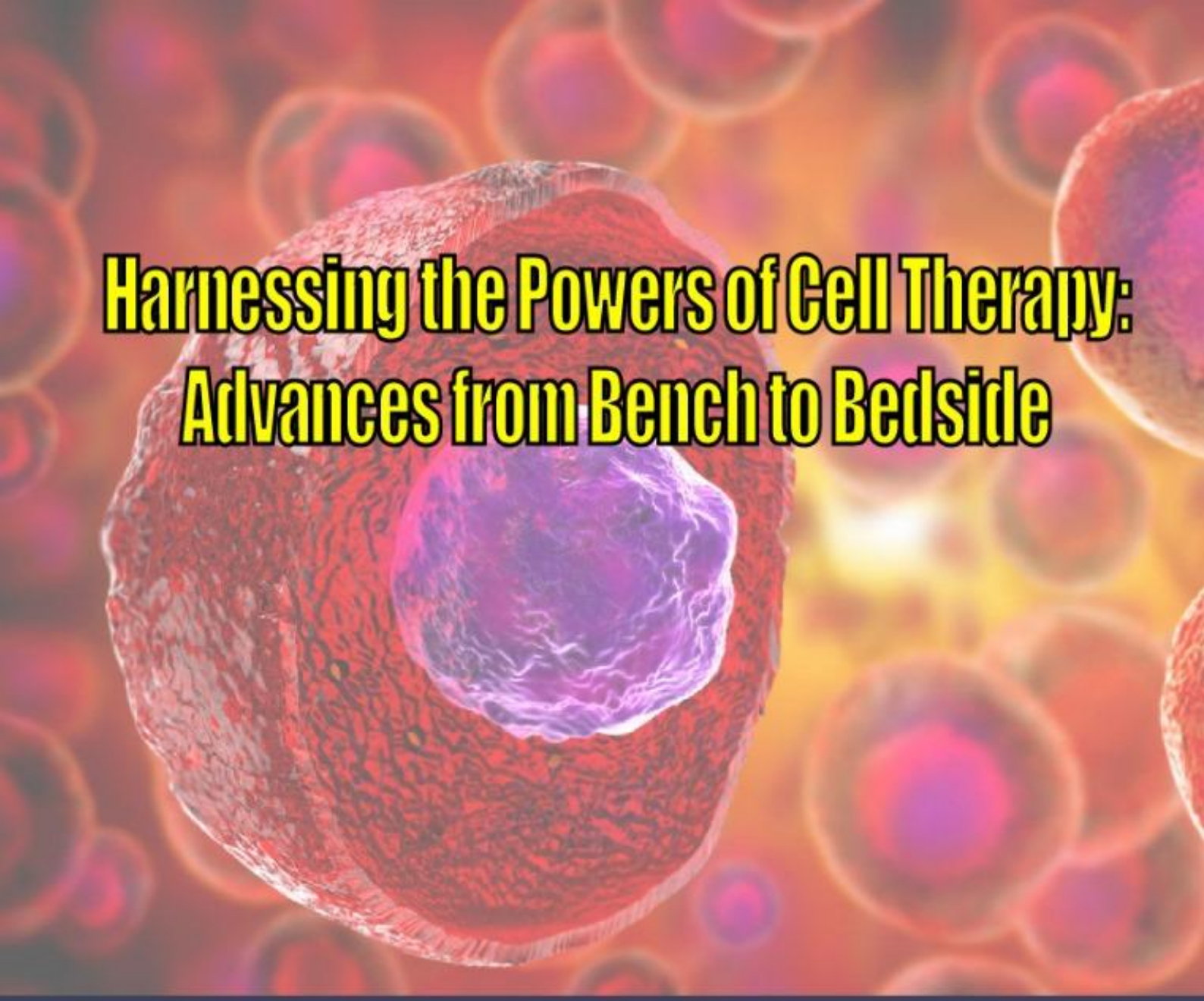

Harnessing the Powers of Cell Therapy: Advances from Bench to Bedside

4th MK FMHS International Conference

M. Kandiah Faculty of Medicine & Health Sciences
Universiti Tunku Abdul Rahman
MALAYSIA

UTAR
UNIVERSITI TUNKU ABDUL RAHMAN

UTAR HOSPITAL
Enriching and Caring for the Community

18 - 19 September 2023

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Message from the Dean

First and foremost, congratulations to the Organising Committee of the 4th MK FMHS International Conference 2023, led by Associate Professor Dr. Ong Hooi Tin, for realising this highly anticipated event. This is the fourth conference organised by the M. Kandiah Faculty of Medicine & Health Sciences, UTAR, since the establishment of the Faculty on 16 November 2009. This fourth edition of the conference holds significant meaning as we gather in person after a challenging period of Covid-19 pandemic to discuss and share insights into the transformative potential of cell-based treatments.

The theme of this conference "Harnessing the powers of cell therapy: Advances from bench to bedside" encapsulates the essence of this conference, where we bridge the gap between pioneering research and real-world applications. The conference will showcase groundbreaking research and discoveries in cell therapy, spanning from fundamental laboratory work to its practical application in patient care. Participants will gain a comprehensive understanding of how cell therapy is revolutionising the treatment of various non-communicable diseases and oncology and have the opportunity to explore the latest technologies that are driving progress in cell therapy.

This conference offers ample opportunities for networking, collaboration and knowledge exchange among professionals, fostering new partnerships and initiatives in the field. It serves as a platform for stakeholders in the cell therapy community to come together, learn from each other, and collectively advance the field towards improved patient outcomes and medical breakthroughs.

Finally, it gives me great pleasure to warmly welcome you to this conference. I wish you a successful and fruitful meeting. My sincere appreciation to all the speakers and sponsors for their generous support to make this meeting a successful one.

Thank you.

Academician Emeritus Professor Dr. Cheong Soon Keng
Dean
M. Kandiah Faculty of Medicine & Health Sciences, UTAR

Message from Chairpersons

On behalf of the organising committee, we welcome everyone to our 4th MK FMHS International Conference 2023, which takes place on 18th – 19th September at The Everly Hotel, Putrajaya Malaysia. Being a biennial event, this year marked the fourth conference organised by the M. Kandiah Faculty of Medicine and Health Sciences (MK FMHS), UTAR, Malaysia. This fourth edition of the conference is made more meaningful as it is organised in collaboration with the new UTAR Hospital in Kampar, Perak.

Over the years, we have seen tremendous development in cell therapy, translating it into a therapeutic "product" in multiple areas, such as generative medicine, immunotherapy and cancer therapy. In line with this year's theme, "Harnessing the Power of Cell Therapy: Advances from Bench to Bedside," we have decided to put together a comprehensive scientific programme ranging from different types of cell therapy to its therapeutic clinical benefits.

The organising committee has worked tirelessly for months prior to the event to try to make this year's conference a successful one. We are also honoured to be able to invite so many eminent and experienced speakers, both locally and internationally, to speak at the conference, sharing their knowledge.

We hope that this conference will provide an excellent opportunity for researchers, clinicians, and industry professionals to come together to network, exchange ideas and discuss the latest research findings in cell therapy. We also hope that the conference will stimulate new collaborations and partnerships that will further enhance the development and translation of cell therapy into clinical practice. Lastly, we would like to express our gratitude to our sponsors and partners for their support in making this event possible.

We look forward to an exciting and fruitful conference ahead!

With warm regards,
Organising Chairperson & Co-Chairperson
Associate Professor Dr. Ong Hooi Tin
Clinical Associate Professor Dr. Lee Bee Sun

Organising Committee Members

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THE 4TH MK FMHS INTERNATIONAL CONFERENCE 2023

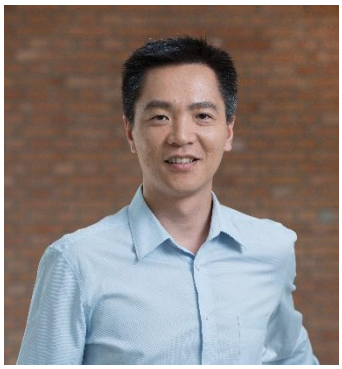
HARNESSING THE POWERS OF CELL THERAPY: ADVANCES FROM BENCH TO BEDSIDE

18 -19 SEPTEMBER 2023 | THE EVERLY PUTRAJAYA, MALAYSIA

Day-1: Monday, September 18, 2023		
0830	Opening and welcome address	
0845	**Dr Wu Lien-Teh Memorial Lecture** The in-vitro circle of life -using embryonic stem cells to build human reproductive organoids *Prof. Dr. Kehkooi Kee, Tsinghua University, China* *Chairperson: Prof. Dr. Yap Sook Fan, Universiti Tunku Abdul Rahman, Malaysia*	
0930	**Symposium I:** **New-generation vaccines** *Chairperson:* *Assoc. Prof. Dr. Chua Jia Xin, Universiti Tunku Abdul Rahman, Malaysia*	Newcastle disease virus as a therapeutic vaccine candidate against cancer *Prof. Dr. Khatijah Mohamad Yusoff, Universiti Putra Malaysia, Malaysia*
		Phage display technology – A promising platform for cancer therapeutic antibodies discovery *Dr. Leow Chiuan Herng, Universiti Sains Malaysia, Malaysia*
		Vaccines for head and neck cancers *Dr. Lim Kue Peng, Cancer Research Malaysia, Malaysia*
1100	Tea break	
1130	**Symposium II:** **Cancer immunotherapy** *Chairperson:* *Dr. Leow Chiuan Yee, Universiti Sains Malaysia, Malaysia*	Isolation of stem memory T cells (TSCMs): Implications for CAR-T therapy *Assoc. Prof. Dr. Chua Jia Xin, Universiti Tunku Abdul Rahman, Malaysia*
		Engineering second, third and next generation CAR-T cells *Dr. Vita Golubovskaya (virtual), Promab Biotechnologies, USA*
		DC vaccines for solid tumours *Assoc. Prof. Dr. Herbert Schwarz, National University Hospital, Singapore*
1300	**Biomed Global Lunch Symposium** Our commitment to cell and gene therapy *Moderator: TBC | Speakers: Dr Suruchi Arora, Bio-Techne (virtual)*	
1400	**Symposium III:** **MSCs as a therapeutic tool** *Chairperson:* *Prof. Dr. Goh Bak Leong, Hospital Sultan Idris Shah, Serdang, Malaysia*	MSCs in GVHD management *Prof. Dr. Chin Sze Piaw, Cytopeutics Sdn. Bhd. / Universiti Tunku Abdul Rahman, Malaysia*
		BM-MSCs in stroke management *Assoc. Prof. Dr. Law Zhe Kang, Universiti Kebangsaan Malaysia, Malaysia*
		Breathing new life: Exploring extracellular vesicles as therapeutic agents in respiratory diseases *Assoc. Prof. Dr. Badrul Hisham Yahaya, Universiti Sains Malaysia, Malaysia*
1530	Tea break	
1600 – 1730	ISBT International Society of Blood Transfusion **Symposium IV: Evolving roles of the transfusion services** *Chairperson:* *Prof. Dr. Veera Sekaran Nadarajan, Universiti Tunku Abdul Rahman, Malaysia*	New applications of cord blood *Dr. Zalina Mahmood, National Blood Centre, Malaysia*
		Generation of red cells from iPSC and erythroid cell lines *Dr. Becky Griffiths, Australian Red Cross Lifeblood, Australia*
		iPSC banking from cord blood sources *Assoc. Prof. Dr. Ngaire Elwood, Murdoch Children's Research Institute, Australia*

