper pairing of the TCR subunits, and a dual functional tEGFR based molecular tool.

Methods, Results & Conclusion:

Peripheral blood mononuclear cells were stimulated with WT1 peptides, including the WT137-45, and single reactive cells were captured using interferon-γ capture assays or tetramer staining (Fig1A-B). Four unique HLA-A2+ TCRab sequences specific for the WT137-45 epitope were identified using 10X Chromium single cell TCR sequencing. Murinisation of TCR constant chains, Cys disulphide bond addition, and inclusion of C-terminal leucine zipper chains (Fig1C) promoted correct pairing of VLD1 TCR subunits without compromising functionality, as confirmed with tetramer binding, effector cytokine release upon specific activation and cytotoxicity of target cells (Fig1D-E). A novel tEGFR linked to a CD28 and a CD3 domain (Fig1C) molecular tool aided expansion of these new TCR T-cells via stimulation with irradiated K562 feeder cells modified to express a cetuximab scFv. In addition, this tool can serve as a safety switch for in vivo elimination via complement-dependent cytotoxicity with cetuximab administration.

The leading TCR candidate (VLD1) demonstrated specific HLA-A*02:01 restriction without cross reactivity to other HLA alleles (Fig1F) and cytotoxicity against endogenously WT1 expressing leukaemic (Fig1G), primary ovarian cancer and osteosarcoma cell lines (Fig1H), with comparable response to a previously published benchmark TCR (HD1) targeting the same epitope.

The identified TCR and novel TCR T-cell product shows promise for the treatment of WT1+ malignancies.

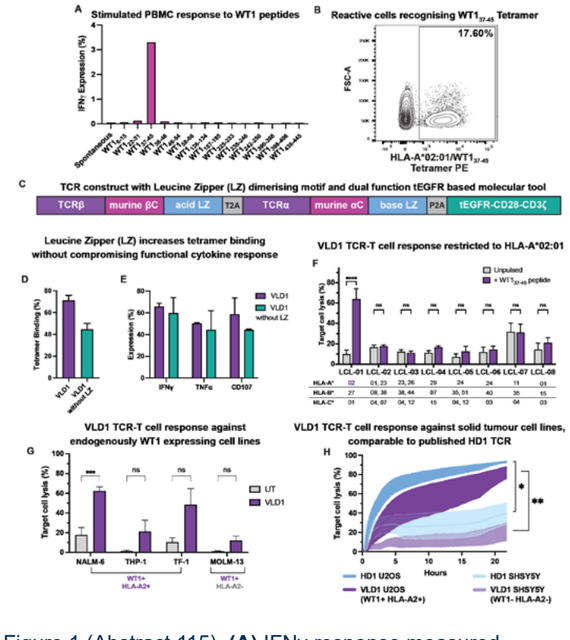

Figure 1 (Abstract 115). **(A)** IFNγ response measured by intracellular flow cytometry either at spontaneous baseline (Spontaneous) or following 4h incubation with individual peptides. **(B)** Flow cytometry dot plot showing CD8+ subsets of T cells binding to HLA-A*02:01/WT137-45 tEGFR-CD28-CD3ζ as an expansion tool. αC; α Constant chain, βC; β Constant chain, LC; Leucine zipper. **(D)** Flow cytometry-based measurement of CD3+, VLD TCR+, CD8+ subset of TCR-T cell binding to HLA-A*02:01/WT 137-45 Tetramer-PE (n=2, SD). **(E)** Intracellular cytokine release if IFNγ, TNFα and degranulation marker CD107 expression detected by flow cytometry following co-culture of TCR-T cells with K562-A2 + WT137-45 peptide pulsed target cells at an E:T ratio of 5:1 (n=2, mean ± SD). **(F)** VLD1 TCR cytotoxicity against a panel of LCLs, either unpulsed or pulsed overnight with WT137-45(VLDFAPPGA) peptide, at a E:T ratio of 10:1, measured by Calcein cytotoxicity assay. HLA alleles of LCLs are noted in table below the graph. n=2 donors, each with 3 technical replicates, mean ± SEM. ns=p>0.5, ***p<0.0001 by mixed effects analysis with Holm-Sidak correction. **(G)** Killing of leaukemic cell lines by untransfected (UT) T-cells and VLD1 TCR-T cells at an E:T ratio of 10:1 as measured by Calcein-AM cytotoxicity assay. n=3 donors, each with 3 technical replicates, shown as mean ± SEM. ns=p>0.05, p*<0.05 by paired t-tests with Holm-Sidak correction. **(H)** Killing

of solid tumour cell lines U2OS (WT1-HLA-A2+) and SHSY5Y (WT1-HLA-A2-) by TCR-T cells measured by impedance based real time XCELLigence cytotoxicity assay, n=4 independent donors, data shown as mean ± SEM. *p<0.05, **p<0.01 by paired t-test with Holm-Sidak correction.

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

ANTIGEN-HETEROGENEOUS SOLID TUMOUR TARGETING WITH TUMOUR-LOCALISED T CELL ENGAGER-EXPRESSING T CELLS

Y. Huang[1,2], T. Hoang[1], D. Nguyen[2], P. K. Darcy[1,2], C. Wang[3], P. Beavis[1,2]

KEYWORDS: CAR T cell, T cell engager, solid tumour.

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2. Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, VIC, Australia.

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Background & Aim:

Background

Adoptive Cell Therapy (ACT) and bispecific T Cell Engager (TCE) are potent immunotherapies that direct T cells to kill tumour cells. CAR T cells are genetically engineered for sustained, antigen-specific cytotoxicity, while TCEs are synthetic antibodies that transiently link T cells to tumour antigens via CD3 binding, enabling rapid activation without additional genetic modification. However, both approaches face challenges in solid tumours due to heterogeneous antigen expression and off-tumour/dose-limiting toxicities. Our lab has previously developed a novel CRISPR/HDR knock-in (KI) method to drive payload expression in T cells under a tumour-localised promoter of NR4A2. Here we explore tumour-specific armouring of T cells with TCEs to overcome solid tumours with multiple antigens.

Methods, Results & Conclusion:

Methods

Murine CAR and OT1 T cells were engineered to secrete HER2-targeting TCEs (1) constitutively (retrovirus) and (2) tumour-specifically (CRISPR/HDR KI). In vitro evaluation and in vivo therapeutic efficacy and toxicity were evaluated using an immune competent HER2 transgenic murine model with subcutaneous and mammary fat pad tumour models expressing different tumour antigens.

Results

Both TCE-expressing T cells demonstrated enhanced therapeutic efficacy in different solid tumour models with enhanced T cell activation and expansion. However, 30% of mice treated with constitutive TCE-expressing T cells experienced rapid weight loss (>20%). This adverse effect was eliminated when the TCE was regulated by NR4A2 at the tumour site. Tumour-localised control of TCE reduced systemic T cell expansion, detectable serum level of TCE and PD1/CD101 expression on intra-tumoural cytotoxic T cells.

Conclusions

Tumour-localised control of TCE delivery in ACT provide a safer, and more effective solution to targeting antigen-heterogeneous solid tumours.

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

AUTOMATING CELL ISOLATION FROM BUFFY COATS FOR CELLULAR THERAPY APPLICATIONS

G. Rodrigues Rossi[1], D. Kelk[1], F. Chong[1], B. Griffiths[1]

KEYWORDS: counterflow centrifugation system , PBMCs.

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Background & Aim:

Cell isolation from buffy coats is a critical upstream step in the manufacture of cellular therapies, including T and natural killer (NK) cell-based immunotherapies and emerging allogeneic cell therapy platforms. However, conventional density gradient centrifugation remains labour-intensive, time-consuming, and poorly adaptable for selective and reproducible enrichment of defined cell subsets. Protocols often require additional manual processing steps to remove platelets and red blood cells. These constraints limit the development of rapid, standardised, and scalable workflows that are essential for robust, GMP-compliant cellular therapy manufacturing and clinical translations.

Methods, Results & Conclusion:

Using a counterflow centrifugation system (Rotea, Thermo Fisher), we established multiple isolation workflows tailored to distinct cellular outputs. Isolated cells were characterised by flow cytometry and haematology analysis (Sysmex), and functional performance of T and NK cells was evaluated post-culture, including expansion capacity, cytotoxic activity, and cytokine production (tumour necrosis factor (TNF)-α and interferon (IFN)-γ).

Our optimised protocols enabled flexible manufacturing outputs, ranging from high-yield preparations (recovering ~77% of leukocytes from a buffy coat) enriched in granulocytes, monocytes, and lymphocytes, to highly purified lymphocyte fractions (95% purity) with reduced overall cell recovery (~8% of starting leukocytes). Expanded T and NK cells demonstrated cytokine production (TNF-α and IFN-γ), while NK cells also exhibited cytotoxic activity, confirming functional integrity. Overall, these findings demonstrate that automated counterflow centrifugation provides a flexible, scalable, and standardised platform for buffy coat processing, enabling tailored cell isolation workflows with strong potential for integration into GMP-compliant and translational cellular therapy manufacturing.

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

DEVELOPMENT OF ANTI-CAR ANTIBODY RESPONSES IN CAR-T THERAPY: PRELIMINARY DATA FROM PHASE 1 CLINICAL TRIALS IN ADULT AND PEDIATRIC BRAIN TUMORS

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KEYWORDS: CAR-T, GBM, DIPG, HACA.

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Background & Aim:

Glioblastoma multiforme (GBM) and diffuse intrinsic pontine glioma (DIPG) are aggressive and life-threatening brain tumors in adults and children respectively, with poor survival outcomes and high rates of recurrence. Current standard treatments, including surgery, radiation, and chemotherapy for GBM and radiation for DIPG, provide limited long-term benefit, highlighting the urgent need for more effective therapies. Chimeric antigen receptor (CAR)-T cell therapy has emerged as a promising immunotherapy approach for targeting GBM and DIPG.

Translational oncology lab is conducting two CAR-T cell therapy clinical trials using GD-2 targeting CAR-T cells for GBM (KARPOS) and DIPG (LEVI'S CATCH). In both trials, 3 adults and 3 paediatric patients were given multiple infusions. We observed that CAR-T cell expansion decreased following multiple infusions in all patients. This finding suggested that an immune response against the CAR construct may be limiting CAR-T persistence and activity. One possible mechanism is the development of human anti-CAR antibodies (HACA), which can recognise and neutralise CAR-T cells.

Methods, Results & Conclusion:

To investigate this, we analysed plasma /serum and cerebrospinal fluid (CSF) samples collected from both adult and pediatric patients treated with repeated CAR-T infusions. HACA was detected in most of the patients, in both plasma/serum and CSF, appearing after 4-6 weeks. In one pediatric DIPG patient, HACA appeared after the second CAR-T infusion and was associated with reduced CAR-T expansion. Neutralisation of CAR-T activity was confirmed ex vivo in a real-time cytotoxicity experiment. The patient then received 4 weeks treatment with B-cell–depleting therapy (daratumumab), HACA levels became undetectable in both plasma and CSF. If eligible, this patient will next receive a repeat infusion and CAR-T expansion following B cell depletion will be directly assessed.

These findings suggest that anti-CAR immune responses can develop after repeated CAR-T dosing in CNS malignancies and may contribute to reduced CAR-T expansion. The loss of HACA following B-cell depletion indicates that these antibodies are likely maintained by short-lived antibody-producing cells. Our study highlights the importance of monitoring immunogenicity during repeat CAR-T therapy and suggests that B-cell–targeted approaches may help improve CAR-T persistence and efficacy in brain tumor patients.

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

DEVELOPMENT OF T CELL-TARGETED LENTIVIRAL VECTORS FOR IN VIVO DELIVERY OF THE BRIDGE ADAPTOR CAR SYSTEM

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KEYWORDS: Adaptor CAR, in vivo CAR, Immunotherapy.

