Candidate: Elected Member MD (2023-2025)

Claudia C dos Santos, MD, MSc
Associate Professor of Medicine
University of Toronto
Canada

Summary of academic and professional background:

I am a clinician-scientist. I completed Medical School, Internal Medicine, and Critical Care Medicine Fellowship at the University of Toronto. My basic science degree is from the Department of Molecular and Medical Genetics. I am a practicing critical care intensivist and I run my own basic science laboratory at the Keenan Research Centre for Biomedical Science. My research is aimed at building a world-class program in translational acute care medicine. My program has three distinct domains: 1) patient-based discovery (omics/bioinformatics); 2) in-vitro mechanistic research (cell models); and 3) in-vivo pre-clinical research (animal models). My laboratory has significant interest in the application of mesenchymal stromal cell, cell derived and cell-free, including extracellular vesicles, technology to acute care medicine. My focus is specifically in sepsis and acute respiratory distress syndrome (ARDS). In addition to the pre-clinical and translational studies we do in the laboratory, I am also involved in clinical studies to advance the application of stem cell technology to the care of critically ill patients. I was an investigator in the first Dose Escalation Safety Trial of Cell Immunotherapy for Septic shock (CISS-1, led by Dr. L. McIntyre) and a translational co-lead to identify biomarkers of potency and efficacy of MSC treatment. I am a co-investigator for CISS-2 (Phase 2 funded by Ontario Institute of Regenerative Medicine [OIRM] and Stem Cell Network [SCN]). I was a co-applicant in the Solutions for Cardio-pulmonary Organ Repair and Regeneration (SCORR, led by Dr. D Stewart) and Extracellular Vesicles (EV) Options for Lung and Vascular Diseases (EVOLVD) consortiums – to bioengineer EVs with precision medicine determined cargoes - for optimized cell-free therapeutics. I am the site PI for AMETHYST - Advanced Mesenchymal Enhanced cell THerapY for SepTic patients - a first in-human study of genetically modified MSCs for the treatment of sever sepsis (sponsored by NorthernTherapeutics). My current work focuses on bioengineering lipid nanoparticles to deliver proprietary microRNA mimics or inhibitors derived from our regenerative medicine discovery studies in humans for testing in pre-clinical models of sepsis and ARDS. I am the co-founder of NorthMiRs a new student start-up dedicated to advancing this technology for regulatory approval and first-in-human studies.

Affiliated professional and commercial associations and any perceived or potential conflict of interests:

I hold the University of Toronto Pitts Research Chair in Acute and Emergency Medicine. My clinical appointment is that of staff physician, Department of Critical Care Medicine (CCM) at Saint Michael's Hospital (SMH). I am a Fellow of the Royal College of Physicians of Surgeons of Canada. I am a Scientist at the Keenan Research Centre for Biomedical Science, appointed to the Institute of Medical Sciences, cross appointed to the Departments of Laboratory Medicine and Pathology, and Physiology. I am a scientist with the Institute of Biomedical Engineering Science and Technology (iBEST). I am a member of the Collaborative Graduate Program in Genome Biology and Bioinformatics, the Canadian Critical Care Trials (CCCTG) and Translational Biology Groups (CCCTBG) and member of the Canadian Sepsis Network. I am a Parker B. Francis and Canadian Institutes of Health Research (CIHR) Fellow; a recipient of a CIHR New Investigator Award, Clinician-Scientist from the Heart and Stroke Foundation, and an Early Research Award from the Ministry of Research and Innovation. I received of the Department of Medicine (DOM) Merit award. My work has been funded by the Canadian Institute of Health Research (CIHR), Natural Sciences and Engineering Research Council (NSERC), National Research Council of Canada (NRC), Canadian Foundation for Innovation (CFI), Ontario Research Fund (ORF), the Stem Cell Network (SCN), the Ontario Institute for Regenerative Medicine (ORIM) and the McLaughling and St. Michael's Foundation. I am the creator and current director of the Unity Health Toronto Critical Care Medicine Biobank and a lead of the University of Toronto COVID19 biobank. I am a member of CoVaRR-Net Biobank and Data Alliance National group for pandemic preparedness – Biobanking. The Canadian COVID-19 Prospective Cohort Study (CANCOV). I am the Scientific Director for the Canadian Critical Care Society, and a member of the Canadian Critical Care Forum Executive. I am the Scientific Officer for NorthMiRs - the start-up I co-founded with Gilbert Walker Director of the Canadian Nanomedicine Innovation Network and our graduate students. The goal of NorthMiRs is to design and test innovative formulations for therapeutic RNA/miRNA delivery. I see my leadership, administrative and scholarly activities not in conflict with a future role in ISCT, but as a natural extension of my national and international interest and commitment to the advancement of translational research and the application of stem cell technology to clinical practice.

List of top notable contributions to the field (e.g. publications, patents, reports, products advanced to clinical trial or regulatory approval, asset development, mergers, acquisitions, etc.) from the last 10 years:

I have published over 135 manuscripts with over 7,678 citations with impact factors ranging from 3-91, over 50 in the last 5 years, 23 as lead author, and presented over 40 invited talks (21 international talks). My overall h-index is 46 (36 since 2017), and my i10-index is 93 (Google Scholar, 81 since 2017). My publications can be found:

https://www.scopus.com/authid/detail.uri?authorId=57214144197

Website to my Lab: https://research.unityhealth.to/labs/dos-santos/

Intellectual Property Patents (#1). Transcriptomic signatures of mechanical stress. Spain. 2022/02/18. Patent Status: Pending (#2). Invention Disclosure - Transcriptomic signatures of

mechanical stress. Spain. 2021/01/08. Patent Status: Pending Dr. Claudia dos Santos 15 (#3). Methods Of Treating A Vascular Leakage-Associated Disease Or Disorder. United States. 62/797,979. 2019/01/29. Patent Status: Allowed Disclosures 1. Start-Up company "NorthMiRs" Disclosed Filing Date: 2022/07/28