Day-2: Tuesday, September 19, 2023		
0845	**Plenary I** Cell therapeutics: New treatment paradigms for blood disorders *Prof. Dr. John EJ Rasko, AO, University of Sydney, Australia* *Chairperson: Emeritus Prof. Dr. Cheong Soon Keng, Universiti Tunku Abdul Rahman, Malaysia*	
0930	**Symposium V: Advances in CAR-T therapy** *Chairperson:* *Assoc. Prof. Dr. Leong Pooi Pooi, Universiti Tunku Abdul Rahman, Malaysia*	Exploring the impact of T-cell exhaustion on CAR-T cell therapy *Dr. Leow Chiuan Yee, Universiti Sains Malaysia, Malaysia*
		Cytokine-induced killer (CIK) cells and dendritic cell (DC) vaccines have emerged as promising tools in cancer immunotherapy *Prof. Dr. Ho Gwo Fuang, Universiti Malaya, Malaysia*
1030	Tea break	
1100	ISBT International Society of Blood Transfusion **Symposium VI: CAR-T therapy in the clinical setting** *Chairperson:* *Prof. Dr. Gan Gin Gin, Universiti Malaya, Malaysia*	Managing CAR-T complications *Dr. Michaela Seng, KK Women's and Children's Hospital, Singapore*
		CAR-T therapy in Malaysian public hospitals Dr. *Tan Sen Mui, Ampang Hospital, Malaysia*
		Overview of CAR-T therapy in haematological malignancies *Dr. Chang Kian Meng, Sunway Medical Centre, Malaysia*
1220	**Symposium VII: Cell therapy and nursing care** *Chairperson:* *Prof. Dr. Hamidah Hassan, Universiti Tunku Abdul Rahman, Malaysia*	Cell therapy: Roles and functions of nurses in navigating the patient through the treatment process *Ms. Amanda Choong Jyeyi, Sunway Medical Centre, Malaysia*
		Stem cell transplantation treatment: Specific population with financial implication *Ms. Seery Zaliza Azura binti Zaider, Universiti Kebangsaan Malaysia, Malaysia*
1310	**Cryocord Lunch Symposium** Cord blood - is it a biomedical waste or gold mine? *Moderator: Emeritus Prof. Dr Cheong Soon Keng | Speakers: Assoc. Prof. Dr Lee Bee Sun & Dr Fann Rui Jeat*	
1400	**Plenary II** Pelareorep as an enabling technology for both chemotherapies and immune-oncology therapies *Dr. Houra Loghmani, Oncolytics Biotech, Canada* *Chairperson:* *Assoc. Prof. Dr. Ong Hooi Tin, Universiti Tunku Abdul Rahman, Malaysia*	
1440	**Symposium VIII: Cell therapies for aging joints** *Chairperson:* *Prof. Dr. Tunku Kamarul Zaman Tunku Zainol Abidin, Universiti Sains Malaysia, Malaysia*	MSC and cartilage tissue-derived extracellular vesicles to treat osteoarthritis *Dr. Law Jia Xian, Universiti Kebangsaan Malaysia, Malaysia*
		The use of platelet-derived extracellular vesicles for musculoskeletal tissue regeneration: from basic research to clinical outcome *Dr. Chong Pan Pan, Universiti Malaya, Malaysia*
1540	Tea break	
1610	**Symposium IX: Engineered cells for disease modelling** *Chairperson:* *Prof. Dr. Alan Ong Han Kiat, Universiti Tunku Abdul Rahman, Malaysia*	Application of genomic editing technology in retinal diseases *Prof. Dr. Chiou Shih-Hwa (virtual), National Yang Ming Chiao Tung University*
		Modelling heart disease from animal to *in vitro* models *Assoc. Prof. Dr. Tan Jun Jie, Universiti Sains Malaysia, Malaysia*
1710	Oral Papers	Establishment of hiPSCS derived 3D lung organoids as disease modelling for respiratory diseases *Ms. Nalini Devi Verusingam, Universiti Tunku Abdul Rahman, Malaysia*
		Multiple Dosing of Cytopeutics® Human Umbilical Cord Mesenchymal Stem Cells is Safe in BALB/c Mice Toxicity Evaluation Dr. *Natasha Najwa, Cytopeutics Sdn. Bhd., Malaysia*
		Analysis of Secretome Profile in Umbilical Cord-derived Mesenchymal Stromal Cells Co-cultured with Senescent Normal Human Dermal Fibroblast *Ms. Lee Soke Sun, Universiti Tunku Abdul Rahman, Malaysia*
1740 - 1750	Closing, prize giving and farewell address	

Dr Wu Lien-Teh Memorial Lecture



Professor Dr. KehKooi Kee
Deputy Director of Department of Basic Medical Sciences
School of Medicine
Tsinghua University, China

Dr. Kee received his Bachelor and Master degrees in Biochemistry at Iowa State University in 1997. He studied meiotic recombination during his graduate school at Weill Cornell Medical School and Sloan Kettering Institute in Professor Dr. Scott Keeney laboratory. After his PhD study, he joined Professor Dr. Renee Reijo Pera lab as a postdoctoral fellow at UCSF and became a research associate at Stanford University in 2007. He started his own lab and became a principal investigator at School of Medicine, Tsinghua University since 2010.

His research team is interested in understanding the molecular mechanisms underlying human germ cell development, initiation of meiosis, and impacts of human germ cells on early embryo development. Their current research projects include developing in vitro models of human germ cell development and studying mutations causing infertility manifested in clinical setting. He has published in *Nature, EMBO J, Nature Communications, Human Reproduction Update* and other journals reporting many pioneering discoveries and derivation methods in stem cell and reproductive medicine. The *in vitro* differentiation methods of human pluripotent stem cells to different cell types that his team developed have been used in many basic research and translational applications including China space projects to study the effect of microgravity on human germ cell developments.

Abstract

The *In-vitro* Circle of Life - Using Embryonic Stem Cells to Build Human Reproductive Organoids

Kehkooi Kee[1,2]

1 Center for Stem Cell Biology and Regenerative Medicine, Department of Basic Medical Sciences, School of Medicine, Tsinghua University, Beijing, China
2 The State Key Laboratory for Complex, Severe, and Rare Diseases; SXMU-Tsinghua Collaborative Innovation Center for Frontier Medicine; School of Medicine, Tsinghua University, Beijing, China

Germ cells perform many unique and fascinating mechanisms which are vastly different from somatic cells. Understanding mechanisms of human germ cell development is important for building basic knowledge and clinical treatments of infertility, genetic diseases, and tumorgenesis in human reproductive systems. However, genetic and molecular studies of

human germ cell development are limited by the ethical and technical constraints to obtain the desired cell type and cell number to conduct molecular and cellular experiments. Realising that differentiating human embryonic stem cells (hESCs) to germ cell will provide a novel platform for studying human germ cell development and developing treatment reproductive medicine, we have developed several *in vitro* differentiation systems to study human germ cells at different developmental stages, including primordial germ cells (PGCs), oocytes and spermatids. Strategy and methodology of building the *in vitro* differentiation systems will be described. The differentiated systems have been utilised to investigate molecular mechanisms of human PGC development, causative effect of infertility mutations, and studying the microgravity of spaceflight on germ cell development.

Plenary I

John E. J. RASKO AO
BSc (Med), MBBS (Hons), PhD, MAICD, FFSc(RCPA), FRCPA, FRACP, FAAHMS

Professor John Rasko is an Australian pioneer in the clinical application of adult stem cells and gene therapies. Since 1999 he has directed the Department of Cell & Molecular Therapies at Royal Prince Alfred Hospital and the Gene and Stem Cell Therapy Program, Centenary Institute, University of Sydney. He was appointed Deputy Director of Research Development & Partnerships at the Centenary Institute in 2023.

He is a clinical haematologist, pathologist and scientist with an international reputation in gene and stem cell therapy, experimental haematology and molecular biology. In over 220 publications he has contributed to the understanding of stem cells and blood cell development, gene therapy technologies, cancer causation and treatment, human genetic diseases and molecular biology. He has delivered the Australian Broadcasting Commission's prestigious Boyer Lectures for 2018, Life Re-engineered. With historian Carl Power, he published Flesh Made New: the unnatural history and broken promise of stem cell research.

He serves on Hospital, state and national bodies including the longest-serving Chair of The Gene Technology Technical Advisory Committee, OGTR, and past inaugural Chair of the TGA Advisory Committee on Biologicals. He co-founded and was past-President of the ANZ regional division of the International Society for Cell & Gene Therapy and served as ISCT's President and Board member 2016-2022.

Abstract

Cell Therapeutics: New Treatment Paradigms for Blood Disorders

John EJ Rasko, AO[1,2,3]

1 President 2018-20, International Society for Cell & Gene Therapy
2 Professor, Sydney Medical School, University of Sydney; Head, Gene and Stem Cell Therapy Program, Centenary Institute
3 Head of Department, Cell & Molecular Therapies, Royal Prince Alfred Hospital, Sydney, Australia

Advanced therapeutic medicinal products based on gene and stem cell therapies are increasingly being approved throughout the world. Immunotherapies including checkpoint inhibitors and CAR-T cells have captured the attention of many scientists, physicians and

cancer sufferers. The convergence of substantial incremental technical advances towards combined cell and gene therapy has led to improved clinical outcomes in immune deficiencies, haemoglobinopathies, immunotherapies and other inherited diseases.

In the regenerative medicine field to be detailed in this talk, there is a pressing need to standardize cell manufacturing protocols for widespread clinical assessment and implementation. Strict compliance with government regulation and oversight is essential to maintain the safety of all therapeutic products. In 2020 we reported the first ever completed trial of iPSC-derived Mesenchymal stromal cells in Steroid-Resistant Acute GvHD and in now report the two year follow up. MSCs have been widely investigated as a treatment for graft versus host disease (GvHD), but with mixed results. Factors such as MSC donor variability and the effects of prolonged culture expansion may contribute to inconsistent or disappointing outcomes. The novel Cymerus™ manufacturing process facilitates virtually limitless production of well-defined and consistent MSCs from a single human iPSC bank, using clonogenic progenitor-based technology. This avoids both inter-donor variability, batch-to-batch variation and the need for prolonged *in vitro* expansion of MSCs.

In the area of *ex vivo* gene therapies, we have been the first site in the southern hemisphere pursuing lentivirus modified autologous haemopoietic stem/progenitor transplantation for transfusion dependent beta-thalassaemia (TDT) – the commonest human genetic blood disease. Although advances in red blood cell transfusion and iron chelation have improved the prognosis of patients with TDT, allogeneic haemopoietic stem cell transplantation has been the only curative therapy. Since 2011, we have been a foundation site with BlueBird Bio evaluating LentiGlobin gene therapy in patients with TDT. We have reported results from the completed phase 1/2 Northstar and phase 3 Northstar-2 studies, including 7-Year Post-Infusion Follow-up. From mid-2019 to 2022, Zynteglo was available for the treatment of patients 12 years and older with TDT as approved by the European Medicines Association and the US FDA approved this in 2023. Zynteglo (betibeglogene autotemcel), represents the first cell-based gene therapy for the treatment of adult and paediatric patients with beta-thalassemia who require regular red blood cell transfusions.

However, in parallel with objectively proven therapies, ‘stem cell tourism’ has become a billion dollar industry with increasing examples of false claims. These data should be of immediate concern to governments and ethicist being lobbied to amend laws governing the manufacture, distribution and clinical use of human cell-based medical products. Unregulated, untested or unsafe stem cell ‘therapies’ place the field at a difficult crossroad. Blurring the lines that distinguish evidence-based cell therapies from those that are not remains a fundamental public health concern.