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2. St George and Sutherland Clinical School, the University of New South Wales, Sydney, NSW, Australia.

3. Westmead Institute for Medical Research, The University of Sydney, Westmead, NSW, Australia.

Background & Aim:

Background

We previously developed BRiDGE CAR, a modular fully human adaptor CAR platform currently configured for ex vivo CAR T-cell generation. To leverage the advantages of in vivo CAR approaches, including off-the-shelf availability, avoidance of lymphodepletion, simplified logistics and reduced cost, we investigated whether

the BRiDGE CAR system could be adapted for in vivo delivery.

Methods, Results & Conclusion:

Methods

Using a third-generation lentiviral vector (LVV) system, we generated engineered vectors pseudotyped with modified ("blinded") VSV-G and Cocal glycoproteins to eliminate native tropism and retarget delivery toward T cells. Vectors were designed to target pan-T-cell markers including CD3, CD5 and CD7. A bispecific CD3/CD80 targeting strategy was also evaluated to enhance selective T-cell delivery.

Results

Following optimisation of LVV production, engineered vectors were generated at titres of 1–9 × 10e8 TU/mL, with successful expression of T-cell-targeting molecules on packaging cells. In vitro studies demonstrated selective T-cell transduction, with an MOI of 30 achieving ~50–90% CAR expression in T cells while maintaining minimal transduction of other major blood cell populations. Preliminary assessment of the CD3/CD80 strategy further supported the feasibility of dual-targeted delivery and improved selective T-cell transduction. Importantly, CAR T cells generated using this in vivo-compatible LVV approach showed strong in vitro antitumour activity in CD19-positive lymphoma and CD33-positive acute myeloid leukaemia models, confirming functional CAR expression following targeted delivery.

Conclusion

These findings support the feasibility of transitioning the BRiDGE CAR platform from an ex vivo manufacturing process to an in vivo CAR delivery system. Ongoing studies will assess efficacy, off-target transduction and safety in animal models, alongside development of GMP-compatible vector manufacturing to support future clinical translation.

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

DEVELOPING SINGLE OR MULTI-TARGETING CAR-T CELL THERAPY IN THE TREATMENT OF PAEDIATRIC BRAIN TUMOURS

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KEYWORDS: Paediatric brain tumour, CAR-T cells.

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4. Ben Towne Center for Childhood Cancer Research, Seattle Children's Research Institute, Seattle, WA, United States.

Background & Aim:

Diffuse midline glioma (DMG) isong the most aggressive paediatric brain cancers and accounts for most brain tumour-related deaths in children. The 5-year survival rate is ~2%, with no effective treatments identified to date. We are developing novel Chimeric Antigen Receptor (CAR)-T cell therapies for DMG and other paediatric brain tumours by targeting one or more tumour-specific antigens. This includes the established targets GD2 and B7-H3, which are the focus of current clinical trials for DMG, and fibroblast activation protein (FAP), a promising target strongly expressed in tumour-associated vasculature but not yet studied in paediatric brain tumours. Here, we aimed to survey expression of these antigens in aggressive paediatric brain tumours and characterise the activity of CAR-T cells directed toward these antigens, alone or in combination, to treat otherwise incurable childhood brain tumours.

Methods, Results & Conclusion:

In our studies, we have investigated the expression of GD2, B7-H3, and FAP in paediatric DMG (n=3) and medulloblastoma (n=5) tissues using immunohistochemistry (IHC) and multiplex immunofluorescence (multi-IF). GD2 and B7-H3 showed consistent medium-to-high expression throughout tumour tissue, while FAP expression was restricted to tumour-associated vasculature. Multi-IF analyses revealed strong co-expression of all three antigens within tumour regions and minimal expression in normal brain tissue. Patient-derived DMG cell lines (n = 5) were uniformly positive for GD2 and B7-H3, with variable FAP expression. We generated second-generation (CD28) GD2, FAP, and third-generation (CD28/4-1BB) B7-H3 CAR-T cells. CAR expression ranged from 40–90% in single CAR-T products, with up to 20% dual-positive cells in co-transduced CAR-T populations. In cytolysis assays across five DMG cell lines, B7-H3 CAR-T cells demonstrated potent tumour killing in all lines, while GD2 CAR-T cells were effective in four. Notably, FAP CAR-T cells also showed significant efficacy and outperformed GD2 CAR-T cells in three of five lines. These findings demonstrate that GD2, B7-H3, and FAP are promising targets for paediatric DMG and support the development of multi-targeted CAR-T cell approaches. The strong tumour-specific antigen expression and potent in vitro cytotoxicity, particularly of B7-H3 and FAP CAR-T cells, highlight their potential as effective immunotherapies for paediatric brain tumours.

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

COOPERATIVE CAR T AND CAR NK CELL THERAPY FOR DURABLE TUMOUR CONTROL

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KEYWORDS: CAR T, CAR NK, Non-Hodgkin Lymphoma.

1. Microbiology and Immunology, University of Otago, Dunedin, Otago, New Zealand.

Background & Aim:

Chimeric antigen receptor (CAR) T cell therapy revolutionised the treatment of haematological malignancies, achieving complete remission rates of 50-90% in relapsed or refractory blood cancers. Despite this, relapse remains a major limitation, driven by antigen escape, T cell exhaustion, and treatment-associated toxicities such as cytokine release syndrome (CRS). This study investigates the use of Natural Killer (NK) cells in combination with CD19-directed CAR T cells to improve therapeutic efficacy and overcome antigen escape in Non-Hodgkin Lymphoma (NHL) and Acute Lymphoblastic Leukaemia (ALL).

Methods, Results & Conclusion:

Using humanised NSG mouse models, the combination of CAR T and NK cells demonstrated enhanced tumour control compared to CAR T cells alone, supporting a synergistic interaction between these cell populations (Figure 1). Notably NK cells may also target CD19-negative tumour populations that evade CAR T cell recognition; this is currently being evaluated in NSG models using RFP-positive, CD19-negative Raji cells.

In vitro analysis further demonstrated that NK cells cultured in CAR T cell-conditioned media exhibited increased expression of CD16 and TIM-3, alongside potent cytotoxicity compared to standard IL-2 stimulation (Figure 2). This suggests cytokines released by activated T cells provides a favourable environment for NK cells. Ongoing studies aim to further characterise these mediators through proteomic analysis providing mechanistic insight into the CAR T-NK synergy.

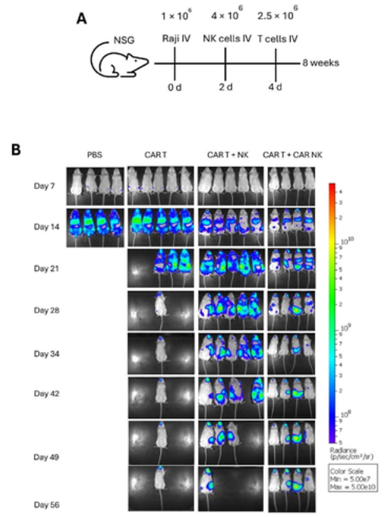

Figure 1 (Abstract 121). Representative IVIS images depicting overall Raji tumour burden in NSG mice.

(A) Schematic overview of injection timeline. (B) Weekly bioluminescence images showing systemic tumour burden in PBS, CAR T, CAR T + NK, and CAR T + CAR NK groups, measured in photons/second. Colour scale reflects total photon flux intensity.

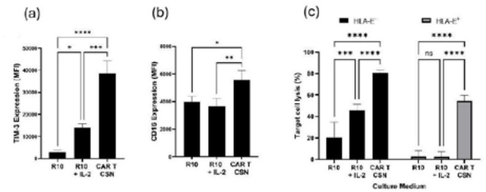

Figure 2 (Abstract 121). CAR T supernatant benefit on NK cells

(A, B) Culturing NK cells in activated CAR T cell supernatant heightened expression of TIM-3 and CD16. (C) CAR T cell supernatant-stimulated NK cells displayed improved lysis of both HLA-E- and HLA-E+ tumour cells.

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

NEXT-GENERATION CAR-T CELLS THROUGH TRANSCRIPTIONAL REPROGRAMMING

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KEYWORDS: CAR-T cells, Immunotherapy, CRISPR.

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Background & Aim:

Chimeric antigen receptor (CAR) T cell therapy has revolutionised the treatment of haematological malignancies by enabling a patient's own immune cells to recognise and eliminate cancer cells. However, translating this success to solid tumours remains a major challenge, largely due to poor CAR-T cell persistence and rapid functional exhaustion within the tumour microenvironment.

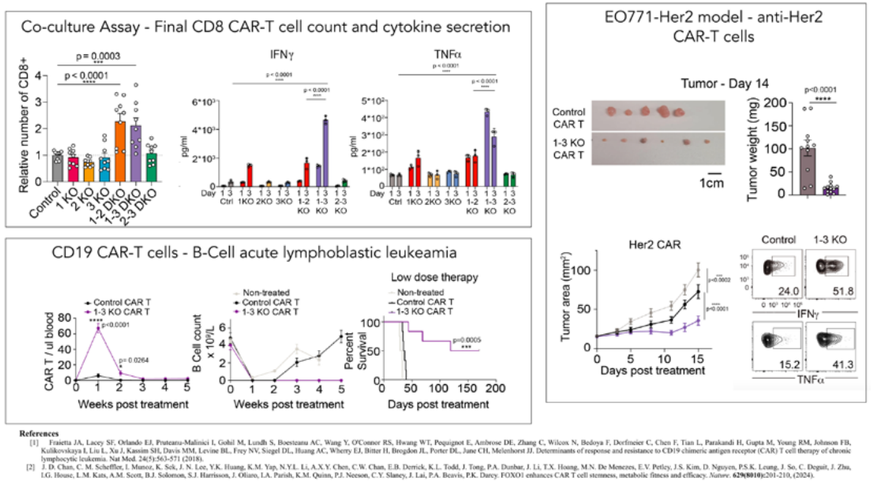
To address this, we have explored strategies to preserve a "less differentiated," stem-like state in CAR-T cells, which is associated with enhanced metabolic fitness and therapeutic durability[1]. Our recent work demonstrates that overexpression of the transcription factor FOXO1 maintains this stem-like state and significantly improves CAR-T cell persistence and anti-tumour efficacy in solid tumour models (Nature 2024[2]). This supports the idea that preserving T cell stemness through transcriptional reprogramming is key to sustaining CAR-T cell functionality in challenging tumour environments.

Building on this concept, we sought to identify novel transcriptional regulators driving CAR-T cell exhaustion. By comparing gene signatures from exhausted vs non-exhausted CD8 T cells, we identified the Ikaros family of transcription factors, as being strongly upregulated in exhausted cells. However, their specific roles in CAR-T cell exhaustion remain unclear. To further investigate their functions, we employed CRISPR to knock out 3 members of the Ikaros family in mouse/human CAR-T cells, testing each member individually and in combinations (7 combinations).

Methods, Results & Conclusion:

Using chronic tumour co-culture systems, we identified two genetic combinations that markedly enhanced CAR-T cell fitness, leading to increased proliferation, cytokine secretion, and killing capacity. Importantly, these engineered CAR-T cells demonstrated superior tumour control, prolonged cytokine production, and significantly improved survival in preclinical mouse models compared with conventional CAR-T cells, which rapidly became exhausted. Mechanistically, we found that loss of IKZF1/IKZF3 was linked to an epigenetically "promiscuous" state, with enhanced chromatin accessibility at both stemness and effector associated transcription factor motifs (under revision at Cell).

Together, our findings demonstrate that precise transcriptional programming can durably reprogram CAR-T cell fate and function, offering a robust framework to create next-generation CAR-T cells with superior persistence and enhanced efficacy against solid tumours.