Selected recent contributions (2021-:

1. Rapid and Low-Cost Detection and Quantification of SARS-CoV-2 Antibody Titers of ICU Patients with Respiratory Deterioration Using a Handheld Thermo-Photonic Device. Biomedicines 10(6), 2022
2. Identifying clinical subtypes in sepsis-survivors with different one-year outcomes: a secondary latent class analysis of the FROG-ICU cohort. Critical Care 26 (1), 1-12.2. 2022
3. The relationship between antithrombin administration and inflammation during veno-venous ECMO. Panigada M, Spinelli E, De Falco S, Consonni D, Novembrino C, Boscolo Anzoletti M, Panarello G, Occhipinti G, Dos Santos CC, Pesenti A, Arcadipane A, Grasselli G. Sci Rep. 2022 Aug 22;12(1):14284. doi: 10.1038/s41598-022-17227-7.
4. Diversity in the Expressed Genomic Host Response to Myocardial Infarction. Circulation Research 131 (1), 106-108,1. 2022
5. Redefining critical illness. Nature Medicine 28 (6), 1141-1148.10. 2022
6. DJ-1 binds to Rubicon to Impair LC-3 Associated Phagocytosis. Cell Death & Differentiation, 1-10; 2022
7. Proceedings of the ISCT scientific signature series symposium, “advances in cell and gene therapies for lung diseases and critical illnesses”: International society for cell and gene therapy. Cytotherapy. 2022
8. MicroRNA regulatory networks associated with abnormal muscle repair in survivors of critical illness. Journal of cachexia, sarcopenia and muscle 13 (2), 1262-1276; 2022
9. Comprehensive Multi-cohort Transcriptional Meta-analysis of Muscle Diseases Identifies a Signature of Disease Severity. Sci Rep 12, 11260. 2022.
10. Mesenchymal stromal (stem) cell therapy modulates miR-193b5p expression to attenuate sepsis-induced acute lung injury. Eur Respir J. 2022 Jan 6;59(1):2004216.
11. Predicting sepsis severity at first clinical presentation: The role of endotypes and mechanistic signatures EBioMedicine 75, 103776; 13. 2022
12. Mesenchymal stromal (stem) cell therapy modulates miR-193b-5p expression to attenuate sepsis-induced acute lung injury. European Respiratory Journal 59 (1); 6; 2022
13. Mesenchymal stem/stromal cell-based therapies for severe viral pneumonia: therapeutic potential and challenges. Intensive care medicine experimental 9 (1), 1-21. 1; 2021
14. National Preclinical Sepsis Platform: developing a framework for accelerating innovation in Canadian sepsis research. Intensive Care Medicine Experimental 9 (1), 1-19;1.2021
15. Healthy versus inflamed lung environments differentially affect mesenchymal stromal cells European Respiratory Journal 58 (4).5. 2021 25. Mesenchymal stem/stromal cells increase cardiac miR-187-3p expression in a polymicrobial animal model of sepsis. Shock (Augusta, Ga.) 56 (1), 133 4;2021

Summary of involvement with ISCT in the past five years:

My involvement with ISCT can be divided into 2 parts: (a) Research collaborations and (b) scholarly administrative contributions. I actively collaborate with various ISCT scientists (Weiss, Rocco, McIntyre, Mei, Stewart, Giebel, and Matthay) both at the pre-clinical as well as clinical research level. In terms of contributions to the Society, I became significantly involved working with Dr. Rachele Ciccocioppo with Gastrointestinal Committee, in an advisory capacity as an

expert on innate immune function of macrophages in response to MSCs. We published together various proceedings of the meetings and I helped develop the strategic plan for this committee. I also co-organized the first Stem Cell Work shop in Toronto in 2016 - a 2 day even that brought together various world experts. Results of this symposium contributed to the generation of the dossier that was to submitted to Health Canada to support regulatory approval for the first clinical trials of MSCs for the treatment of septic shock (published in 2018). I also co-organized with Dr. Rocco the ISCT symposium on Success and Failure of Cell Therapy Clinical Trials for Acute and Chronic Lung Diseases for the meeting in Paris 2020; “MSC-Derived EVs: Cell Therapy without Cells In New Orleans in 2021 (scientific signature event), and participated in the Pulmonary Signature event "Advances in Cell and Gene Therapies for Lung Diseases" in 2021. I contributed to the meeting proceedings; these were published in Cytotherapy.

Summary of strategic vision for the Global Society:

My vision moving forward is to advance translation and deployment of cell and gene therapy technology to clinical practice; with a focus on advancing innovative technology for the generation of robust products for clinical testing, including nanotherapeutics, advancing strategies to accelerate regulatory approval, commitment to education of the public, and harmonization of evaluative measures and clinical trial design. My area of expertise is critical care, so much of my focus is on the development of innovative designer therapeutics for acute critical illness. The application of precision diagnostics coupled with advanced enhanced cell therapy and cell-free approaches: including genetically modified, clonally immortalized, application of multi omics, endotyping of patients, coupled with bioengineered personalized nanovesicles and other cell-products for the treatment of ARDS, sepsis and acute (new) organ failure. I am also interested in fostering opportunities for "incubator" collaborations between industry and academia to accelerate transition of innovative ideas to first-in-human clinical trials, development of business models for advancement of innovative products, participation of regulatory agencies in pre-clinical research to fast-track regulatory approval, and engagement with industry and patient-partners for creation of seed funds to transition ideas from the bench to commercialize products.