The implementation of cell and gene technologies in the clinical setting have already provided enormous benefits to human health. Vigilant careful planning, ongoing research and longer-term data are needed to overcome current limitations across many therapeutic areas.

Further Reading:

Adrian J C Bloor, Amit Patel, James E Griffin, Maria H Gilleece, Rohini Radia, David T Yeung, Diana Drier, Laurie S Larson, Gene I Uenishi, Derek Hei, Kilian Kelly, Igor Slukvin, John E J Rasko. Production, safety and efficacy of iPSC-derived mesenchymal stromal cells in acute steroid-resistant graft versus host disease: a phase I, multicenter, open-label, dose-escalation study, Nature Medicine 2020 Nov;26(11):1720-1725. doi: 10.1038/s41591-020-1050-x.

Gabrielle M. O'Sullivan, Joshua G. Philips, Heidi J. Mitchell, Michael Dornbusch and John E. J. Rasko. 20 Years of Legislation – How Australia Has Responded to the Challenge of Regulating Genetically Modified Organisms in the Clinic, Frontiers in Medicine, Policy and Practice Reviews, 2022 May 10;9:883434. doi: 10.3389/fmed.2022.883434.

Gabrielle M. O'Sullivan, Joshua G. Philips, and John E. J. Rasko. Clinical gene technology in Australia: building on solid foundations, Medical Journal of Australia, 2022 Jul 18;217(2):65-70. doi: 10.5694/mja2.51629.

Shreyashee Mallik, Charles G Bailey, John E J Rasko, Approved gene therapies in Australia: coming to a store near you, Internal Medicine Journal, 2022 Aug;52(8):1313-1321doi: 10.1111/imj.15880.

Thompson AA, Walters MC, Kwiatkowski J, Rasko JEJ, et al. Gene Therapy in Patients with Transfusion-Dependent β-Thalassemia. N Engl J Med. 2018 Apr 19;378(16):1479-1493. doi: 10.1056/NEJMoa1705342. PMID: 29669226.

John EJ Rasko & Carl Power, Flesh Made New: The Unnatural History and Broken Promise of Stem Cells, Harper Collins Book 2021. ISBN: 9780733340147.

Carl Power & John EJ Rasko. The deadly legacy of a stem cell charlatan BMJ 2023; 381 doi: https://doi.org/10.1136/bmj.p1367 (Published 21 June 2023).

David Cyranoski, Douglas Sipp, Shreyashee Mallik, John E.J. Rasko. Too little, too soon: Japan's experiment in regenerative medicine deregulation 30:7, p913-916, July 06, 2023 doi.org/10.1016/j.stem.2023.06.005.

Plenary II

Dr Houra Loghmani
Oncolytics Biotech, Canada

Abstract

Pelareorep as an Enabling Technology for Both Chemotherapies and I–O Therapies, Including Checkpoint Inhibitors and Chimeric Antigen Receptors (CAR T) Therapy

Houra Loghmani[1], Richard Trauger, Matt Coffey[1], Richard Vile, Thomas Heineman

1 Oncolytics Biotech Inc. Calgary, Canada
2 Oncolytics Biotech Inc. San Diego, USA
3 Department of Molecular Medicine, Mayo Clinic, Rochester, USA

Pelareorep (pela) is a naturally occurring oncolytic reovirus, which has a double-stranded RNA (dsRNA) genome that selectively infects transformed cells. It promotes anti-tumour responses through the dual mechanisms of direct cell lysis and stimulation of tumour-directed innate and adaptive immune responses. The combination of productive infection leading to cell lysis and the introduction of dsRNA into tumour cells promotes the recruitment and activation of anti-tumour immune cells and remodels the tumour microenvironment through enhanced cytokine and chemokine expression, which in turn reverses the immunosuppressive environment of cold tumours. Pela is uniquely suited for clinical applications. It is not genetically modified and, therefore, can be administered in a chemotherapy suite without special precautions. In addition, it is transported to tumours bound to immune cells allowing it to evade neutralization in the blood, which permits intravenous administration in contrast to most other oncolytic viruses that must be given intratumorally. Prior studies support the clinical benefit of pela. In the phase 2 IND-213 trial, treatment with pela + paclitaxel resulted in a near doubling of overall survival in HR+/HER2- metastatic breast cancer patients compared to standard-of-care paclitaxel monotherapy. In the AWARE-1 window of opportunity trial, in which newly diagnosed breast cancer patients were treated with letrozole + pela +/- atezolizumab, pela activated T cells and enhanced their infiltration into tumours. In addition, pela increased the expression of PD-L1 by activating the interferon gamma signalling pathway, thus priming the tumour for checkpoint blockade therapy. Synergy with checkpoint blockade therapy was also observed in the GOBLET trial in first-line metastatic pancreatic cancer patients with a near tripling of the overall response rate for the pela and atezolizumab + chemotherapy arm compared to historical controls. Because of its ability to bind T cells that traffic to the tumour, another potential application of pela is as a partner in chimeric antigen receptor T cell (CAR T) therapy for solid tumours. In pre-clinical tumour models, pela-loaded CAR Ts exhibited enhanced expansion,

longer persistence, and a more prominent memory phenotype. These expanded functions resulted, in part, from the expansion of dual-specific CAR Ts that are specific to both the CAR target as well as to pela-specific epitopes. This, in turn, allowed them to expand after a single IV pela boost. Accordingly, the combination of pela and CAR Ts has shown better efficacy than either pela or CAR T treatment alone in several pre-clinical tumour models, including pancreatic cancer, glioma and melanoma and warrants clinical investigation.

Symposium I

Professor Dr. Khatijah Mohd Yusoff
PhD, DSc (honoris causa) (La Trobe)
FASc, FTWAS, FIAS, FMSA
National Institutes of Biotechnology Malaysia

Professor Khatijah is currently a Subject Matter Expert at the National Institutes of Biotechnology Malaysia (NIBM). She has extensive engagement and network with industry, professional bodies and academies; she is currently the Vice-President of Islamic World Academy of Sciences (IAS), a member of the Council of Scientific Advisors of International Centre for Genetic Engineering and Biotechnology (ICGEB), a Senior Fellow of the Academy of Sciences Malaysia (ASM), Fellow of the Malaysian Scientific Association (MSA) and Fellow and former Vice-President of The World Academy of Sciences for the advancement of science in developing countries (TWAS). Her 5-year stint as the Deputy Secretary-General of Ministry of Science, Technology and Innovation Malaysia (2008-2013) gave her an opportunity to promote science through national policies and development of a strong framework in managing science in the country. She believes strongly on the need for translating science into tangible benefits to people around the world; she previously sat on the Board of Trustees of the International Livestock Research Institute, SEAMEO-BIOTROP Governing Board, Advisory Board for La Trobe Asia, and the Technical Advisory Panel for COMSATS as well as several agencies in Malaysia. She is involved in promoting science to the communities; she was formerly a member of the National Science Research Council and the National Bioethics Council. She is currently the Chairman of the National Committee on Research Integrity and the Advisor of the Talent Development Committee under ASM. Her research focuses on the molecular biology of Newcastle disease virus, a poultry virus which kills cancer cells without affecting the normal cells. Through reverse genetics, she is currently developing an NDV-based cancer vaccine for the treatment of colorectal and bladder cancers. Her work has received many awards, the most recent being the Anugerah Tokoh Akademik Negara 2022. She was also featured in a 2021 special edition of DC Comics "Wonder Women: Wonderful Women of The World. Her special message to young Malaysian scientists looking to impact their field is to "never give up and value the importance of teamwork".

Abstract

Newcastle Disease Virus as a Therapeutic Vaccine Candidate Against Cancer

Khatijah Yusoff, FASc

National Institutes of Biotechnology Malaysia

The Newcastle disease virus (NDV) is an avian paramyxovirus which has a non-segmented negative stranded RNA genome. The virus infects poultry inducing several levels of pathogenicity. Interestingly, NDV does not pose any threat to humans in terms of pathogenicity, though it might trigger mild conjunctivitis and flu-like symptoms. Nevertheless, the virus has demonstrated a remarkable ability to selectively target and destroy human cancer cells, making it a highly promising therapeutic vaccine candidate for oncovirotherapy. This intrinsic feature of selectively lysing cancer cells with a high degree of specificity and sensitivity, leaving normal cells unharmed provides a strategic avenue to harness NDV's potential for cancer treatment. Multiple clinical trials attest to this potential. The mechanisms underlying its oncolytic prowess encompass two pathways: direct selective infection and killing of tumour cells, as well as indirectly through induction of specific host immune response acting against the tumour tissue. By manipulating the viral genome through reverse genetics, NDV can orchestrate the recruitment of immune cells towards cancer cells, thus enhancing the effectiveness of oncolysis. This dynamic development heralds an exciting and challenging frontier in cancer therapy and opens up new possibilities for leveraging the virus's potential to combat cancer while inflicting minimal harm to healthy cells. This innovative approach holds great promise for advancing cancer treatment and offers hope for improved therapeutic outcomes.

Dr. Chiuan Herng Leow
Institute for Research in Molecular Medicine
Universiti Sains Malaysia

Dr. Chiuan Herng Leow is a senior lecturer at the Institute for Research in Molecular Medicine, Universiti Sains Malaysia. He received his PhD from the University of Queensland, Australia, and has supervised several PhD and Master's projects. Dr. Leow has published over 40 scientific articles and presented over 50 talks/posters at international conferences. His research interests include developing single domain antibodies using phage display technology and investigating adaptogens from higher basidiomycetes as potent adjuvants for immunodiagnostic and immunotherapeutic applications.

Abstract

Phage Display Technology – A Promising Platform for Cancer Therapeutic Antibodies Discovery

Chiuan Herng Leow

Institute for Research in Molecular Medicine (INFORMM), Universiti Sains Malaysia

Monoclonal antibodies (mAbs) have emerged as a pivotal class of biopharmaceutical products in the medical market. The groundbreaking potential of phage display technology, acknowledged by the 2018 Nobel Prize in Chemistry, plays a significant role here. This innovative approach involves identifying high-affinity target-binding peptides from a vast collection of displayed peptides on phages within a combinatorial library. The process is further honed through biopanning, showcasing its effectiveness in identifying peptides with exceptional precision and specificity. Phage display's value extends to probing protein ligand interactions, investigating receptor binding sites, and amplifying the efficacy of protein binding with their counterparts. Moreover, this technique aids in developing monoclonal antibodies, enhancing their affinity, isolating antibodies from unstable hybridoma cells, and revealing crucial elements like epitopes, mimotopes, and functional sites on antigens. Remarkably, the applications of phage display-derived methods extend to diverse domains including transfusion medicine, neurological disorders, mapping vascular destinations, and directing peptides to specific tissues. Notably, phages find significance in immunisation therapies, potentially introducing fresh tools for addressing autoimmune and cancer-related conditions. This presentation strives to expound upon the core principles of phage display technology, simultaneously shedding light on recent advancements in its therapeutic application, particularly in tackling cancer, underscored by the notable number of FDA-approved phage-displayed monoclonal antibodies for combating cancer.