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

LEVERAGING ENDOGENOUS GENE REGULATION TO ENABLE TUMOR-RESTRICTED ARMORING OF CAR T CELLS WITH ENHANCED SAFETY AND EFFICACY

K. Yap[1, 2], A. Chen[1, 2], I. House[1, 2], P. K. Darcy[1, 2], P. Beavis[1, 2]

KEYWORDS: Cancer Immunotherapy, CAR T, CRISPR/Cas9.

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2. Sir Peter MacCallum Department of Oncology, University of Melbourne, Parkville, VIC, Australia.

Background & Aim:

Chimeric antigen receptor (CAR) T cell therapy has transformed the treatment of blood cancers but remains largely ineffective against solid tumors. Armoring CAR T cells with cytokines is a promising strategy to overcome immunosuppression in solid tumors. However, this is often limited by toxicities arising from systemic cytokine expression, despite attempts to restrict cytokine production to the tumor using synthetic inducible systems. To address this, we aimed to develop a CRISPR/Cas9-mediated knock-in (KI) strategy that leverages endogenous gene regulation to enable tumor-restricted transgene expression in CAR T cells (Fig. 1; Chen & Yap et al., Nature, 2025).

Methods, Results & Conclusion:

RNA-seq was performed on CAR T cells isolated from tumors and spleens of mice. 27 genes upregulated in intratumoral relative to splenic CAR T cells were identified as potential KI sites. As KI disrupts target gene expression, the impact of knocking out each gene on CAR T cell function and phenotype was first assessed. 8 genes with no adverse impact following knockout had GFP knocked in.

NR4A2 and RGS16 emerged as optimal KI sites (Fig. 2). While the highly tumor-restricted activity of NR4A2 enabled the safe delivery of potent cytokines like IL-12, the robust intratumoral activity of RGS16 was optimal for mediating the efficacy of less potent cytokines like IL-2. However, the high peripheral transgene expression observed following KI at the RGS16 locus was unexpected, as RNA-seq detected only minimal endogenous RGS16 expression in CAR T cells isolated from the same site. This discrepancy suggested that termination of RGS16 transcription following KI likely interfered with its native regulatory control. To this end, we developed a next-generation strategy that preserves endogenous target gene transcription following transgene KI (Fig. 3). At the RGS16 locus, this strategy markedly tightened transgene activation, resulting in highly tumor-localized delivery of IL-12 and IL-2. Mechanistically, this improved control was mediated by preservation of the 3′ untranslated region (UTR), a regulatory feature that we confirmed was conserved across multiple genes, supporting 3′ UTR-mediated regulation as a broadly applicable mechanism for refining transgene control.

Together, these findings establish a versatile engineering platform for the safe and effective armoring of CAR T cells with diverse therapeutic payloads to address the multifaceted challenges of solid tumors.

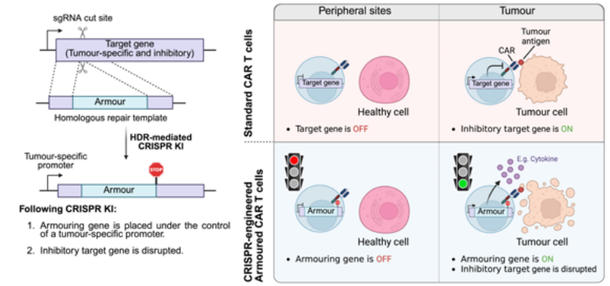

Figure 1 (Abstract 123). **CRISPR KI strategy for generating next-generation armored CAR T cells with enhanced safety and efficacy**. Targeted insertion of an armoring gene into an endogenous gene locus, which is specifically expressed by CAR T cells at the tumor site and encodes for a protein inhibitory to CAR T cell function.

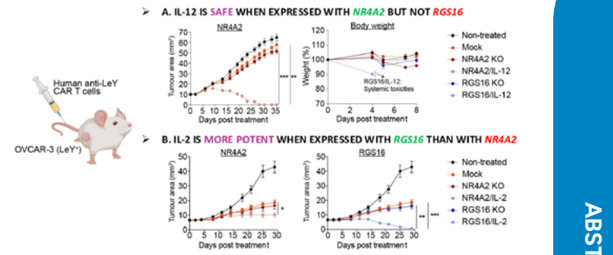

Figure 2 (Abstract 123). **Identification of NR4A2 and RGS16 as optimal tumor-specific genes for generating armored CAR T cells with tumor-restricted transgene expression**. Human anti-Lewis Y (LeY) CAR T cells CRISPR-engineered to express IL-12 or IL-2 from the NR4A2 or RGS16 locus were adoptively transferred into mice bearing subcutaneous OVCAR-3 tumors, following which tumor progression and body weight were monitored.

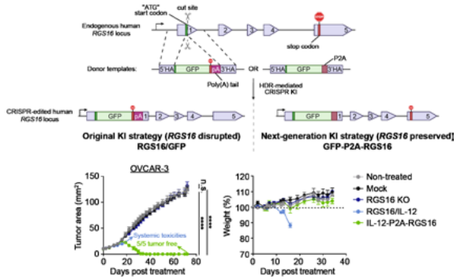

Figure 3 (Abstract 123). **A next-generation CRISPR KI strategy improves the tumor specificity of RGS16.**

Human anti-Lewis Y (LeY) CAR T cells CRISPR-engineered to express IL-12 from the RGS16 locus, where RGS16 transcription was either disrupted or preserved, were adoptively transferred into mice bearing subcutaneous OVCAR-3 tumors, following which tumor progression and body weight were monitored.

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

COMBINING CAR-T CELL THERAPY WITH SMAC-MIMETICS TO IMPROVE OUTCOMES FOR PATIENTS WITH MULTIPLE MYELOMA

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KEYWORDS: Multiple Myeloma, CAR-T cell, SMAC-mimetic.

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Background & Aim:

Multiple myeloma (MM) in an incurable cancer that develops from abnormal plasma cells in the bone marrow. Chimeric Antigen Receptor (CAR)-T cell therapy is now a standard of care immunotherapy for patients with relapsed/refractory MM. However, the majority of these patients relapse due to the lack of a durable response, highlighting the clinical challenge associated with treating relapsed/refractory MM. Accordingly, there is growing interest in combining CAR-T cells with therapeutics that boost their survival and efficacy. Our lab was the first to discover that the second mitochondria-derived activator of caspases (SMAC)-mimetic, birinapant, sensitises tumour cells to CAR-T cell killing in a murine model. Evidence suggests that SMAC-mimetics may also modulate the immune response by co-stimulating T cells, further supporting the potential these small molecule drugs can be an adjuvant to CAR-T cell therapy.

In this study we aimed to determine the effects of the SMAC-mimetic, xevinapant, on human T cells and investigate the efficacy of CAR-T cell and xevinapant combination therapy in preclinical models of multiple myeloma.

Methods, Results & Conclusion:

The effects of xevinapant on T cell survival, proliferation, and death was determined by flow cytometry and cyton modelling. The in vivo effects of combining xevinapant and CAR-T cell therapy was assessed in both xenograft and syngeneic models of anti-BCMA CAR-T cell therapy. NSG or C57BL/6 mice were engrafted with BCMA positive myeloma cells and treated with CAR-T cells and xevinapant, alone or in combination. Efficacy was assessed by monitoring tumour burden by bioluminescence imaging in NSG mice or by levels of plasma IgG2b in immunocompetent C57BL/6 mice, and flow cytometry was used to quantify and phenotype the number of CAR-T cells in xevinapant treated and untreated mice.

Our data demonstrates that xevinapant has potent costimulatory activity on naïve human T cells. Xevinapant treatment also resulted in greater CAR-T cell persistence and tumour control in preclinical NSG models of human myeloma. In the syngeneic model, combining CAR-T and xevinapant treatments also resulted in a more potent and durable anti-tumour response.

Collectively, our data demonstrates that enhancement of CAR-T cell survival, proliferation, and function by xevinapant may address the issues limiting CAR-T cell efficacy for the treatment of multiple myeloma.

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

ARMOURING GD2 CHIMERIC ANTIGEN RECEPTOR (CAR)-T CELLS WITH CHEMOKINE RECEPTORS AND INTERLEUKIN (IL)-15 TO TREAT GLIOBLASTOMA

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KEYWORDS: CAR T-cell therapy, Glioblastoma, Armouring.

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Background & Aim:

Glioblastoma multiforme (GBM) is the most common and aggressive malignant brain tumour. Several CAR T-cell therapies targeting GBM-associated antigens have been tested, but most patients did not exhibit long-lasting clinical benefit. Major challenges include inefficient T-cell infiltration and a harsh immunosuppressive microenvironment. To address these challenges, we engineered GD2 CAR-T cells co-expressing chemokine receptors that target GBM-associated chemokines and investigated the effect of IL-15 co-expression to improve CAR T-cell survival and potency.

Methods, Results & Conclusion:

Single-cell RNA sequencing and high-parameter flow cytometry were used on primary GBM specimens to identify which chemokines and chemokine receptors are upregulated in GBM. We next constructed murine GD2 CAR by murinising the corresponding human GD2 CAR, and manufactured mouse GD2 CAR-T cells from splenic T cells. CAR-T-mediated cytotoxic activity was then investigated in an orthotopic syngeneic mouse model, where CT-2A cells expressing GD2, GFP, and luciferase were administered intracranially to C57BL/6 mice, and the mice were treated with mouse GD2 CAR-T cells via tail-vein injection. To armour the GD2 CAR-T cells, we constructed a panel of bicistronic vectors in which the murine GD2 CAR is co-expressed with either the GBM-relevant murine chemokine receptors or murine IL-15.

From the patient GBM specimens, we identified that T-cell subsets expressing chemokine receptors CCR2, CCR5, CXCR3, and CXCR6 are enriched in GBM tumours relative to peripheral blood, and that other cells in the GBM microenvironment express complementary chemokines: CCL2, CCL3, CCL5, CXCL9, and CXCL16. These chemokine patterns were also observed in C57BL/6 mice with intracranially implanted GD2+ CT-2A or GD2+ GL-261 murine glioma cell lines. High transduction efficiency was observed upon manufacturing mouse GD2 CAR-T cells co-expressing the chemokine receptors or IL-15, and the co-expression did not compromise CAR-T-cell mediated cytotoxic activity in vitro. Co-expression of the GBM-relevant murine chemokine receptors showed an effect on tumour growth kinetics in vivo, and co-expression of murine IL-15 showed significant improvement in CAR T-cell persistence in vivo without any apparent systemic tissue damage.

We show successful development of mouse GD2 CAR-T cells from construct design to in vivo study. Also, constitutive IL-15 promotes CAR T-cell persistence in vivo without toxicity even in the presence of an intact immune system.

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TUMOUR-INFILTRATING LYMPHOCYTE (TIL) MANUFACTURING FEASIBILITY AND OPTIMISATION IN APPENDICEAL CANCER

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KEYWORDS: Tumour Infiltrating Lymphocyte, Appendiceal Cancer, CD4 T cells.

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Background & Aim:

Tumour-infiltrating lymphocyte (TIL) therapy is a promising approach for solid tumours; however, translating this approach to rare cancers such as appendiceal cancer has not previously been explored. This study aimed to optimise TIL manufacturing by evaluating the effects of cytokine support, co-stimulation strategies, and CD137-based enrichment on TIL phenotype and function capacity. In parallel, we also investigated the impact of tumour heterogeneity on CD8+ T cell expansion.