Dr. Lim Kue Peng
Cancer Research Malaysia

Dr. Lim Kue Peng obtained her PhD from the University of Bristol and currently she leads the Cancer Immunology and Immunotherapy research team in Cancer Research Malaysia. Her research goal is to identify ways by which the immune system can be modulated for cancer treatment and develop effective immunotherapy for cancers that are common in the Asian region. Her recent work demonstrated that the vaccine that was developed based on the discovery of important cancer proteins can successfully induce anti-tumour response and clinical trials are currently being planned to evaluate this in patients. Dr. Lim is the recipient of the prestigious Loreal for Women in Science Award and has successfully received research grants both from local and international funding bodies including the Ministry of Science, Technology & Innovation Malaysia, the Newton-Ungku Omar Fund and the Global Challenges Research Fund from the Medical Research Council in the United Kingdom.

Abstract

Vaccine for Head and Neck Cancers

Kue Peng Lim[1*], Syafinaz Zainal[1], Natasha Zulaziz[1], Chai Phei Gan[1], San Jiun Chai[1], Chuan Wang[2], Christian Ottensmeier[2,3], Emma King[2], Gareth Thomas[2], Natalia Savelyeva[2,3] and Sok Ching Cheong[1]

1 Cancer Research Malaysia, 47500 Subang Jaya, Malaysia
2 Cancer Sciences, University of Southampton, UK.
3 Head and Neck Centre, Institute of Systems, Molecular and Integrative Biology, University of Liverpool, UK
*Corresponding author: kuepeng.lim@cancerresearch.my

The clinical benefit of immunotherapies relies heavily on the ability of T cell to identify antigens presented by tumour cells. As checkpoint blockade therapy has limited efficacy, tumour antigens have the potential to be exploited as a complementary treatment to this therapy. Our team identified MAGED4B and FJX1 to be overexpressed in head and neck cancers and promote tumour growth. Subsequent studies confirmed the immunogenic nature of these two tumour-associated antigens (TAAs) by demonstrating the presence of inherent antigen-specific T cells and the ability of these antigens to stimulate T cell expansion *ex vivo*. Full length DNA of these two TAAs was used to develop vaccine in the form of DNA plasmid. Encouragingly, this novel approach shown to be efficacious in controlling tumour growth *in vivo* and tumour inhibition is further enhanced when the cancer vaccine is used in combination with checkpoint blockade therapy. A bioinformatics study suggested our vaccine works to stimulate antigen presentation and hence augment T cell responses. This observation was confirmed when cancer vaccine-trained T cells successfully restored the antigen presentation in nasopharyngeal cancer cell lines that have compromised antigen presentation. As checkpoint blockade therapy works

by re-invigorating CD8 T cells, the ability to restore antigen presentation can complement its efficacy, especially in patients who have downregulated antigen presentation.

Symposium II

Associate Professor Dr. Chua Jia Xin
Universiti Tunku Abdul Rahman, Malaysia

Associate Professor Dr. Jia Xin Chua is a cancer immunologist with 14 years of experience in translational research. She is the member of AACR, EACR and BSI. She received her PhD degree in Oncology in 2016 (University of Nottingham, UK). During her PhD, she succeeded in developing a new technology to generate ultraspecific monoclonal antibodies against carbohydrate antigens and contributed to the development of the Avidimab antibody engineering technology, which enhances the avidity of monoclonal antibodies. The Avidimab platform has been patent protected and ready to be licensed. Two monoclonal antibodies she made during her PhD showed excellent efficacy to be used for near-infrared fluorescent (NIRF) imaging of gastrointestinal tumours with desirable safety profile. The monoclonal antibodies were patent protected and going into phase I clinical trial in cancer patients. Dr. Chua was first to demonstrate that these 2 monoclonal antibodies had potent anti-tumour efficacy in a metastatic colorectal tumour model, leading to significant long-term survival. In 2015, the discovery was recognised to contribute to the excellence in biomedical research by Medicine Innovates, which is a global leader in trustworthy and timely medical research news. In 2019, she generated a unique agonistic monoclonal antibody, which discovered a novel marker on stem memory T cells. The monoclonal antibody has been patent protected and currently being evaluated in the area of adoptive T cell transfer and CAR-T therapy. In 2022, her research work on COVID-19 was published in iScience (Cell Press), and she was invited to develop a Podcast on the work by Researchpod, UK.

Abstract

Isolation of Stem Memory T Cells (TSCMs): Implications for CAR-T Therapy

Chua Jia Xin

M. Kandiah Faculty of Medicine & Health Sciences, Universiti Tunku Abdul Rahman, Malaysia

Stem memory T cells (TSCMs) have self-renewal capacity and multipotency. TSCMs can reconstitute the full diversity of effector/memory T cell compartments and are superior in eradicating tumours. However, clinical exploitation of TSCMs remaining challenging due to their relative low percentage (2-4%) in the peripheral blood. This study describes an ultra-specific monoclonal antibody (mAb), 2811 against SSEA-4 and SSEA-4 expression on human and mouse TSCMs. Expression of SSEA-4 on human TSCM was determined by indirect

immunofluorescence with 2811 and co-stained with mAbs for CD3, CD122, CD45RA, CD45RO, CD62L and CD95. Purified T cells from healthy donors were labelled with CSFE, followed by stimulation with 2811 mAb and assessed *in vitro* for T cell proliferation by CSFE dilution. To confirm the SSEA-4+ T cells were TSCMs, we applied RNA sequencing to examine the transcriptome of SSEA-4+ T cells. The T cell agonistic effect of 2811 mAb *in vivo* was investigated in C57/B6 mice. 2811 stained 0.8-2.3% of PBMCs, which co-expressed CD3+CD45RA+CD62L+CD95+CD122+, suggesting that they were TSCMs. 2811 mAb could induce proliferation and differentiation of these cells, which remained viable for more than 2 months *in vitro* in the absence of exogeneous cytokines. Multiplexed cytokine assay revealed IL-7 and IL-21 cytokines were the key self-maintaining cytokines of TSCM cells. Transcriptomic analysis of SSEA-4+ T cells confirmed that they had a similar profile to putative TSCMs. Splenocytes harvested from C57/B6 mice immunised with 2811 showed increased percentage of different T cell subsets, which remained viable *in vitro* for over a month. 2811 is a unique mAb for identifying, isolating and inducing proliferation of putative TSCM cells, which may address the ongoing debate regarding the methodology for isolating and expanding TSCMs. We envision that 2811 mAb is a potential T cell agonistic mAb and 2811-isolated SSEA-4+ TSCMs are potential candidates for genetic manipulation to express cancer specific T cell receptors or chimeric antigen receptors (CARs).

Dr. Vita Golubovskaya
Promab Biotechnologies, USA

Abstract

Engineering Second, Third, and Next Generation CAR-T Cells

Vita Golubovskaya[1,*], John Sienkiewicz[1], Alan Zhang[1], Jinying Sun[1], Yanwei Huang[1], Liang Hu[1], Hua Zhou[1], Hizkia Harto[1], Shirley Xu[1], Robert Berahovich[1], Walter Bodmer[2] & Lijun Wu[1,3]

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3 Forevertek Biotechnology, Janshan Road, Changsha Hi-tech Industrial Development Zone, Changsha, Hunan 410205, China

Chimeric antigen receptor (CAR) T cell therapies such as CD19-CAR-T cells and BCMA-CAR-T cells have recently been approved by the FDA to treat lymphoma and multiple melanoma. Novel CAR-T cell therapies need to be developed to target resistant or recurrent haematological cancers as well as solid tumours. Novel second, third generation and next-generation CAR-T cells were developed and functionally validated, called bispecific CAR-T cells, that simultaneously targeted two tumour antigens such as CD19-CD37 and CS1-BCMA. In addition, next-generation Her-2-CAR-T cells which secreted GM-CSF or CCL-2 cytokines effectively blocked SKOV-3 ovarian tumour growth *in vivo*. In addition, several T cells engaging bispecific antibodies were designed that effectively killed solid tumours. Recently, a CAR mRNA-LNP platform has been developed to create functional CAR-NK cells. Moreover, mRNA-LNPs encoding an EpCAM-CD3 hFc bispecific antibody were also delivered intratumorally, effectively blocking colon tumour xenograft growth in mice. These novel CAR-T cell therapies, and mRNA-LNP applications for developing CAR-NK cells and bispecific antibodies can be used for future clinical trials.

Associate Professor Dr. Herbert Schwarz
National University of Singapore

Abstract

DC Vaccines for Solid Tumours

Herbert Schwarz

Yong Loo Lin School of Medicine, National University of Singapore

Cancer immunotherapy has finally reached a stage where it is able to prolong patient survival. Immune checkpoint inhibitors and chimeric antigen receptors can be very successful in the treatment of haematological malignancies but their efficacy for solid cancers is limited. Cancer vaccination offers the possibility to induce effective immune responses also against solid cancers. This talk will give an overview on the different available cancer vaccination methods. We developed a cancer vaccine based on a new type of dendritic cell (DC), that are being generated by a CD137 ligand (CD137L) agonist, and that display enhanced potency. In a phase I study, 12 nasopharyngeal carcinoma (NPC) patients were administered CD137L-DC that were pulsed with Epstein-Barr virus (EBV) antigens. Treatment was well tolerated. One partial response (PR) was obtained, and 4 patients are still benefitting from a progression free survival (PFS) of currently 4 years. Patients with clinical benefit had lower plasma EBV DNA levels, and a reduction after vaccination, indicating that this vaccine induces an anti-EBV and anti-NPC immune response, and warranting further studies.

Symposium III

Professor Dr. Chin Sze Piaw
Cytopeutics Sdn. Bhd., Cyberjaya, Selangor, Malaysia
Universiti Tunku Abdul Rahman, Malaysia

Dr. Chin Sze Piaw is a co-founder of Cytopeutics. He is also a practicing medical specialist who obtained his MBBS in 1995 and his MRCP in 1998. Dr. Chin is an Adjunct Professor and Honorary Fellow of the Centre for Stem Cell Research at UTAR, and a Lecturer at UMSC focusing on the Advanced Masters in Regenerative Medicine. Dr Chin has served on expert committees for clinical practice guidelines, and several research and registry steering committees for cardiovascular disease and stem cell research. Dr Chin has over 60 publications in international peer-reviewed journals and presented at international medical conferences for the demonstration of clinical anti-inflammatory and immunomodulatory actions of mesenchymal stem cells (MSC) in cardiomyopathy, stroke and diabetes complications and osteoarthritis. Dr Chin was jointly awarded patents from the USA for his pioneering use of MSC treatment for acute stroke, vernal keratoconjunctivitis and diabetes and has been a joint recipient of numerous grants including the MOSTI Technofund. Most recently, Dr. Chin was nominated by MOSTI and endorsed by the MOE for the UNESCO Life Sciences Researcher Award.

Abstract

MSCs in GVHD Management

Sze-Piaw Chin[1,2]

1 Cytopeutics Sdn. Bhd., Cyberjaya, Selangor, Malaysia
2 M. Kandiah Faculty of Medicine & Health Sciences, Universiti Tunku Abdul Rahman, Malaysia

Mesenchymal stem cells (MSCs) have attracted attention for their immunomodulation property that is achieved through the release of various mediators in response to injury with subsequent tissue regeneration. We have demonstrated the therapeutic potential of Cytopeutics® MSCs in various ischemic and inflammatory disorders such as ischemic stroke, diabetes and acute graft-versus-host disease (aGVHD). aGVHD is a devastating complication of bone marrow transplant for lymphoma and leukaemia with up to 50% 1-year mortality. Survival appears to be correlated with promptness and completeness of response to initial therapy. In 2016, Japan had approved the use of allogenic mesenchymal stem cell for children with aGVHD refractory to steroid treatment. MSC therapy improved overall response but mortality rate was still high. In 2018 Cytopeutics along with senior haematologists in Malaysia decided to explore the

upfront use of Cytopeutics® MSCs in combination with standard treatment instead. The study was approved by the MREC and NCERT. We obtained the precedent CTX from the NPRA under the new enforcement of CGTP regulations. The study was jointly sponsored by the MOSTI Smartfund. This ambitious double blind randomised placebo-controlled phase I-II clinical trial began at MOH Ampang Hospital and later extended to Sunway Medical Centre, Hospital Universiti Kebangsaan Malaysia and Hospital Sultanah Aminah Johor. The lecture today will provide the interim results of the study which demonstrated faster and sustained complete response with better overall, relapse-free and disease-free survival in aGVHD patients with the upfront use of Cytopeutics MSCs.

Associate Professor Dr. Law Zhe Kang
Universiti Kebangsaan Malaysia

Associate Professor Dr. Law Zhe Kang is a consultant neurologist and an Associate Professor at the Faculty of Medicine, Universiti Kebangsaan Malaysia / Hospital Canselor Tuanku Muhriz. He completed his neurology training in 2016 followed by a PhD in stroke medicine at the University of Nottingham, UK in 2019. He was the national coordinator for the TICH-2 and the ongoing Tranexamic acid for hyperacute spontaneous IntraCerebral Haemorrhage (TICH-3) randomised controlled trial. He was also involved as an investigator for several international stroke randomised controlled clinical trials. He was the first author of "The effects of intravenous infusion of autologous mesenchymal stromal cells in patients with subacute middle cerebral artery infarct: A phase 2 randomized controlled trial on safety, tolerability and efficacy" published in Cytotherapy. He has >70 journal article publications to date including in the Lancet, JAMA Neurology, European Stroke Journal, Stroke, International Journal of Stroke, Translational Stroke Research and Cochrane Systematic Reviews. He is a reviewer for several high impact stroke/neurology journals. He is an editorial board member for the European Stroke Journal and associate editor for Neurology Asia. He is currently a World Stroke Organisation Future Stroke Leader.

Abstract

BM-MSCs in Stroke Management

Law Zhe Kang

Faculty of Medicine, Universiti Kebangsaan Malaysia

Mesenchymal stem cells had been considered a promising treatment for patients with ischaemic stroke. We conducted a phase 2, single-centre, assessor-blinded randomised controlled trial to investigate the safety and efficacy of intravenous autologous bone marrow-derived MSCs (BMMSCs) in patients with subacute middle cerebral artery (MCA) infarct, which is now published in Cytotherapy. We recruited 17 patients with severe ischemic stroke involving the MCA territory within 2 months of stroke onset. Using permuted block randomisation, 9 patients were assigned to receive 2 million BMMSCs per kilogram of body weight (treatment group) and 8 standard medical care (control group). All patients were severely disabled following their MCA infarct (median mRS = 4.0 [4.0 5.0], BI = 5.0 [5.0 25.0], NIHSS = 16.0 [11.5 21.0]). The baseline infarct volume on the MRI was larger in the treatment group (median, 71.7 [30.5 101.7] mL versus 26.7 [12.9 75.3] mL, P = 0.10). There were no between-group differences in median NIHSS score (7.0 versus 6.0), mRS (2.0 versus 3.0) or BI (95.0 versus 67.5) at 12 months. At 12 months, there was significant improvement in absolute change in median infarct volume, but not in total infarct volume, from baseline in the treatment group (P = 0.027). No treatment-related adverse effects occurred in the BMMSC group. In conclusion,

intravenous infusion of BMMSCs in patients with subacute MCA infarct was safe and well tolerated. Although there was no neurological recovery or functional outcome improvement at 12 months, there was an improvement in the absolute change in median infarct volume in the treatment group. In this talk, other trials of stem cell therapies in ischaemic stroke will also be discussed. The design of an ongoing randomised controlled trial on allogenic MSCs for ischaemic stroke will also be shared.

Associate Professor Dr. Badrul Hisham Bin Yahaya
Advanced Medical and Dental Institute, Universiti Sains Malaysia

Dr. Badrul Hisham Bin Yahaya, PhD, currently serves as the Principal Investigator at the Department of Biomedical Sciences within the Advanced Medical and Dental Institute at Universiti Sains Malaysia. Dr. Badrul has a rich professional background, having previously held the position of Director at the Animal Research and Service Centre (ARASC) at Universiti Sains Malaysia in Penang. Dr. Badrul's educational journey includes obtaining a Bachelor of Science degree with Honors in Genetics from Universiti Kebangsaan Malaysia in 2002, followed by a Master of Science in Human Genetics from Universiti Sains Malaysia in 2006. His academic pursuits took him to the Roslin Institute and Royal (Dick) School of Veterinary Studies at the University of Edinburgh, Scotland, where he completed his PhD degree. In the realm of professional associations, Dr. Badrul is an active member of various national and international societies. His expertise in stem cell and regenerative medicine has led to numerous invitations from both local and international organisations to present his groundbreaking research findings at global scientific gatherings. He plays an integral role in the Tissue Engineering and Regenerative Medicine Society of Malaysia (TESMA) and the Malaysian Society for Stem Cell Research and Therapy.

Additionally, Dr. Badrul currently holds the position of Visiting Professor at Xinxiang Medical University (XXMU) in Henan Province, China. He plays a pivotal role in international collaborations, serving as the coordinator for research and academic initiatives with Xinxiang Medical University, China; Mahidol University, Thailand; and Universitas Padjadjaran, Bandung, Indonesia. In the realm of scholarly publications and editorial responsibilities, Dr. Badrul is the Editor-in-Chief of the Journal of Biomedical and Clinical Sciences (JBCS), published by AMDI USM. He also serves as an Editor for Stem Cell Biology and Regenerative Medicine (Springer-Nature) and Series Editor for Tissue Engineering - Part A. His editorial contributions extend to other esteemed journals, including Biomedical Research and Therapy (BMRAT) in Vietnam, Majalah Kedokteran Bandung, The Global Medical and Health Communication (GMHC) journal in Bandung, and Stem Cells in Clinical Applications (Springer-Nature).

With a passionate focus on stem cell and regenerative medicine, Dr. Badrul has secured research grants from various funding bodies, including Universiti Sains Malaysia, the Ministry of Science, Technology and Innovation (MOSTI) of Malaysia, the National Institute of Health/Ministry of Health (NIH/MOH) in Malaysia, and the Ministry of Higher Education, Malaysia, among others. He has also received international grants, such as those from the Nippon Sheet Grant Foundation (NSGF) and funding from Henan Province, China, as well as industry matching grants, notably from Cryocord Sdn. Bhd., to advance research in various facets of stem cell and regenerative medicine. Dr. Badrul's remarkable contributions to the field are reflected in his extensive publication record, which includes over 95 articles in various indexed journals and chapters in books related to stem cell research, cell therapy, tissue

engineering, cancer stem cells, and disease modelling. He has also played a pivotal role in postgraduate education, supervising 33 postgraduate students, with 18 of them successfully completing their studies under his guidance, focusing on various aspects of research related to stem cell and regenerative medicine.

Abstract

Breathing New Life: Exploring Extracellular Vesicles as Therapeutic Agents in Respiratory Diseases

Badrul Hisham Yahaya*, Lian Jie, Noridzzaida Ridzuan, Nur Shuhaidatul Sarmiza Abdul Halim, Egi Kardia, Syahidatulamali Che Shaffi

Lung Stem Cell and Gene Therapy Group, Department of Biomedical Sciences, Advanced Medical and Dental Institute (IPPT), SAINS@BERTAM, Universiti Sains Malaysia, Penang, Malaysia
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Over the past decade, there has been an industrial expansion, and patient interest surrounding stem cell-based interventions. This heightened attention has also given rise to a growing number of direct-to-consumer enterprises offering stem cell "therapies" across various medical conditions, often with limited empirical evidence substantiating their safety and efficacy. Concurrently, the utilization of stem cell secretomes and/or extracellular vesicles (EVs) as a viable alternative to stem cell transplantation has gained prominence within the realm of regenerative medicine. Currently, multiple clinical trials are underway to evaluate the safety and effectiveness of these agents. Nevertheless, this burgeoning field has not been immune to opportunistic businesses and private clinics, which are capitalising on the trend by offering secretome/extracellular-based interventions despite the paucity of supporting data. One specific area where stem cell-based approaches are receiving considerable attention is chronic obstructive pulmonary disease (COPD). Secretomes and EVs, released by a variety of cell types, play a pivotal role in paracrine and extracellular communication. Recent breakthroughs in this field have brought to light the therapeutic potential of stem cell-derived EVs, demonstrating their comparability to the parent cells in terms of efficacy. This study presents a novel exploration into the molecular mechanisms through which extracellular vesicles, derived from mesenchymal stem cells (EV-MSCs), enhance pulmonary inflammatory injury. Our findings indicate that MSC-derived EVs exhibit a remarkable capacity to mitigate inflammation induced by COPD. These discoveries open the door to a promising avenue of research, suggesting that EVs could serve as a novel cell-free therapeutic approach for the treatment of respiratory diseases. This research not only contributes to our understanding of the intricate interplay between stem cell-derived EVs and respiratory disease but also underscores the potential of EV-based therapies as a groundbreaking advancement in regenerative medicine. As we delve deeper into this uncharted territory, it becomes increasingly evident that the utilisation of EVs holds immense promise, offering a new dimension in our quest to alleviate the burden of respiratory diseases and potentially revolutionise treatment strategies for various other medical conditions.

Symposium IV

Dr. Zalina Mahmood
MD (USM), MMED (TRANSFUSION MEDICINE, USM)
National Blood Centre Malaysia

Dr. Zalina graduated from the University Science Malaysia in 2000 and later she completed her Masters of Medicine (MMed) in Transfusion Medicine, University Science Malaysia in 2011. Dr. Zalina had recently finished off her subspecialty training in regenerative medicine focusing on the cell & plasma/serum therapy involving blood component and cord blood. She is currently the Head of Production, Plasma Fractionation & Blood Supply Management Division at National Blood Centre Malaysia.

Abstract

New Applications of Cord Blood

Zalina Mahmood

National Blood Centre, Kuala Lumpur, Malaysia

Umbilical Cord Blood (UCB) contains relatively heterogeneous cell populations including haematopoetic stem cells (HSC), mesenchymal stem cells (MSCs), multipotent adult progenitor cells, unrestricted somatic stem cells, endothelial progenitor cells and immature immune cells. These cells are capable of giving rise to hematopoietic, epithelial, endothelial, neural and other tissues. Thus, it has a potential to treat a wide variety of diseases including cardiovascular, ophthalmic, orthopaedic, neurological and endocrine diseases. Among all, the most commonly studied was neurological disorders such as cerebral palsy (CP), hypoxic ischaemic encephalopathy (HIE) and autism spectrum disorder (ASD). Other disorders include diabetes mellitus, cardiac and vascular diseases as well as hepatic diseases. Even though many preclinical and initial clinical (safety and feasibility) studies are quite convincing, the lines of investigation are still in the early stages as evidenced by the fact that the majority of the clinical studies are Phase 1 or combined Phase 1/2.