Methods, Results & Conclusion:

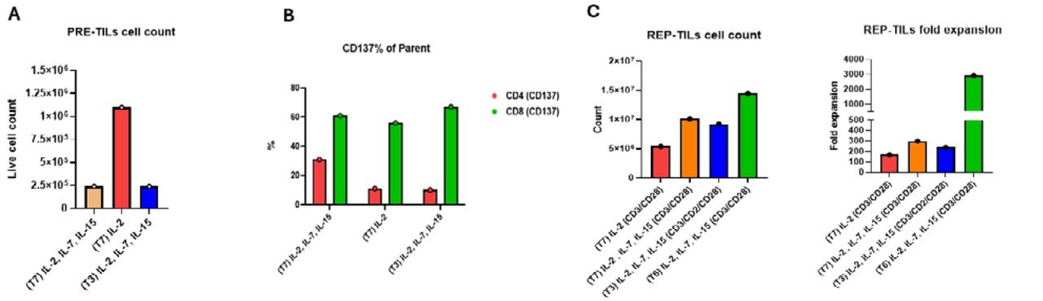
Methods:

TILs were generated from appendiceal tumour fragments from a single patient. PRE-TIL cultures were established in IL-2 alone or in combination IL-2/IL-7/IL-15. After ~14

days, CD137-based enrichment was undertaken to isolate tumour-reactive populations, and then expanded (rapid expansion phase; REP) using CD3/CD28 or CD2/CD3/CD28 mediated stimulation. Phenotypic profiling at PRE-TIL and REP stages was undertaken by flow cytometry to assess T cell subsets (CD4+, CD8+, memory), activation (CD137), and regulatory markers (FOXP3).

Results:

PRE-TIL cultures were successfully expanded (Fig 1A) from all tumour fragments with >99% viability. Culturing with IL-2/ IL-7/IL-15 improved CD8+ T cell subsets compared with IL-2 alone (Fig 1D). IL-2 alone produced the highest overall cell expansion but was associated with increased FOXP3+ Treg frequencies. T cell profiling showed a predominance of effector memory phenotypes, consistent with prior tumour antigen exposure and retained functional potential. CD137 expression was higher in CD8+ T cells (Fig 1B), supporting a tumour-reactive cytotoxic phenotype, and CD137-based enrichment enhanced expansion of these populations during REP (Fig 1C & D). Co-stimulation with CD2/CD3/CD28 did not result in substantial improvements compared with CD3/CD28. Interestingly, TILs derived from spatially separate fragments demonstrated marked variability in CD8+ T cell expansion and subset composition, indicating intra-tumour heterogeneity (Fig 1D).



D

	CD4 (% CD3)		CD8 (% CD3)	
	PRE-TILS	REP	PRE-TILS	REP
T7 (IL-2, IL-7, IL-15)	85	99	10	0.2
T6 (IL-2, IL-7, IL-15)	n/a	87	n/a	40
T3 (IL-2, IL-7, IL-15)	30	59	22	30
T7 (IL-2)	94	100	3	0.16

Figure 1. Phenotypic and expansion analysis of PRE-TILs and REP-TILs cultured with different cytokine combinations and co-stimulatory signals.
(A) Live cell counts of PRE-TILs generated from tumour tissue fragments cultured in IL-2 alone or IL-2/IL-7/IL-15 conditions. Tumour fragment cultures supplemented with IL-2 alone demonstrated greater expansion compared with IL-2/IL-7/IL-15 conditions. **(B)** Frequency of CD137⁺ cells within CD4⁺ and CD8⁺ T-cell populations in PRE-TIL cultures. CD8⁺ T cells showed consistently higher CD137 expression compared with CD4⁺ T cells across all culture conditions, indicating enhanced activation of the CD8 compartment. **(C)** REP-TILs total cell counts and fold expansion following rapid expansion protocol using different cytokine combinations and co-stimulatory molecules (CD3/CD28 or CD2/CD3/CD28). Addition of IL-7 and IL-15 together with CD3/CD28 stimulation resulted in the highest REP-TIL expansion. **(D)** Summary table showing flow cytometric analysis of CD4⁺ and CD8⁺ T-cell frequencies at PRE-TILs and REP-TILs phase under different cytokine and stimulation conditions. REP culture using IL-2/IL-7/IL-15 in combination with CD3/CD28 stimulation demonstrated the highest fold expansion and CD8⁺ T cells, suggesting enhanced expansion of activated cytotoxic tumour-reactive T-cell populations compared with CD2/CD3/CD28 stimulation.

Figure 1 (Abstract 126). **Phenotypic and expansion analysis of PRE-TILs and REP-TILs cultured with difference cytokine combinations and co-stimulatory signals.**

(A) Live cell counts of PRE-TILs generated from tumour tissue fragments cultures in IL-2 alone or IL-2/IL-7/IL-15 conditions. Tumour fragment cultures supplemented with IL-2 alone demonstrated greater expansion compared to with IL-2/IL-7/IL-15 conditions.

(B) Frequency of CD137+ cells withing CD4+ and CD8+ T-cell populations in PRE-TIL cultures. CD8+ T cells showed consistently higher CD137 expression compared with CD4+ T Cell across all culture conditions, indicated enhanced activation of the CD8+ compartment. **(C)** REP-TILs total cell counts and fold expansion follow rapid expansion protocol using different cytokine combinations and co-stimulatory molecules (CD3/CD28 or CD2/CD3/CD28). Addition of IL-7 and IL-15 together with CD3/CD28 stimulation resulted in the highest REP-TIL expansion.

(D) Summary table showing flow cytometric analysis of CD4+ and CD8+ T-cell frequencies at PRE-TILs and REP-TILs phase under different cytokine and stimulation conditions. REP culture using IL-2/IL-15 in combination with CD3/CD28 stimulation demonstrated the highest fold expansion and CD8+ T cells, suggesting enhanced expansion of activated cytotoxic tumour-reactive T-cell populations compared with CD2/CD3/CD28 stimulation.

Conclusion:

Optimisation of cytokine support and CD137 enrichment resulted in improved expansion of CD8+ T cell population. Intra-tumour heterogeneity was observed and represents a factor in manufacturing TILs. Confirmation of the results are underway in other patient tissues as well as confirming tumour killing ability of expanded TILs. These findings will further support the development of a standardised TIL manufacturing strategies for appendiceal cancer.

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

OPTIMISATION OF MULTI-TAA MANUFACTURE USING VST AS A MODEL SYSTEM

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KEYWORDS: Tumor, Immuno, T Cell.

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Background & Aim:

Multi-tumour associated antigen (multi-TAA) targeted T cells have demonstrated early clinical success most notably within Baylor college of medicine and the resultant spinoff company, Marker Therapeutics, in both haematologic and solid tumours. These therapies are safe and can be delivered as an outpatient therapeutic while also circumventing the costs associated with lentiviral vectors characteristic of CAR-T. However, optimisation of expansion regimes for multi-TAA therapeutics are challenging given the need for often extended duration of manufacture and complexity associated with initial antigen presentation and priming. As such, it is worthwhile to use more robust and technically less challenging antigen-specific systems to model multi-TAA manufacture.

Methods, Results & Conclusion:

Within the host laboratory, we have utilised viral specific T cell (VST) manufacture as a model system to optimise multi-TAA manufacture in the G-Rex™. Utilising this system we have optimised media formulations, seeding densities and feeding frequencies within the G-Rex™ that promote more efficient VST manufacture. These findings have subsequently been applied to a multi-TAA culture protocol and have shown outgrowth of a CD8+ T cell population with significant antigen reactivity within a 33-day culture window as shown below in figure one.

Further investigations will aim to assess cytokine consumption and/or degradation of key cytokines utilised in multi-TAA workflows in the G-Rex™ as well as compare the use of whole PBMC or isolated T cells as starting materials utilising a VST manufacturing run as a model system. These findings will then be used to inform best practice for multi-TAA manufacture in our cultures.

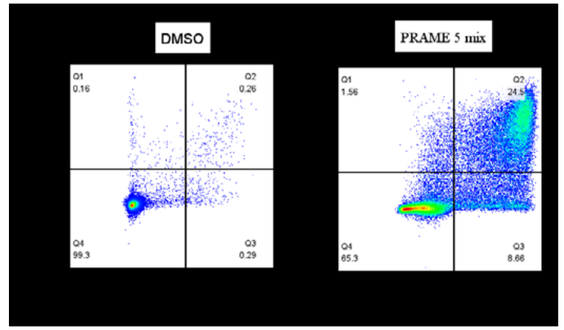

Figure 1: Intracellular cytokine staining of CD8+ T cells on day 33 of multi-TAA culture with DMSO (vehicle) restimulation shown on the left and a pepmix of five distinct HLA-A2 restricted PRAME epitopes shown on the right.

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BEYOND COMPENDIAL STERILITY TESTING: AN IMPLEMENTATION FRAMEWORK FOR RAPID MICROBIOLOGICAL RELEASE IN CAR-T MANUFACTURING

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KEYWORDS: Sterility, CAR-T, Manufacturing.

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Background & Aim:

Chimeric antigen receptor (CAR)-T cell therapies have revolutionised the treatment of haematological malignancies, yet patients with aggressive, time-sensitive disease remain vulnerable to manufacturing-

related treatment delays. Current compendial sterility testing under United States Pharmacopoeia (USP) <71> requires a 14-day culture period. This is incompatible with the clinical timelines of short shelf-life cell therapy products and exposes a structural mismatch between retrospective compendial sterility testing and clinical release timelines demanded by both decentralised and centralised CAR-T manufacturing models. Rapid sterility testing methods represent a promising means of addressing this limitation, although their translational integration remains poorly defined. This review therefore aims to evaluate rapid sterility testing technologies, identify translational barriers, and propose a framework for integration into CAR-T release workflows.

Methods, Results & Conclusion:

ATP bioluminescence, solid phase cytometry, and PCR-based assays targeting conserved 16S/18S rRNA sequences have emerged as rapid alternatives to compendial methods, delivering substantially shorter turnaround times. However, in conducting a narrative review of the literature, we identified four barriers to translation including (i) matrix-specific analytical validation, (ii) decentralised site operational readiness, (iii) cross-jurisdictional regulatory acceptability, and (iv) clinical governance for discordant or conditional release decisions. In response, we propose a structured three-phase validation framework for the conditional release of CAR-T products using rapid sterility assays. The framework progresses from analytical qualification through bridging and equivalency to conditional release implementation, with defined decision gates at each phase transition.

Rapid sterility testing represents a meaningful pathway to repositioning sterility assurance from a rate-limiting step to an enabling capability across CAR-T manufacturing models. Widespread adoption will require targeted regulatory reform and prospective multisite validation. By integrating analytical validation, operational readiness, regulatory evidence generation, and clinical risk governance, this framework provides a practical blueprint for converting rapid sterility testing from an adjunct assay to an essential component of CAR-T and broader cellular therapy release workflows.