Dr. Becky Griffiths
Australian Red Cross, Australia

Abstract

Generation of Red Cells from iPSC and Erythroid Cell Lines

Becky Griffiths

Australian Red Cross, Australia

Fully functional cultured red blood cells (cRBCs) can be grown in the laboratory from haematopoietic stem cells (HSCs) isolated from adult peripheral blood, cord blood or bone marrow. There are numerous advantages of cRBCs over donated RBCs: (1) Greater transfusion efficacy due to increased lifespan in comparison to donor RBCs, (2) Reduced immunisation risk for those who have rare blood group antigens or are multi-transfused, (3) Minimisation of infection risk and (4) Constant availability due to stem cell banks. However, primary HSCs have a finite proliferative capability and are technically challenging to genetically manipulate. Alternative stem cell sources for RBC production which are both sustainable and genetically malleable such as iPSC and immortalised erythroid cell lines have been developed and continue to be explored yet fail to recapitulate erythropoiesis as well as primary derived HSC stem cell sources. The benefits and challenges of iPSC and erythroid cell line derived RBCs will be considered and discussed.

Associate Professor Dr. Ngaire Elwood
BMDI Cord Blood Bank, Melbourne, Australia
Murdoch's Children Research Institute, Melbourne, Australia

Associate Professor Dr. Ngaire Elwood is the Director of the BMDI Cord Blood Bank in Melbourne and serves as Chair of the AusCord network of public cord blood banks. Dr. Elwood has played a key role in development of the FACT Standards for Cord Blood Banking, is a FACT Cord Blood Bank inspector, serves on the FACT Accreditation Committee and Regenerative Medicine Taskforce. and is Chair of the Education Committee. She is also Head of the Cord Blood Advanced Therapies Research Laboratory at the Murdoch Children's Research Institute where the current focus is on creation of GMP-grade induced pluripotent stem cells for potential therapeutic use, and clinical trials using cord blood for cardiac repair in children. She is immediate past - Vice President of the FACT Board of Directors, is Chair of the Board of Australian Sickle Cell Advocacy Ltd and holds various board appointments on the Cord Blood Association, National Stem Cell Foundation of Australia, and the International Society for Cell & Gene Therapy.

Abstract

iPSC Banking from Cord Blood Sources

Ngaire Elwood[1,2,3], Keren Abberton[1,2], Junann Whish-Wilson[1,2], Kawa Choi[1,2], Denise Tsoutras[1,2], Trish McDonald[1,2], Pei Tian[1,2]

1 BMDI Cord Blood Bank, Melbourne, Australia
2 Murdoch Children's Research Institute, Melbourne, Australia
3 Department of Paediatrics, University of Melbourne, Melbourne, Australia

Induced pluripotent stem cells (iPSCs) can be differentiated into any cell in the body. Banked cord blood (CB) is an ideal source of starting material for the creation of iPSCs, with many advantages not found in other cell sources. An iPSC bank derived from CB selected on the basis of human leukocyte antigens (HLA) homozygosity could form the basis of future cell-based therapies. The BMDI Cord Blood Bank (CBB) in Melbourne is a government-funded public cord blood bank. The bank holds a Good Manufacturing Practice (GMP) cell-manufacturing licence from the Therapeutic Goods Administration (TGA) and is internationally accredited by the Foundation for the Accreditation of Cellular Therapy (FACT). Our aim is to create and manufacture a bank of GMP-compliant CB-derived iPSCs of HLA homozygous haplotypes for potential therapeutic use. We have developed a process for reconsent of CB donors to use a portion of their banked CB to create iPSC lines for potential new cellular therapies (https://doi.org/10.1093/stcltm/szac060). We have developed methodology to create "GMP-like" iPSCs from banked CB (https://www.frontiersin.org/articles/10.3389/fcell.2022.835321/full). This technology has now been transitioned from the research lab to be GMP-compliant, mimicking the Quality

Systems in place for the CBB. We have established an Institutional Biosafety Committee (IBC)-approved PC2 laboratory co-located within the GMP-compliant CBB facility. In addition to the physical space, we have developed a Quality Systems framework, with processes in-line with the FACT Common Standards for Cellular Therapy, leveraging off those in place for the CBB. A full mock run has been completed to test and validate the process in its entirety, resulting in the creation of new CB-derived "GMP-mock" iPSC lines. We are now in the process of creating our first fully GMP-compliant HLA homozygous CB-derived iPSC line. Collaborations have been established for pre-clinical studies to use our CB-derived iPSC lines for therapies directed towards retinal and neurological repair, NK and CAR-NK immunotherapies. Proof of principle has been established for a GMP-compliant CB-derived iPSC bank, co-located and leveraging the BMDI CBB. Production of iPSC lines for potential clinical use extends the utility of the public CBB inventory, and value-adds to the altruistic donations of those who donate this precious resource.

Symposium V

Dr. Leow Chiuan Yee
Universiti Sains Malaysia

Dr. Leow obtained a PhD in infection and immunity from the University of Queensland, Australia. His PhD thesis worked on the investigation of the potential vaccines targeting against schistosome infection. In 2010, he received an Edward Jenner Award from Australian Centre for Vaccine Development (ACVD) for his scientific contribution in vaccine development against parasitic disease. During his doctoral study, he spent a short-term clinical training at QPharm Pty Ltd at Brisbane, Australia to conduct several human vaccines at clinical level. Upon his doctoral completion, in 2013, he worked as a postdoctoral scientist at Molecular Immunology Laboratory at QIMR Berghofer Medical Research Institute to investigate the roles of T cells in initiating immunity against chronic malaria and human colorectal cancer. In September 2014, Dr. Leow joined School of Pharmaceutical Sciences at Universiti Sains Malaysia as a senior lecturer. In 2019, he received a fellowship from Institute for Glycomics at Griffith University in Gold Coast Australia to investigate the vaccine development against gonorrhoea. Dr. Leow is currently a supervisor of 5 PhD projects while he has graduated 4 PhDs and 7 Master students to date. Meanwhile, he has already been the advisor of 17 research projects and has designed and participated in several international/industrial collaborative projects. Dr. Leow has published more than 40 scientific papers in the international journals and has presented more than 60 lectures/posters in congresses/meetings/public media. Dr. Leow's primary research interest focuses on the understanding of the molecular basis of immunity associated with infectious diseases and cancers. The principal aim of the research is to identity potential vaccine and therapeutics targets for immunotherapeutic development.

Abstract

Exploring the Impact of T-Cell Exhaustion on CAR-T Cell Therapy

Leow Chiuan Yee

School of Pharmaceutical Sciences, Universiti Sains Malaysia, Pulau Pinang, Malaysia

Tumour immunotherapy has emerged as a promising therapeutic approach, with cytotoxic T cells playing a pivotal role in combating cancer. Among these, chimeric antigen receptor T-cell (CAR-T-cell) therapy has revolutionised haematological cancer treatment. Despite the success of CAR-T-cell therapy in haematological cancers, the exhaustion of T cells, particularly in solid tumours, presents a challenge. The interplay between "stimulatory" and "suppressive" signals regulating immune responses is disrupted in cancer and pathogenic invasion, with the

programmed-cell-death-1 (PD-1) receptor and its ligands (PD-L1 and PD-L2) contributing to immune suppression. Intriguingly, PD-L2's interaction with galectin-9 (GAL9) unfolds as a key regulatory mechanism. GAL9's elevated expression on activated immune cells forms lattice-raft structures, fostering dense immune molecule clustering. Innovative approaches utilising multimeric PD-L2 protein and an anti-GAL9 antibody stabilise the lattice-raft, enhancing co-stimulatory molecule expression, TNF secretion, and reducing inhibitory molecules. The anti-GAL9 antibody demonstrates promise *in vitro* and in pre-clinical models, holding potential as a multifaceted immunotherapeutic strategy to counter T-cell exhaustion and reinforce CAR-T-cell therapy outcomes for solid tumours.

Professor Dr. Ho Gwo Fuang
Universiti Malaya, Malaysia

Dr Ho Gwo Fuang is a Professor and clinical oncologist at University Malaya Medical Centre and University Malaya Specialist Centre, Kuala Lumpur, Malaysia. He was trained at Barts and The London National Health Service (NHS) Trust and The Royal Marsden NHS Trust in London. He attained his Certificate for Completion of Specialist Training (CCST) in 2007 and joined the Faculty of Medicine at University Malaya. His research interests involve breast, gastrointestinal and hepatobiliary cancers. He is involved in many national and international collaborative research work, as well as the training of new oncologists in Malaysia.

Abstract

Cytokine-Induced Killer (CIK) Cells and Dendritic Cell (DC) vaccines Have Emerged as Promising Tools in Cancer Immunotherapy

Ho Gwo Fuang

Faculty of Medicine, University Malaya, Malaysia

Cytokine-Induced Killer (CIK) cells exhibit MHC-unrestricted killing. CIK cells have a unique ability to target and eliminate tumour cells without requiring direct recognition of specific MHC-peptide complexes, due to the expression of both NK (natural killer) cell receptors and T cell receptors on CIK cells, enabling them to recognize stress-induced molecules or other factors on the surface of tumour cells. Because MHC-unrestricted killing does not rely on the presence of specific MHC-peptide complexes, it offers potential advantages in cancer immunotherapy, as it can target a broader range of tumour cells and might bypass some immune evasion mechanisms employed by tumours. Dendritic cells, the sentinels of the immune system, play a pivotal role in orchestrating immune responses. DC vaccines involve loading these cells with tumour antigens to enhance antigen presentation and T-cell activation, thereby priming a targeted anti-tumour response. Combining CIK cells with DC vaccines synergistically amplifies the immune cascade, bolstering both innate and adaptive immunity against malignancies. The dynamic interplay between CIK cells and DC vaccines may generate synergistic effect in cancer immunotherapy. By harnessing the inherent strengths of both approaches, a better anti-cancer immune response can be achieved, paving the way for more effective and tailored therapeutic strategies in oncology.

Symposium VI

Dr. Michaela Seng
Department of Paediatric Haematology/Oncology, KK Women's and Children's Hospital, Singapore

Dr. Michaela Seng is a paediatric haematologist/oncologist with a clinical niche in haematopoietic stem cell transplant (HSCT) and a research interest in translational cell therapies. She graduated from NUS, completed paediatric training in Singapore, and further specialised in paediatric oncology and transplant in Sydney, Australia. Dr. Seng is the PI of several early phase novel cell therapy trials including a tandem dual CAR-T trial and an adoptive COVID-specific T cell trial. She has been involved in the entire process from the conceptualization of the studies, manufacturing validations, regulatory submissions, IIT negotiations, setting up of correlative assays, generation of pilot clinical data, and the final authorisation of the investigator-initiated clinical trials. Dr. Seng serves as the BMTCT clinical facility director and BMTCT research lead in the Children's Blood and Cancer Centre, with the goal to drive the collaborative translation of innovative cell therapies in paediatric oncology.

Abstract

Managing CAR-T Complications

Michaela Seng

Department of Paediatric Haematology/Oncology, KK Women's and Children's Hospital, Singapore

Recognising and managing toxicities encountered by patients following CAR-T cell therapy are critical to successful patient outcomes. The lecture will provide an overview of CAR-T associated adverse events, and the set up required in a paediatric CAR-T programme. Using case studies primarily in paediatrics, we will discuss the medical management and interventions employed to address these complications, emphasising the importance of vigilant monitoring and prompt intervention to optimise patient outcomes. Through this lecture, healthcare professionals will gain valuable insights into the nuances of post-CAR-T complications and their management. The presentation aims to foster meaningful discussions and knowledge exchange among attendees, empowering them to provide high-quality, patient-centred care in the realm of cell and gene therapies.