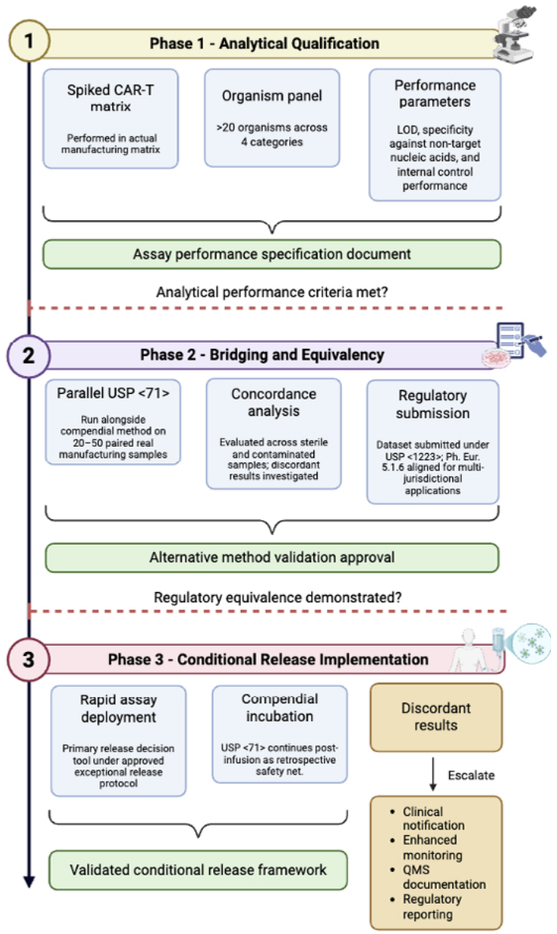

Figure 1 (Abstract 128). **Three-phase pathway for rapid microbiological release authorisation in decentralised CAR-T manufacturing**. Progression through each phase is conditional on satisfying the gate criteria indicated by dashed lines. Phase 1 establishes analytical qualification of the rapid assay in spiked CAR-T matrix using a facility-specific organism panel of >20 organisms across four microbial categories, with performance parameters including limit of detection (LOD), specificity, and internal control performance documented in an assay performance specification document. Phase 2 involves bridging and equivalency testing through parallel running of the rapid assay alongside United States Pharmacopoeia (USP) <71> on 20-50 paired real manufacturing samples, with concordance data submitted to regulatory authorities under USP <1223>, with alignment to European Pharmacopoeia (Ph. Eur.) 5.1 6 for multi-jurisdictional applications. Phase 3 implements conditional release protocol, while USP <71> incubation continues post-infusion as a retrospective safety net. Generation of discordant results including either a positive rapid assay with a negative compendial result and a negative rapid assay with a positive compendial result triggers escalation encompassing clinical notification, enhanced patient monitoring, quality management systems (QMS) documentation, and regulatory reporting.

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

PREDICTING EPITOPE-BINDING TCR FOR T CELL-BASED THERAPIES IN ACUTE MYELOID LEUKEMIA

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KEYWORDS: Epitope prediction, TCR T cell therapy.

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Background & Aim:

Patients with relapsed/refractory (R/R) acute myeloid leukemia (AML) have dismal prognosis with <20% 2-year survival. Adoptive T-cell therapy using transgenic leukemia associated antigen (LAA)-specific T-cell receptors (TCR) is a promising strategy for R/RL. However, identification of suitable TCRs requires significant labor and time investments. Cutting-edge AI models have shown promises in predicting TCR-epitope binding. We aim to develop a computational pipeline aiding in the identification of immunogenic TCR-epitope pairs for experimental validation.

Methods, Results & Conclusion:

Methods In silico X-scanning mutagenesis was applied to the published HD-1 TCR complementarity-determining region 3β (CDR3β) by substituting eachino acid with all other naturally occurring residues. ERGO-II, a deep learning-based TCR-peptide predicting model, was used to predict optimal binding between mutant HD-1 TCRs with VLDFAPPGA epitope from Wilm's Tumor 1 (WT1) protein presented by HLA-A*02:01. The protein structures of peptide-HLA-TCR (pHLA-TCR) complexes identified from ERGO-II were modelled using AlphaFold 3 and analyzed in PyMOL 3.1 to validate TCR-peptide binding strength.

Results Inclusion of HLA alleles shifted predictive scores toward higher values than using TCR sequences alone, suggesting that HLA-restricted peptide presentation contributes positively to the predicted TCR-peptide recognition (Fig 1A).ong the top 20 predicted CDR3β sequences, eight are shared in both settings, indicating consistency of top candidate prediction (Fig 1B). Comparison ofino acid residuesong shared mutant CDR3β sequences shows that positions 251, 252, and 257 exhibit the greatest variability (Fig 1C), suggesting these sites may critically influence TCR-epitope binding. This observation is further supported by the structural model of the pHLA-TCR complexes (Fig 1D), where the CDR3β chain (orange) engages in strong polar interactions with the epitope (green), notably the glycine and tyrosine at positions 251 and 252, respectively. The structure-based predictions of residues mediating polar interactions (in magenta) align with the sequence-based TCRs predicted with high variability in epitope binding.

Conclusion:

The integration of deep learning-based predictive models with protein structural data improves TCR-epitope binding prediction and offers promise for the precise development of TCR-engineered T-cell therapeutics.

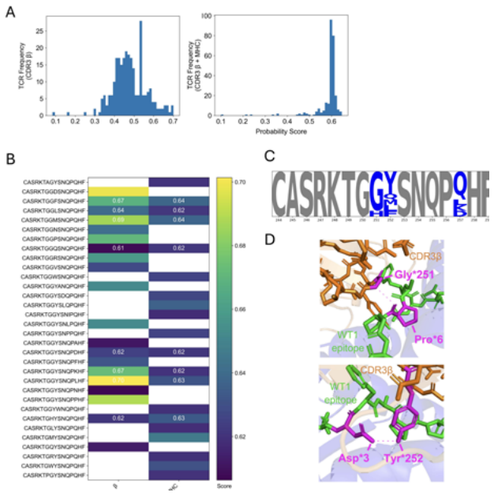

Figure 1 (Abstract 129).

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

OPTIMISATION OF GD2-IL15 CAR-T CELL PRODUCTION FOR A PHASE ONE CLINICAL TRIAL FOR GLIOBLASTOMA

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KEYWORDS: double transduction.

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Background & Aim:

Background: Chimeric antigen receptor T cell (CAR-T) therapy is a promising strategy for solid tumours, including glioblastoma (GBM) and diffuse intrinsic pontine glioma (DIPG), two highly aggressive brain tumours with poor survival outcomes. Several clinical trials on CAR-T cell therapy have been conducted for brain tumours, targeting different types of antigens, such as IL-13Rα2, EGFRvIII, HER2 and GD2. To enhance the efficacy of CAR-T cells, cytokines are designed to co-express with CAR to actively remodel tumour microenvironment, which increase the recruitment of endogenous T cells to tumour sites and facilitate better killing.

Methods, Results & Conclusion:

Methods: We conducted phase I trials, KARPOS and LEVI CATCH, at Royal Adelaide Hospital and Sydney Children's Hospital using GD2-CAR-T cells for GBM and DIPG. In parallel, we optimised a double-transduction manufacturing workflow using clinical-grade GD2-CAR and IL-15 retroviral vectors, with the goal of improving CAR-T persistence and tumour infiltration. We also evaluated a closed-system G-Rex bioreactor platform to reduce contamination risk during autologous CAR-T production.

Results: Early trial data demonstrated safety, together with evidence of in vivo CAR-T cell expansion and antitumour activity. However, GD2-CAR transgene copy number peaked in plasma and cerebrospinal fluid 7–14 days after infusion and declined thereafter. In preclinical work, GD2-CAR-T cells co-expressing IL-15 showed improved engraftment and superior tumour control in an intracranial xenograft model. In process development studies, separate CD3/CD28 activation followed by transduction with RetroNectin Pro achieved 52% transduction efficiency, and G-Rex6M culture supported more than 60-fold cell expansion.

Conclusion: These findings support further optimisation and validation of a closed, G-Rex-based manufacturing platform for GD2-IL-15 CAR-T cells before clinical application in GBM and DIPG.

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

MANIPULATING THE BRAIN TUMOUR MICROENVIRONMENT TO IMPROVE TUMOUR TARGETING

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KEYWORDS: CAR T therapy, glioblastoma, AAV.

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Background & Aim:

The development of successful new treatments for glioblastoma has been hampered for many decades due to the uniquely challenging brain microenvironment in which the influx of immune cells and release of soluble signalling molecules is tightly controlled. IL-2 is a potent T cell stimulator capable of enhancing chimeric antigen receptor (CAR) T cell therapy, but systemic administration can expand regulatory T cells and result in severe cytotoxicity. To combat these challenges an adeno-associated viral (AAV) vector based therapeutic delivery system was developed to modify the brain tumour environment to maximise T cell mediated tumour cell killing.

Methods, Results & Conclusion:

To induce the localised release of IL-2 within the IL-2-limited brain microenvironment, a GFAP promoter was added to an AAV vector to induce the release of IL-2 variants from GFAP positive glioblastoma cells and brain resident astrocytes. This vector system was administered in combination with CAR T cells in an intracranial tumour mouse model. Immune and toxicity profiles of wild-type vs engineered IL-2 were characterised. The combination of CAR T cells with "mutein" beta-gamma receptor targeted IL-2 resulted in tumour clearance and prolonged survival. These changes were accompanied by increased T cells and NK cells within the brain microenvironment.

Ultimately, we demonstrate that cell therapies can benefit from cell and gene therapy combinations to enable brain tumour microenvironments to facilitate tumour control. Cell and gene therapy combinations may enable precise manipulation of other tumour microenvironments to benefit T cell therapies and enable tumour destruction.

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

UNDERSTANDING HOW MYELOID CELLS LIMIT CAR-T CELL THERAPY IN BRAIN CANCER

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KEYWORDS: CAR-T, Cancer, Myeloid .

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Background & Aim:

Glioblastoma (GBM) and diffuse midline glioma (DMG) are aggressive brain cancers with limited treatment options and poor survival outcomes. While chimeric antigen receptor (CAR)-T cell therapy has shown success in blood cancers, its efficacy in brain cancers remains limited. The abundance of myeloid cells may play a key role in creating a suppressive environment that limits CAR-T cell persistence and activity. Here, we aim to define how myeloid populations influence CAR-T cell therapy and identify strategies to overcome myeloid-driven immune suppression.

Methods, Results & Conclusion:

To investigate this, blood and cerebrospinal fluid (CSF) from DMG patients treated with GD2 CAR-T cell therapy were analysed using Olink platforms, while peripheral blood mononuclear cells (PBMCs) were profiled using Parse Evercode Whole Transcriptome assay. To model cellular interactions in vitro, PBMCs from healthy donors and GBM patients were cultured and exposed to patient-derived GBM tumour cells to promote differentiation into tumour-associated myeloid states. These in vitro generated myeloid cells were compared with patient-derived peripheral blood and tumour myeloid populations and assessed for suppressive function.

Preliminary analysis from three patients suggests a role for myeloid cells in limiting CAR-T cell persistence. In a non-responder, CAR T cells showed limited expansion in both peripheral blood and CSF, accompanied by increased levels of myeloid derived suppressor cells (MDSCs) identified by single cell RNA sequencing (scRNA-seq) and flow cytometry compared with responders. Further, CSF proteomic analysis further revealed increased signature of myeloid associated activation alongside signature of T cell activity, suggesting a myeloid response following CAR-T cell infusion in all patients. Lastly, tumour cells derived from different GBM patients promoted distinct myeloid states and induced varying levels of myeloid mediated suppression.

Future work will define how myeloid cells regulate CAR-T cell activity in brain cancers and identify pathways that mediate immune suppression. Targeting these interactions may restore CAR T cell function and inform next generation immunotherapeutic strategies for brain cancers.

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iPSC

TEN YEARS IN THE MAKING: AUSTRALIA'S FIRST GMP-COMPLIANT CORD BLOOD-DERIVED IPSC MASTER CELL BANK FOR TRANSLATIONAL AND CLINICAL RESEARCH

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KEYWORDS: GMP , cord blood, Master Cell Bank.

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1. Abberton et al, 2022 https://academic.oup.com/stcltm/article/11/10/1052/6693980

2. Tian et al., 2022 https://www.frontiersin.org/articles/10.3389/fcell.2022.835321/full

Background & Aim:

The Cord Blood Advanced Therapies Research Laboratory (MCRI, Melbourne) has established Australia's first GMP-compliant induced pluripotent stem cell (iPSC) lines derived from banked cord blood. These lines are now available for research and have potential for future immuno- and regenerative therapies.

Methods, Results & Conclusion:

The BMDI Cord Blood Bank operates under a Therapeutic Goods Administration (TGA) GMP licence and is FACT-accredited. Cord blood units with homozygous HLA haplotypes were identified, and donors re-consented for iPSC generation1. A dedicated PC2-GMP facility was established, alongside a quality framework aligned with existing cord blood bank systems to support compliant iPSC manufacture.

A cord blood unit carrying a common Australian haplotype (A_01:01, B_08:01, C_07:01, DRB1_03:01), with potential to match ~10% of the Victorian population, was selected for reprogramming using the CTS™ CytoTune™-iPS 2.1 Sendai reprogramming kit. The protocol for creation of the iPSC lines has been described2, with upscaling of reagents to fully certified CTS™ GMP-grade reagents. Two clonal iPSC lines met predefined release criteria, enabling generation of Master Cell Banks.

Comprehensive quality testing, in line with international standards, confirmed identity, genomic integrity, pluripotency, sterility, mycoplasma negativity, and clearance of reprogramming vectors. Functional differentiation into retinal, neural, mesenchymal stromal, haematopoietic stem, and natural killer cell lineages has been demonstrated by collaborators. One line (MCRICBi002-B) has been registered and validated in hPSCreg. A Working Cell Bank is available for research or potential clinical application under material transfer agreements, supported by an in-house Certificate of Analysis.

This program demonstrates the feasibility of implementing GMP-compliant iPSC manufacturing in collaboration with a public cord blood bank, leveraging established infrastructure, governance, and donor frameworks to enable scalable and translational cell therapy development

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Mesenchymal Stem/Stromal Cells

TRANSCRIPTOMIC PROFILING OF PELVIC ORGAN PROLAPSE: DELINEATING DISEASE PATHOGENESIS TO INFORM CELL-BASED THERAPEUTIC POTENCY CHARACTERISATION

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KEYWORDS: Birth injuries, MSCs, Pelvic Organ Prolapse.

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Background & Aim:

Pelvic organ prolapse (POP) is a prevalent condition originating from childbirth-related injuries to pelvic floor. Mesenchymal stromal cells (MSCs) and their extracellular vesicles (EVs) have shown preclinical promise in repairing childbirth-related tissue injury; however, clinical translation requires demonstrating potency, operationally defined as quantifiable biological activity mechanistically linked to the intended clinical effect. This necessitates a prospective definition of the pathway targets that the cell product is expected to engage within the disease microenvironment. POP-specific mechanistic substrate remains undefined, representing a critical gap between preclinical promise and regulatory-grade translational readiness. This study compared the transcriptomic profiles of healthy and POP vaginal tissue

Methods, Results & Conclusion:

Methods

This HREC-approved study was conducted with full informed consent. RNA sequencing was performed on anterior vaginal wall samples from 6 POP patients (stage ≥II) and one healthy control. Differential expression was analysed using DESeq2, GO enrichment, KEGG analysis, pre-ranked GSEA, STRING PPI networks, and CytoHubba hub gene prioritisation.

Results

GSEA identified 12 significant Hallmark and 13 KEGG pathways (FDR<0.05). Most upregulated pathways included E2F Targets (NES=1.85), G2M Checkpoint (NES=1.84), p53 Pathway (NES=1.62), Arachidonic Acid Metabolism (NES=1.78), and Estrogen Response Early/Late. Glycosaminoglycan/Chondroitin Sulfate Biosynthesis (NES=−2.15) and Angiogenesis (NES=−2.14) were most significantly downregulated, indicating ECM scaffold loss and impaired vascularisation. MCL clustering identified a dominant hub module of 121 cell cycle genes, implicating CDK1, CDK2, TOP2A, and TP53 as central nodes.

Conclusions

This analysis delineates four converging pathogenic mechanisms in POP: aberrant CDK-mediated cell cycle activation and p53-driven fibroblast senescence; dysregulated estrogen/steroid signalling; prostaglandin-driven chronic inflammation; and glycosaminoglycan ECM scaffold loss with impaired angiogenesis. MSC-EVs carry miRNA cargo capable of addressing each axis: suppressing aberrant cell cycle progression, restoring ECM biosynthesis, promoting angiogenesis, and modulating estrogen-responsive programmes, providing a molecular rationale for mechanism-anchored potency assay design and MSC-EV therapy in POP, with five priority therapeutic axes identified for experimental validation.

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Mesenchymal Stem/Stromal Cells

COMPARATIVE PROTEOMIC PROFILING OF CELL LYSATE AND SECRETOME FROM WHARTON'S JELLY-DERIVED MESENCHYMAL STEM CELLS REVEALS DISTINCT COMPARTMENT SPECIFIC PROTEIN SIGNATURES

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KEYWORDS: Mesenchymal Stem cell, Proteomics, Secretome.

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Background & Aim:

Wharton's jelly-derived mesenchymal stem cells (WJ-MSCs) are widely explored for regenerative and immunomodulatory properties, with growing evidence that therapeutic effects are primarily mediated through paracrine mechanisms. Both cell-intrinsic properties and secreted factors contribute to these effects, but protein-level basis of these two compartments remains poorly characterised. A simultaneous comparison of the intracellular proteome (cell lysate) and extracellular proteome (secretome) from the same WJ-MSC population is lacking, limiting mechanistic understanding of their distinct therapeutic potential.

Methods, Results & Conclusion:

Methods: WJ-MSCs were isolated from human umbilical cords (n=3 donors, passage 5) by explant method and characterised per ISCT criteria. Cells at 80–90% confluence were washed with DPBS and incubated in serum-free DMEM-LG for 48 hours. Conditioned medium was centrifuged and 0.2-µm filtered, while cell pellets were lysed using RIPA buffer. Both fractions underwent in-solution trypsin digestion and LFQ LC-MS/MS on an Orbitrap Exploris (EASY-nLC 1000). Data were processed in Proteome Discoverer v2.5 (SequestHT/Amanda; UniProt Human proteome; 1% FDR), followed by GO, KEGG, and PPI network analysis.

Results: Label-Free LC-MS/MS identified ~2,700 proteins in the lysate and ~4,100 in the secretome (≥2 unique peptides). The lysate was enriched in structural, metabolic, and stress-response proteins: MYH9, FLNA, ACTB, VIM, HSPA5, GAPDH, PKM, ENO1 reflecting cytoskeletal organisation, glycolytic metabolism, and proteostasis. The secretome was characterised by ECM and paracrine signalling proteins: FN1, COL1A2, COL3A1, COL6A1/2/3, THBS1, TGFBI, SERPINE1, LGALS1. Also, ANXA1, ANXA2, and ANXA5 were prominent in the secretome, representing a constitutive, priming-independent anti-inflammatory signature. GO/KEGG enrichment confirmed protein folding and metabolic homeostasis in the lysate, and ECM organisation, cell adhesion, complement/coagulation, and immune regulation in the secretome.

Conclusion: WJ-MSC lysate and secretome have distinct yet complementary protein profiles supporting both cell-based and cell-free therapeutic approaches.

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Process Development & Manufacturing and Commercialization

VALIDATION OF ENDOTOXIN TESTING FOR RELEASE OF VIRAL SPECIFIC T CELL PRODUCTS USING THE ENDOSAFE PTS

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KEYWORDS: Endotoxin, Quality Control testing, Cell therapies.

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Background & Aim:

Adoptive immunotherapy using virus-specific T-cells (VST) have emerged as a promising treatment for viral infections in the hematopoietic stem cell transplant setting. The manufacture of clinical-grade VST cell therapies encompasses multiple complex processes that are tightly regulated under the code of good manufacturing practice (cGMP) to ensure high-quality and safe products. Westmead T Cell Therapies (WTCT) manufacture autologous and banked VSTs (produced from third-party donors).

WTCT Endotoxin testing validation strategy was developed in alignment with regulatory guidelines as part of compliance for a Therapeutic Goods Administration (TGA) manufacturing licence application by the Australian government authority.

Endotoxins are lipo-polysaccharides from gram-negative bacteria and are the most common cause of life-threatening toxic reactions in patients therefore, it is important that therapeutics infused are tested for their endotoxin content. The limulusoebocyte lysate (LAL) test is the most sensitive and specific means to detect and measure bacterial endotoxins.

The Endosafe- Portable Testing System (PTS) is a rapid, point-of use handheld spectrophotometer. The unit utilises USP/EP compliant FDA-licensed disposable cartridges, containing LAL and a chromogenic substrate for real-time BET to form part of the manufacturing quality control test methodologies.

Aim: To verify the Endosafe- PTS performance for BET in compliance with the EP 2.6.14 and USP<85> and establish a test method, i.e. dilution, for BET of VST cell products manufactured by WTCT, for product release.

Methods, Results & Conclusion:

Methods: VSTs were manufactured from three healthy donors with pilot vials cryopreserved for post thaw analysis on the Endosafe- PTS. The validation was performed in three stages.

Firstly, the endotoxin limit, maximum valid dilution were calculated, and dilutions identified for assessment.

Second, method suitability screening for product formulation/matrix interference (i.e. inhibition/ enhancement (I/E)) using I/E LAL cartridges, to determine a defined dilution range to perform BET.

Finally, the accuracy and precision of product FDA-licensed LAL cartridges (5-0.005 EU/mL sensitivity) were assessed by recovery of known endotoxin test samples and triplicate sample testing performance by two different operators over two separate days. In addition, verification of the BET was performed with the VST products, using the dilution factor selected in the screening assay.

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Process Development & Manufacturing and Commercialization

DEVELOPMENT OF A QUALITY TARGET PRODUCT PROFILE (QTPP) FOR CLINICAL TUMOUR INFILTRATING LYMPHOCYTE (TIL) THERAPY FOR MELANOMA

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KEYWORDS: TIL, QTPP, Validation.

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1. Published indicators of TIL clinical response and safety,

2. Regulatory requirements for autologous T-cell ATMPs from TGA, FDA, and EMA; and

3. Measurable process capabilities at CTTWA.

Background & Aim:

We previously reported the successful validation of the manufacture of Tumour Infiltrating Lymphocyte (TIL) therapy for melanoma. All primary objectives were achieved, with exceptional cell expansion results exceeding literature benchmarks. That validation identified key improvements to manufacturing processes, including optimisation of Rotea wash protocols used to prepare PBMC feeder cells and the Rapid Expansion Protocol (REP-TIL) Drug Product, and enabled the development of a Quality Target Product Profile (QTPP) incorporating Critical Quality Attributes (CQAs) for the final product.

Although QTPPs form the foundation for ICH Q8-aligned ATMP development, there is a lack of prospectively defined TIL QTPPs in the literature; instead, existing frameworks must be inferred. This work establishes the formally defined QTPP and employs it to guide a second consecutive validation of the enhanced manufacturing process.

Methods, Results & Conclusion:

Methods

CQAs were identified through a systematic, mechanism-based mapping process. Each candidate attribute was evaluated against:

1. Published indicators of TIL clinical response and safety,

2. Regulatory requirements for autologous T-cell ATMPs from TGA, FDA, and EMA; and

3. Measurable process capabilities at CTTWA.

These were then risk-ranked according to ICH Q9 to determine inclusion in the QTPP (see Table 1). Additionally, modifications were applied to existing protocols using G-Rex devices, as previously described. Rotea wash protocols of the final products were revised, and new format consumable kits were validated. Preliminary product stability data was generated.

Results

All primary objectives were achieved. Three additional consecutive REP-TIL Drug Products passed all currently applicable QTPP acceptance criteria, with excellent cell expansion results that surpassed published benchmarks. Understanding of process parameters governing REP culture expansion was enhanced.