Dr. Tan Sen Mui
Hospital Ampang, Malaysia

Dr. Tan Sen Mui obtained her basic medical degree locally and MRCP in UK. She started haematology training in the Ministry of Health, Malaysia in 2001 and subsequently has her training in stem cell transplantation followed by research in cancer immunotherapy in the University of Wuerzburg, Germany. She has special interest in cancer immunotherapy and actively participated in clinical trials. Currently, she is the senior consultant haematologist & Head of Department for the Department of Haematology in Hospital Ampang, which is the main haematology referral centre in Malaysia. She is also the past secretary of Malaysian Society of Haematology (MSH) and member of the European Society for Blood and Marrow Transplantation (EBMT).

Abstract

CAR-T Therapy in Malaysian Public Hospitals

Dato Dr. Chang Kian Meng
Sunway Medical Centre, Kuala Lumpur, Malaysia

Dato' Dr. Chang Kian Meng is an acknowledged expert in haematologic malignancies and in stem cell and bone marrow transplants. He was previously the head of haematology service of Ministry of Health, Malaysia and head of department of haematology in Ampang Hospital before he retires from public service. He is currently the consultant haematologist and transplanter based in Sunway Medical Centre.

Abstract

Overview of CAR-T therapy in Haematological Malignancies

Symposium VII

Ms. Amanda Choong Jyeyi
Sunway Medical Centre, Kuala Lumpur, Malaysia

Choong Jyeyi is a highly experienced and dedicated nurse with a career spanning 14 years in the healthcare field. She has established herself as a prominent figure in the realm of oncology nursing, with a strong focus on haematology oncology and stem cell transplantation. In 2012, Choong Jyeyi achieved a significant milestone by completing her Oncology Post Basic training, demonstrating an early commitment to specialised care in the field of oncology. This foundation sets the stage for a remarkable journey in cancer care.
Choong Jyeyi further solidified her expertise by obtaining a Bachelor of Nursing degree in 2015, which enriched her knowledge and skill set, making her an even more valuable asset to the healthcare community. Since 2012, Choong Jyeyi has been an integral part of the oncology nursing community, dedicating her career to providing compassionate and comprehensive care to cancer patients. She specialised in haematology oncology, a field known for its complexities, and thrived in the challenging environment of stem cell transplantation. In recognition of her expertise and passion for oncology nursing, Choong Jyeyi transitioned into the role of an Oncology Nurse Educator in 2016. For four years, she shared her extensive knowledge and experiences with aspiring nurses, shaping the next generation of oncology caregivers. Currently, Choong Jyeyi holds the prestigious position of Senior Manager at Sunway Cancer Centre, where she leads and influences cancer care initiatives. Her leadership is instrumental in the success of the center, and she continues to drive innovation and excellence in patient care. Choong Jyeyi's contributions to the field of oncology nursing extend beyond the clinical setting. She is widely respected for her dedication, empathy, and commitment to improving the lives of cancer patients and their families. Her work reflects her enduring passion for oncology and her unwavering commitment to advancing patient care.

Abstract

Cell Therapy: Roles and Functions of Nurses in Navigating the Patient Through the Treatment Process

Choong JyeYi

Cancer Centre, Sunway Medical Centre, Kuala Lumpur, Malaysia

Cell therapy is a rapidly evolving treatment modality that offers a new hope for patients with a variety of diseases and conditions. As cell therapy becomes increasingly available to patients, nurses play a critical role in guiding patients through the treatment process. The roles and

functions of nurses are navigating patients through the cell therapy treatment process, including patient education, assessment, and coordination of care. There are many unique challenges and opportunities presented by cell therapy, including issues related to patient selection, adverse events, and long-term follow-up. Patient education in the context of cell therapy, including the need to inform patients about the potential benefits and risks of treatments as well as the need for close monitoring and follow-up care, is important. Nurses plays a critical role in facilitating communication and collaboration among members of the healthcare team, including physicians, pharmacists, and other healthcare providers. In addition, nurses also need to address the ethical and legal considerations that arise in the context of cell therapy, including issues related to informed consent, privacy, and confidentiality. Ultimately, nurses play a critical role in the successful implementation of cell therapy. By providing patients with high-quality care and support throughout the cell therapy treatment process, nurses can help optimize patient outcomes and improve the overall quality of care for patients undergoing this promising treatment modality.

Ms. Seery Zaliza Azura binti Zaider
Hospital Canselor Tuanku Muhriz - UKM Medical Centre

Staff Nurse Seery completed 3 years of basic nursing training in 2005 at KPJ University College. She obtained her Degree in Nursing from Open University Malaysia and also underwent a special attachment at the National University Hospital in Singapore for a match unrelated transplant. She has 18 years of working experience in haematology as a stem cell transplant nurse, transplant coordinator and study nurse coordinator. She is currently working at Hospital Canselor Tuanku Muhriz - UKM Medical Centre.

Abstract

Stem Cell Transplantation Treatment: Specific Population with Financial Implication

Seery Zaliza Azura binti Zaider

Hospital Canselor Tuanku Muhriz - UKM Medical Centre, Kuala Lumpur, Malaysia

Hematopoietic stem cell transplantation (HSCT) is a high intensity procedure with the intention of curing acute leukaemia, high grade or relapsed lymphoma, multiple myeloma and benign haematological diseases such as thalassemia in both paediatric and adult patients. It is categorised according to the source of stem cells: autologous (patient's own stem cells), allogeneic (related or unrelated HLA-matched donor, related and unrelated HLA-mismatch donor) or haploidentical family donors. Since the first procedure in 1987, HSCT services are now widely offered in thirteen Malaysian healthcare providers, i.e., government subsidised public hospitals and university hospitals with partial funding from the Ministry of Education and private institutions. HSCT procedures involve a complex coordination between clinicians, diagnostic laboratory, stem cell laboratory, stem cell registry and pharmacy. In addition, financial hardships incurred to patients often becomes a limiting factor for a timely transplant. In cases of allogeneic unrelated donors, the cost of HLA typing and stem cell procurement are individually funded although the actual transplant itself is heavily subsidised, especially in government institutions. The government's HSCT fund assistance offers care package inclusive of the first 100 days, however this often excludes the costs of non-formulary drugs, including immunoglobulin and new generation antifungal or antiviral prophylaxis. Most patients often required time off from work upon the initial diagnosis of cancer. In addition, the majority of patients have already exhausted a large amount of savings and / or insurance at initial disease work-up investigations and during hospitalisations for induction, consolidation, or re-induction chemotherapies. In view of segregation of facilities between the three major healthcare sector providers in Malaysia, access to HSCT services and subsequent patients' eligibility for funding assistance are subjected to a thorough socio-economic evaluation by the stem cell coordinator and hospital social worker. In general, the cost of HSCT in public institution is estimated at RM 50,000 (USD 15,000) while the cost is higher at RM200,000 (USD 50,000) in private

institutions. Financial hardships experienced by HSCT patients, especially those with a lower socio-economic status, those with no regular income, and those with limited to no insurance coverage, have unfavourable impacts on their long-term survival outcomes. They are less likely to adhere to post-transplantation treatment regimens due to difficulty paying hospital bills or to be less compliant with outpatient appointment schedules due to travel costs. Unfortunately, there is no easy and immediate solution to address this issue. However, current efforts from both government agencies and non-governmental organisations may be improved further by rising awareness and health education in the community. Innovative financial hardship screening tools and subsequent models for access to government assistance must be improvised to better support those high-risk patients so that they are not discouraged from having access to this potentially life-saving procedure.

Symposium VIII

Dr. Law Jia Xian
Centre for Tissue Engineering and Regenerative Medicine (CTERM), Faculty of Medicine, Universiti Kebangsaan Malaysia

Dr. Law Jia Xian is a senior lecturer at the Centre for Tissue Engineering and Regenerative Medicine (CTERM), Faculty of Medicine, Universiti Kebangsaan Malaysia (UKM). In 2011, he successfully obtained his Bachelor's degree in Biomedical Science from UKM, and later in 2016, he completed his PhD in Tissue Engineering, also at UKM. Throughout his doctoral studies, his research focused on exploring the potential of utilising a combination of skin cells and platelet-rich plasma to enhance the healing process of full-thickness wounds. Presently, clinical trials are underway to further investigate this innovative approach. Dr. Law has contributed significantly to the scientific community with over 50 published articles in international peer-reviewed journals and book chapters, resulting in a h-index of 18 according to Web of Science. Moreover, he has served as a reviewer for several esteemed journals known for their high impact. Additionally, Dr. Law plays a pivotal role as the Head of Internationalisation Frontiers in CTERM, actively fostering collaborations with international and industrial partners for research endeavours. Dr. Law's research interests encompass the exploration of stem cells, particularly mesenchymal stem cells (MSCs), and stem cell-secreted extracellular vesicles (EVs) in regenerative medicine, ranging from their therapeutic applications in various medical conditions to the development of improved production methods. His ongoing projects revolve around exploring the applications of stem cells and EVs in treating various conditions, including osteoarthritis, atopic dermatitis, frailty, and skin rejuvenation. Furthermore, he actively explores methods such as utilising bioreactors and developing in-house preparations of human platelet lysate (HPL) to enhance the production of stem cells and EVs on a larger scale. Another area of his research involves investigating the use of natural killer cell-derived EVs (NK-EVs) as an immunotherapy for the treatment of malignancies.

Abstract

MSC and Cartilage Tissue-derived Extracellular Vesicles to Treat Osteoarthritis

Chiew Yong Ng[1], Min Hwei Ng[1], Ying Yang[2], Jhi Biau Foo[3], Chee Wun How[4], Kien Hui Chua[5], Nor Hamdan bin Mohamad Yahaya[6], Jia Xian Law[1]
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Extracellular vesicles (EVs) are membrane-bound vesicles secreted by cells. EVs are rich in biological molecules, including nucleic acids, proteins and lipids, that are known to promote tissue regeneration, including the cartilage tissue. As the content of the EVs varies according to its parent cells, it is important to compare the functionality and efficacy of different sources of EVs in supporting cartilage repair in order to identify the optimal source of EVs for the treatment of cartilage injury. In this study, experiments were performed to compare the efficacy of human umbilical cord mesenchymal stem cell (UC-MSC)-derived EVs (MSC-EVs) and human cartilage tissue-derived EVs (cartilage-EVs) in promoting cartilage regeneration. EVs were collected from passage five UCMSCs and partially digested cartilage tissue using the ultrafiltration and tangential flow filtration methods. The isolated EVs were characterised using the nanoparticle tracking analysis, bicinchoninic acid assay and Western blot in accordance to the MISEV2018 recommendation. Then, the effects of EVs on chondrocyte viability, proliferation, migration and extracellular matrix (ECM) gene expression were analysed. Results showed that the size of MSC-EVs and cartilage-EVs were 85.1 ± 1.4 nm and 95.8 ± 0.6 nm, respectively. The MSC-EVs were positive for CD63 and HSP70 as well as negative for GRP94 whilst cartilage-EVs were negative for all these markers. The EVs were readily uptake by the chondrocytes. The MSC-EVs were found to increase the chondrocyte proliferation but did not influence the migration and ECM gene expression. On the other hand, cartilage-EVs increased the gene expression of type II collagen and cartilage oligomeric matrix protein but demonstrated no effect on chondrocyte proliferation and migration. These findings indicated that the functionality of EVs varies according to its cell origin, and this is likely due to differences in the EV's cargo. Thus, it is important to characterise the protein and nucleic acid contents of EVs to understand its functionality and mechanism of action. Based on the findings, it is also postulated that combination of MSC-EVs and cartilage-EVs might be more efficient in promoting cartilage regeneration.