Conclusions

We have our first prospectively defined QTPP for clinical TIL therapy, filling a gap in the literature where QTPPs had previously been inferred (Lievense et al., 2025). Next, we plan to publish the QTPP along with the derivation, so it can serve as a helpful reference for other groups to follow. We'll also work on harmonising standards through engagements with manufacturing facilities at the Australian Collaborative Centre Program for Advanced Therapies (CCPAT) and the regulator.

Table 1 (Abstract 137): TIL Drug Product Quality Target Product Profile (QTPP)

QTPP Element	Sub-element	Test & Method	Criteria from Literature	Acceptance Criteria Set
Identity	Cell Phenotype	CD45+CD3+% (Flow)	Detected or ≥90%	CD45+CD3+% ≥90%
	Viability	Viable CD3+ cells % (Flow)	≥70%	≥70% viable CD3+
Purity	Non-T Immune cells	CD19+ B cell % (Flow)	Not Described	CD45+CD3- ≤2%
	Other cells	Residual cells with tumour markers (Flow)	Not Detected	Not Detected; MCSP Assay TBC
	Irradiated Feeder cells	In-Process Control checks	Not Described	No increase in feeder cell viability or number
	Mycoplasma	Mycoplasma (PCR)	Not Detected	Not Detected
	Endotoxin	Endotoxin (Pyrogent LAL)	≤1.17 EU/ml	≤1.17 EU/ml
	Microbial contamination	BacTEC	Negative	Negative
Quantity	Viable T-cell count	Viable CD3+ cells count (Flow)	1x10^9 ≤ n ≤150x10^9	≥1.0x10^9 live CD3+
Potency	T-cell reactivity	IFNγ release assay (Flow)	≥200pg IFNγ/ml	Flow: CD3+ IFNγ+% ≥48%; CD3+ CD8+ IFNγ+% ≥60%; Secretion assay TBC to complement flow
Stability	Maintain CQAs within specification limits for storage duration and conditions			
Dosage form, container, route of administration	Cells suspended in infusion formulation in sterile bag suitable for dropwise intravenous administration			

ABSTRACTS

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Process Development & Manufacturing and Commercialization

AN EAST-TO-WEST BUSINESS MODEL FOR COMMERCIALISING SOLID TUMOUR CAR-T THERAPIES: LEVERAGING CROSS-BORDER PARTNERSHIPS, ADVANCED MANUFACTURING AND CAPITAL-EFFICIENT DEVELOPMENT

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KEYWORDS: CAR-T, Asia, Cancer.

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Background & Aim:

Despite rapid innovation in cellular immunotherapy across Asia, many promising cell therapies remain inaccessible to Western markets due to regulatory, manufacturing and commercialisation barriers. Autologous CAR-T therapies for solid tumours also face scalability challenges including manufacturing complexity, high cost and limited portability between sites. AdAlta Ltd has developed an "East-to-West" commercialisation model combining Asian innovation with Australia's manufacturing, translational and regulatory ecosystem. The business model, partnering strategy and enabling manufacturing collaborations supporting scalable global development are described.

Methods, Results & Conclusion:

The AdAlta model in-licenses clinically validated cellular immunotherapy assets from Asia, conducting manufacturing transfer and US FDA-aligned Phase I development in Australia, and subsequent out-licensing to larger biopharmaceutical partners for registrational studies and commercialisation. The model aims to create substantial value inflection using a capital-efficient structure and Australia's quality manufacturing and clinical ecosystem.

To support scalable, commercially viable manufacturing, AdAlta established collaborations with Ori Biotech and Cell Therapies Pty Ltd. These partnerships aim to deploy Ori's IRO® automated manufacturing platform within Australia and Asia-Pacific to improve throughput, reduce variability, accelerate technology transfer and lower CAR-T production costs. This demonstrates how partnerships between originators, technology providers, CDMOs and translational developers can de-risk development and improve partnerability of cell therapy assets.

AdAlta's collaboration with Shanghai Cell Therapy Group ("SHcell") is an exemplar of the model. BZDS1901 is a mesothelin-targeted, anti-PD1-armoured CAR-T therapy for mesothelioma and other solid tumours. Investigator-initiated studies in China demonstrated encouraging activity, including multiple tumour responses and two difficult to achieve complete tumour clearances in advanced mesothelioma patients, supporting progression toward Western regulatory development. SHcell continues China-based development while AdAlta leads manufacturing transfer, US FDA engagement and global Phase I development outside greater China.

This model demonstrates a scalable pathway for globalising innovative Asian cellular immunotherapies while strengthening advanced manufacturing capability within Australia and the Asia-Pacific region.

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Process Development & Manufacturing and Commercialization

ALBUMEX20 TO ALBUREX20: SIMPLE SUBSTITUTION OR MULTI-LAYERED MASTERPIECE?

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KEYWORDS: Material, Substitution.

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Background & Aim:

Human serum albumin (HSA) is a critical material in cell therapy manufacturing, supporting cellular stability, maintaining product quality and is a key component in final product formulation. Within our GMP manufacturing process for virus-specific T cells (VST), HSA in the form of Albumex20 (CSL Behring) was routinely used for buffer supplementation, cell processing, and final product formulation. Following discontinuation of Albumex20 in 2023, CSL Behring introduced Alburex20 as a replacement. Although both are ARTG-listed 20% human albumin solutions, differences in excipient and stabiliser composition required formal evaluation prior to substitution.

Methods, Results & Conclusion:

A risk assessment was undertaken to evaluate potential impacts of the Albumex20 to Alburex20 substitution on manufacturing, quality control testing, validation and quality systems. The assessment informed development of a change control strategy. Key considerations included document revision, revalidation of microbial bioburden, mycoplasma and endotoxin assays, potential effects on product stability and the requirement for process verification to assess impact on critical process parameters.

Manufacturing runs for process verification were performed using whole blood starting material from three independent donors. For each donor, equivalent process arms were established, with one arm using Albumex20 and the second arm using Alburex20, while all other manufacturing parameters remained unchanged. This design assessed the impact of the HSA product substitution on the reproducibility of process performance and product quality. Increased monitoring of cell yield and viability at each HSA exposure point, including washes, cell selection, and product formulation, generated ten analytical timepoints across the 12-day manufacturing process. Final VST cell products underwent standard product release testing, including cell enumeration, viability assessment, immunophenotypic characterisation and CD107 expression functional assays. No adverse impacts attributable to substitution of Albumex20 for Alburex20 were observed at any in-process or final product testing point. Long-term stability assessment activities are ongoing.

Replacing Albumex20 with Alburex20 had no impact on the quality of the VST products. This work demonstrates the importance of a risk-based approach when verifying and implementing changes in critical material in GMP manufacturing to maintain process control and product quality.

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Process Development & Manufacturing and Commercialization

NOVEL 3D CULTURE STRATEGY OF STEM CELL USING ALGINATE HYRDROGEL ENCAPSULATION TECHNOLOGY.

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KEYWORDS: Alginate Hydrogel, Encapsulation, Expansion Culture.

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Background & Aim:

Stem cells offer a strong capability that can be differentiated to multiple cell types with determined protocol by preferred therapeutic targets. Nevertheless, the scalability of MSC and iPSC manufacturing presents unique challenges in terms of labor-intensive handling when it comes with conventional culture. In this poster, we demonstrate how the "CellFiber", a novel cell encapsulation technology can be integrated as a 3D, closed and scalable expansion platform for stem cell.

Methods, Results & Conclusion:

Human MSCs were recovered from cryopreservation and pre-cultured for 4 days in T75 flasks. The collected MSCs are encapsulated in the tubular alginate hydrogel for 2-step fiber culture, followed by harvesting the expanded cells by dissolving hydrogel. A final yield of 1.10 x 109 cells (70.5-fold increase), maintaining 97.5% viability. Flow cytometry confirmed high expression (>99.7%) of CD73 and CD105. In a theoretical cost assumption, utilizing CellFiber technology can save up to 70% manufacturing cost at the expected batch yield of 1.0 x1010 cells.

Cryopreserved iPSCs were thawed and cultured under adherent conditions, followed by being encapsulated and cultured for 7 days of fiber culture. The culture at 1L-scale yielded 1.11 × 1010 iPSCs. The overall expansion fold during the culture period was 55.5-fold, and cell viability at harvest reached 97.4%. Key pluripotency markers, including OCT3/4, NANOG, SSEA-4, and TRA-1-60, remain highly expressed after expansion. This indicates that the cells maintain an undifferentiated state. By maintaining a stable and high viable cell density in production scale, suggesting it is potential to achieve a high yield within a manageable culture scale.

Both of the above platform are developed with automated, closed rocking motion cell bag bioreactor (XuriTM W25, Cytiva) and harvest systems, which strongly imply the potential of CellFiber encapsulation technology being utilize in a regulation complied and efficient cell therapy manufacturing processes.

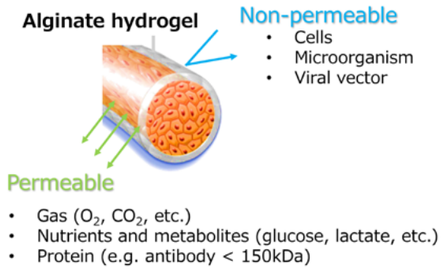

Figure 1 (Abstract 140). Alginate Hydrogel of CellFiber technology

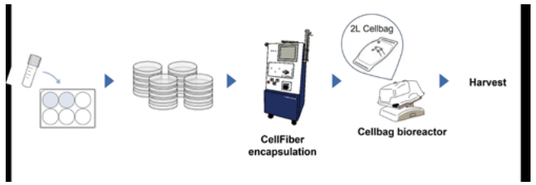

Figure 2 (Abstract 140). Workflow of CellFiber integrated Stem Cell manufacturing process

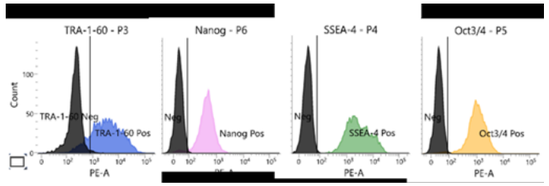

Figure 3 (Abstract 140). Pluripotency marker expression of expanded iPSC harvested from fiber culture

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Regulatory Affairs, Quality Systems, Policy

USE OF THE MIRCA TOOL TO GUIDE IMPROVEMENTS IN MICROBIAL CONTAMINATION RATES AT NEW ZEALAND BLOOD SERVICE

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KEYWORDS: Microbial contamination, haematopoietic stem cell, risk management.

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Background & Aim:

Assessment of microbiological contamination risk is critical when haematopoietic stem cell processing requires an open manipulation or when a closed system is breached, introducing potential routes for contamination. The European Directorate for the Quality of Medicines and Healthcare (EDQM) has developed the Microbiological Risk of Contamination Assessment (MiRCA) tool, an online open resource designed to support organisations in systematically evaluating microbiological risks within laboratory processes.

Methods, Results & Conclusion:

Method

New Zealand Blood Service (NZBS) applied 5 years of sterility results for cryopreserved haematopoietic stem cells, apheresis (HPC-A) (n=2360), collected and stored through New Zealand to the MiRCA tool, to determine our greatest areas of risk with procurement and processing. These parameters were evaluated to determine their contribution to overall microbiological risk.

As per the below Figure 1, overall risk was determined as 'possible' with a score of 91/695. This was determined by answering a series of questions about the processing methods employed at NZBS, including contamination strategies, single use items, cleaning regimes and personnel factors.

The MiRCA too extrapolates upon the specific areas of risk, and Equipment was determined as our area of contributing the largest area of risk, with a score of 9 of a possible 15. However, this was from a single question and in our opinion does not capture the full risk profile. This structured approach enabled NZBS to identify high-risk process steps and from the positive products (n=43), each associated incident was evaluated for the potential source of contamination.

Discussion

The MiRCA tool is data driven but this more qualitative and results are largely driven by the quality of the data available. Further, in our opinion, conclusions are drawn by the tool about the robustness of cleaning and personnel requirements (such as the quality of aseptic process simulations) which may skew results in a positive light. Finally, the tool is also theoretical, assuming that all processes and steps are completed perfectly each time. We felt a review of Standard Operating Procedures and audit of processes should be performed in parallel for any areas of risk identified. Nevertheless, the tool provides an alternative to a risk assessment for a quick analysis of potential microbial contamination issues.

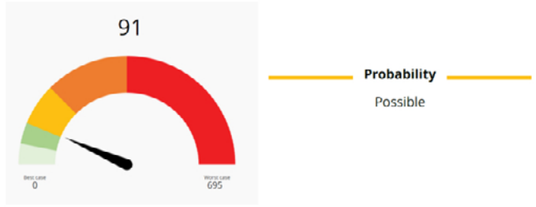

Figure 1 (Abstract 141). Illustrates overall risk as "possible" using the MiCRA tool.

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Tissue Engineering

BIOENGINEERED PLCL-MSC VAGINAL IMPLANTS PROMOTE TISSUE REGENERATION IN AN OVINE MODEL OF PELVIC ORGAN PROLAPSE

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KEYWORDS: Pelvic Organ Prolapse, Mesenchymal Stem Cells, Electrospun Nanofibres.

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Background & Aim:

Pelvic Organ Prolapse (POP) remains a common condition with limited safe and effective long-term surgical treatment options. Previously used polypropylene meshes have been widely restricted due to complications including mesh erosion, exposure, prolonged inflammation, and undesirable foreign body response (FBR). Therefore, regenerative approaches that promote tissue repair without triggering deleterious FBR are needed. Electrospun nanofibrous scaffolds provide a biomimetic architecture that supports cell–cell and cell–biomaterial interactions, while Mesenchymal Stem Cells (MSCs) may further enhance tissue regeneration through immunomodulatory and pro-angiogenic effects. This study investigated the efficacy of bioengineered vaginal implants used alone or combined with xenogeneic human endometrial mesenchymal stem/stromal cells (eMSCs) in an ovine model of vaginal surgery.

Methods, Results & Conclusion:

eMSCs isolated from human endometrial tissue were seeded onto electrospun poly-L-lactide-co-□-caprolactone (PLCL) nanofibres and implanted into multiparous sheep with vaginal weakness across three groups: native tissue repair (NTR), PLCL only, and PLCL + eMSC implants. Tissues collected at 30 and 90 days post-implantation were assessed using histology, immunohistochemistry, and quantitative PCR to evaluate foreign body response (FBR), tissue integration, angiogenesis, extracellular matrix (ECM) formation, and inflammatory gene expression.

Both PLCL-only and PLCL + eMSC implants showed excellent tissue integration, with only one implant exposure observed. Smooth muscle and collagen content significantly increased in both implant groups compared with non-operative controls. At 30 days, the PLCL + eMSC group showed increased expression of inflammatory markers (Nos2, Icam1, Ccl5, and Vcam1) together with upregulation of angiogenesis- and ECM-related genes (Cxcl12, Pecam1, Vegfr, Col1a1, and Col3a1) compared with PLCL-only and NTR groups.

PLCL vaginal implants, particularly when combined with eMSCs, promoted favourable tissue integration and regenerative responses in an ovine vaginal repair model. Although transient inflammatory upregulation was observed, this was accompanied by increased angiogenic and ECM-remodelling activity, suggesting a regenerative rather than chronic inflammatory response. These findings support the potential of PLCL + eMSC implants as a promising tissue-engineered strategy for pelvic floor reconstruction and POP treatment.

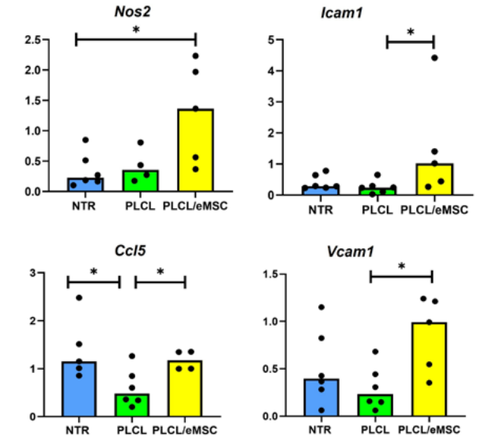

Figure 1 (Abstract 142). Inflammatory gene expression 30 days after implantation of PLCL and PLCL+eMSC. Fold change in total RNA expression of ovine inflammatory genes by quantitative PCR in explanted vaginal tissues consisting of PLCL and PLCL mesh, with and without

endometrial mesenchymal stem/stromal cells (eMSCs) after 30 days. Data are median of n=5-7 samples/group analyzed by Mann-Whitney t test

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Tissue Engineering

A HUMAN IPSC-DERIVED MODEL FOR STUDYING CELL-STATE-SPECIFIC RESPONSES TO MECHANICAL AND HYPOXIC REGULATION OF HEMOGENIC ENDOTHELIAL DEVELOPMENT

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KEYWORDS: iPSC derived microfluidic model, Haemogenic Endothelium , Shear stress–hypoxia interaction.

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4. School of Biomedical Science, Medicine & Health, University of New South Wales, Randwick, NSW, Australia.

Background & Aim:

Blood stem and progenitor cell formation during human development depends on coordinated biomechanical and microenvironmental signalling within the embryonic aortic niche. While inflammatory pathways are required for hemogenic endothelial specification, the upstream microenvironmental cues that regulate these processes in the absence of infection remain incompletely defined. Biomechanical forces generated by embryonic blood flow, together with low-oxygen conditions, are key candidate regulators.

Methods, Results & Conclusion:

Here, we developed a human induced pluripotent stem cell (iPSC)-derived co-culture system consisting of cardiomyocytes and aortic niche populations, maintained in interconnected microfluidic chambers with controlled flow (Fig. 1A,B). From day 9 of differentiation, cells were exposed to eight defined conditions in a balanced factorial design incorporating shear stress and hypoxia (Fig. 1C). Single-cell RNA sequencing was performed across all conditions, profiling ~10,000 cells per condition at an average depth of 20,000–35,000 UMIs per cell. Transcriptomic responses were analysed using clustering, population composition, and differential expression modelling to define condition-specific effects across populations (Fig. 1D).

Shear stress preserves arterial and hemogenic-associated endothelial states under hypoxia (Fig. 2A–E). Endothelial cells form a continuous transcriptional landscape, with hemogenic programs enriched within a defined region rather than a distinct cluster (Fig. 2B). Shear increases expression of flow-responsive pathways, including mechanotransduction and KLF-associated programs, and reduces hypoxia-associated metabolic and stress pathways (Fig. 2D). In contrast, hypoxia without shear increases inflammatory and metabolic stress pathways and reduces hemogenic-associated states (Fig. 2D–E). Responses vary across endothelial subtypes, with distinct populations showing differential sensitivity to combined shear and hypoxia (Fig. 2E).

Together, these results show that shear and hypoxia exert opposing effects on endothelial transcriptional programs, supporting a model in which mechanical cues partially counteract hypoxia-induced stress to maintain hemogenic-associated states. These findings provide a framework for understanding microenvironmental regulation of hemogenic fate and highlight engineered systems for disease modelling and cell therapy.

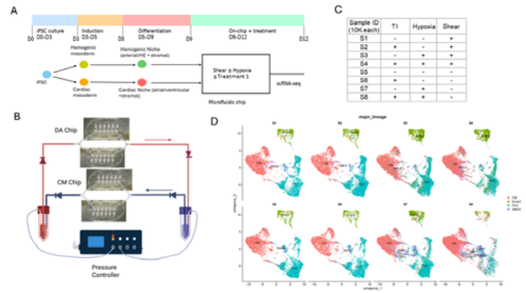

Figure 1 (Abstract 143). Experimental platform and single-cell landscape of iPSC-derived cardiovascular co-culture system. (A) Directed differentiation of iPSCs into cardiac and hemogenic mesoderm lineages, giving rise to cardiomyocyte-containing cardiac niches and aortic niche populations. Cells are co-cultured in a microfluidic system and exposed to controlled shear stress, hypoxia, and treatment from day 9 to day 12 prior to scRNA-seq analysis. (B) Microfluidic flow system used for controlled circulation and environmental perturbation. (C) Experimental design showing eight conditions in a balanced factorial design incorporating shear, hypoxia, and treatment. (D) UMAP embedding of single-cell transcriptomes across all conditions, showing major cardiomyocyte, endothelial, and stromal populations and their condition-dependent distribution.

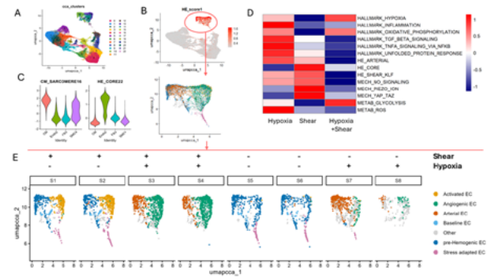

Figure 2 (Abstract 143). Shear and hypoxia exert opposing effects on endothelial state organisation and transcriptional programs. (A) UMAP embedding of endothelial cells coloured by transcriptional subtype, revealing a continuous endothelial manifold comprising activated, angiogenic, arterial, baseline, pre-hemogenic, and stress-adapted states. (B) Overlay of hemogenic endothelial score (HE score) showing spatial enrichment within a defined region of the endothelial manifold. (C) Violin plots of representative gene signatures illustrating differential pathway activity across endothelial subsets, including structural/contractile and hemogenic associated programs. (D) Heatmap of pathway activity changes in endothelial cells under hypoxia, shear, and combined shear–hypoxia conditions. (E) UMAP projections split by experimental condition (S1–S8 showing redistribution of endothelial cells across transcriptional states in response to shear and hypoxia.

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Workforce Development

FROM CLASSROOM TO CLEANROOM: A PRACTICAL FRAMEWORK FOR BUILDING THE CELL AND GENE THERAPY WORKFORCE

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KEYWORDS: Workforce Development, CGT Education, GMP Training.

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Background & Aim:

Rapid growth in cell and gene therapy (CGT) has exposed a persistent gap between academic training and the capabilities required for Good Manufacturing Practice (GMP) environments, quality systems, regulatory requirements, and manufacturing operations. This gap now affects onboarding, consistency, scalability, and the sector's capacity for safe and efficient delivery. We aimed to develop a practical, evidence-informed framework to guide workforce preparation and an implementation roadmap to support coordinated action across academia, industry, professional societies, and government.

Methods, Results & Conclusion:

Through an ISCT Early Stage Professionals-led initiative, with input from senior contributors across academia, industry, clinical, and regulatory settings, we synthesised published evidence and sector experience to develop a CGT workforce framework and implementation roadmap. The analysis focused on recurring mismatches between university training and workforce needs, particularly in GMP, quality systems, regulatory requirements, manufacturing operations, and opportunities for structured experiential learning.

We propose a five-pillar framework for CGT workforce readiness comprising: (1) curriculum innovation, (2) interdisciplinary integration, (3) scalable and inclusive delivery, (4) structured experiential learning, and (5) competency-based credentialing. The framework is paired with an implementation roadmap outlining specific actions, timelines, and measurable outcomes for key stakeholders. Priorities include earlier integration of GMP, quality, and regulatory concepts; stronger industry-linked and hands-on training; flexible delivery models that expand access; and portable, competency-based credentials.

Building a future-ready CGT workforce cannot be left to universities alone. It requires coordinated action across academia, industry, professional societies, and government. This framework provides a practical roadmap to strengthen workforce preparation, onboarding, consistency, and scalability across the sector, moving beyond ad hoc initiatives toward a more coherent, outcomes-driven approach.

Notes

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