Dr. Chong Pan Pan
Faculty of Medicine, Universiti Malaya, Malaysia

Dr. Chong Pan Pan is highly qualified with B.Sc. (Hons) in Microbiology, M.Sc. Biochemistry and successfully completed PhD on her research on mesenchymal stem cells (MSCs) and skeletal tissue engineering. After that, she worked as a post-doctoral research fellow (2013-2016) and was later inducted as a senior lecturer (2016-now) at the National Orthopaedic Centre of Excellence in Research and Learning (NOCERAL), Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya (UM), Malaysia. Additionally, she is in charge of setting up the Good Manufacturing Practice (GMP) Laboratory in NOCERAL. She has also been put in charge of the newly provided clinical service using platelet-derived extracellular vesicles (P-EVs) to treat lateral epicondylitis, plantar fasciitis, osteochondral defect, delayed union and knee osteoarthritis, etc. The P-EVs service is provided at the University of Malaya Medical Centre (UMMC) and the University of Malaya Specialist Centre (UMSC). Her research interest involves the current and innovative area of tissue engineering and manipulation of adult mesenchymal stem cells (MSCs) for future use as biological therapies for poorly regenerating tissues. Her work focuses on driving adult MSCs from bone marrow, peripheral blood and adipose tissue along chondrogenic lineages for later transplantation to replace worn-out joint cartilage in patients suffering from joint disorders, including trauma or osteoarthritis. To attest to her work, Dr. Chong has published in several high-quality (Q1/high impact factor) peer-reviewed journals and presented her works extensively and globally at numerous international conferences. At that time, she also won a number of awards, including top prizes at the regional level, such as the Young Investigator Awards, Young Investigator Best Paper Award, L'Oréal Malaysia for Women in Science, Best Poster / Oral Presentations and travel fellowships, etc. In addition, she has participated in several biotechnology exhibitions and business idea competitions. Furthermore, she won many innovation awards for her work on MSCs and P-EVs as biological therapies for tissue regeneration. She has also developed intellectual property related to the novel work, which has been successfully patented.

Abstract

The Use of Platelet-derived Extracellular Vesicles for Musculoskeletal Tissue Regeneration: From Basic Research to Clinical Outcome

Pan Pan Chong[1,*], Nur Hidayah Hassan[1,2], Jonas Fernandez[1], Shani Samuel[1], and Tunku Kamarul[1]

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The increasing number of musculoskeletal injuries has produced a concurrent stimulus in both the number and the effectiveness of different treatments of these lesions, especially in the search for minimally invasive procedures or adjuvants. It is well known that platelet-rich concentrate (PRC), a high concentration of platelet within a small amount of plasma, is widely used in promoting tissue repair. PRC appears to be very potent in inducing chondrogenic differentiation of human mesenchymal stromal cells, and offers the additional benefit of suppressing chondrocyte hypertrophy, rendering it a promising approach for providing an abundant pool of chondrogenic mesenchymal stromal cells (MSCs) for application in cartilage tissue engineering. Moreover, PRC enhances the reparative effects of MSC in treating focal articular cartilage injuries. Platelet-derived extracellular vesicles (PEV) are believed to work in a similar method as PRP, and further research has led to a better understanding of its mechanism of action in the process of tissue repair. The most apparent difference between PRC and PEV is in its size. PEV was isolated via differential gradient centrifugation. The characterisations of the PEV were performed using a scanning transmission electron microscope (SEM), and nanoparticle tracking analysis (NTA), followed by chondrocyte culture in vitro. The PEV treatment is carried out using the accredited Good Manufacturing Practice (GMP) laboratory at the NOCERAL. Patients with Kellgren-Lawrence grade I or II knee osteoarthritis based on a knee x-ray were enrolled. They were then asked to complete the questionnaire before the treatment and again one month later. A total of 58 osteoarthritis patients were recruited. Seventeen patients were injected with autologous PEV, 20 with hyaluronic acid, and 21 were treated conservatively (control). The KOOS, WOMAC, and SF36v2 questionnaires were filled out before and one month after the treatment. Data obtained were analysed using the SPSS. The activated platelets and vesicles were observed in SEM. Visualisation by electron microscopy revealed that activated platelet released EVs of a typical shape, i.e., irregular round vesicles, membrane-bounded, and no contaminants, could be observed. Moreover, the NTA demonstrated a poly-dispersed population of PEV with a particle size range of 50-500 nm. Two distinct populations of particles with sizes at 100-200 nm correspond to exosomes, and a substantial proportion of larger particles with sizes at 250 to 500 nm fall into the size range of microvesicles. The cell cultured in 10% PEV attained 100% confluence at day 7 of expansion, while only 80% confluence for 5% PEV and 50% confluence for 10% FBS. The overall morphology of growing cells is fibroblastic and identical in size. Cell counting analysis revealed an increase in the chondrocytes that were cultured in 10% PEV supplementation, 9 times and 5.5 times higher than those chondrocytes cultured in 10% FBS and 5% PEV, respectively. For the clinical outcome, PEV can improve the symptoms and lifestyle of a patient with mild or moderate knee osteoarthritis. Although not statistically significant in all subscales, when comparing the differences in scores among the groups, patients treated with PEV showed the most improvement, especially compared to patients in the control groups.

Symposium IX

Professor Dr. Shih-Hwa Chiou
National Yang Ming Chiao Tung University, Taiwan PRC

Professor Dr. Shih-Hwa Chiou is a physician-scientist, the director of the Department of Medical Research in Taipei Veterans General Hospital, and a distinguished chair professor at the Institute of Pharmacology and the Institute of Clinical Medicine & Genomic Center, National Yang-Ming University in Taiwan. As a visiting researcher, he was trained in the Department of Molecular Biochemistry at the Boston Children's Hospital of Harvard Medical School and the Department of Molecular Biochemistry at the Scripps Research Institute. He won the Young Investigator Award at the Annual Meeting of the Society of Molecular Imaging (Germany) and the Achievement Award from the Society of Asia-Pacific Academy of Ophthalmology (Australia). He was invited to serve as Chairman and Keynote Speaker at the Cancer Stem Cell Section of the Japan Cancer Association (JCA)'s 69th Annual Meeting in Japan. His current focus is on the application of iPSC-derived 3D organoids as disease models for research on genetic-mutation diseases, drug screening, and nanomedicine based genomic editing technology for personalised medicine.

Abstract

Application of Genomic Editing Technology in Retinal Diseases

Chiou Shih-Hwa

National Yang Ming Chiao Tung University, Taiwan PRC

CRISPR-Cas9 is a potential technology that can edit the genome by removing, adding, or modifying certain sections of a DNA sequence. This technology provides the opportunity for scientists and researchers to manipulate the interested gene. X-linked juvenile retinoschisis (XLRS) is an early-onset retinal degenerative disease that can cause visual impairment and retinal detachment. We have successfully established personalized iPSC-derived retinal organoids and further used the latest CRISPR/Cas9 technology to repair the mutated genes and the "schisis" phenotype in the retinal organoids. This advanced CRISPR-Cas9 gene editing may hold promise in the treatment of inherited diseases and will be extended to clinical application in the near future.

Associate Professor Dr. Tan Jun Jie
Universiti Sains Malaysia

Dr. Tan Jun Jie has been working on cardiac regeneration, tissue engineering and stem cell research for 15 years with the ambition to introduce new therapeutic strategies to treat heart diseases. He is now an Associate Professor at Universiti Sains Malaysia, with his primary focus on human induced pluripotent stem cells, differentiation and disease modelling *in vitro*. His research work focuses on proepicardial cell differentiation and its application in cardiac cell therapy and regeneration. He has also started a Heart Failure Research Program to examine the emerging disease, heart failure with preserved ejection fraction, and examine the effects of repurposed drugs on cardiac fibrosis.

Abstract

Modelling Heart Disease from Animal to *In Vitro* Models

Jun Jie Tan

Advanced Medical and Dental Institute, Universiti Sains Malaysia, Pulau Pinang, Malaysia

Heart disease remains a significant contributor to high morbidity and mortality, imposing a substantial healthcare burden worldwide. The race to successfully regenerate myocardium lost in ischemic hearts is ongoing, but the methods used to model the disease and mimic the diseased phenotype for regenerative research have heavily relied on animals, ranging from rodents to non-human primates. The emergence of the *in vitro* tissue-engineered heart tissue and the development of cardiac organoids have piqued substantial interest in the research community, offering the potential to reduce animal usage and facilitate personalised testing. However, both animals and the *in vitro* tissue engineered heart tissue or organoid models remain indispensable in research and testing at this stage due to the unique advantages and limitations of each. In general, myocardial regenerative research must consider factors such as post-transplantation cell survival, fate, engraftment, synchronisation with the host myocardium, and immune rejection when interpreting observed cardiac function. These parameters involve the complex interplay between cardiac haemodynamics and the systemic immune response, which are challenging to replicate *in vitro*. On the other hand, organoids derived from patient-specific induced pluripotent stem cells provide a personalised genetic makeup that comprises individual regulatory proteins or phenotypes. This genetic individuality is crucial for understanding responses and sensitivities to drugs, enabling more personalised and effective drug treatments by considering genetic variations among patients. The cellular composition and maturity, tissue structure and function are keys to developing good resemblance to human heart for such testing. In this lecture, the current use of animals and *in vitro* models, the limitations and as well as the future applications in heart regeneration study will be discussed.

Oral Papers

Abstract Code: A01
Establishment of hiPSCS Derived 3D Lung Organoids as Disease Modelling for Respiratory Diseases

Nalini Devi Verusingam[1,2,3,4], Habeebat Aderonke Mustapha[2,3], Soon-Keng Cheong[1,4], Alan Han-Kiat Ong[1], Shih-Hwa Chiou[2,3,5] & Mong-Lien Wang[3,6]

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4 Department of Research and Development, Majlis Kanser Nasional (MAKNA), Kuala Lumpur, Malaysia
5 Genomic Research Center, Academia Sinica, Taipei, Taiwan
6 Institute of Food Safety and Health Risk Assessment, National Yang-Ming University, Taipei, Taiwan

Introduction: Three-dimensional (3D) lung organoids are a groundbreaking platform to model respiratory diseases, derived from human induced pluripotent stem cells (hiPSCs) through stepwise differentiation. Current therapeutic options for respiratory diseases are limited due to disparities between animal models and human lung physiology. Therefore, relevant lung model systems are needed to develop effective therapies. Recent advances in single-cell transcriptomic analysis have shown that human lung organoids (hLO) from hiPSCs significantly replicate human lung development, making them an ideal model for studying the development of lung-related respiratory diseases. In our study, we focused on the generation of hLO in disease modelling for respiratory diseases.
Materials & Methods: HiPSCs were differentiated into definitive endoderm (DE) for 4 days and then into anterior foregut (AF) within 10 days using induction medium. Next, AF cells were further induced to form hLO using organoid medium for 14 days. The hLOs were molecularly characterised for pulmonary-alveolar markers using qRT-PCR, western blot and immunofluorescence (IF) staining.
Results: Characterisation results indicated upregulation of SFTPB+, SFTPC+, SOX9+, and NKX2.1+ expression in hLOs, suggesting the presence of alveolar type II cells.
Discussion: We successfully generated hLO *in vitro* as evident by phenotypic and genotypic characterisation. HLOs can serve as personalised disease models in clinical settings, enhancing our understanding of respiratory diseases like lung cancer, SARS-CoV-2 lung injury, and idiopathy pulmonary fibrosis (IPF).

Abstract Code: A02
Multiple Dosing of Cytopeutics® Human Umbilical Cord Mesenchymal Stem Cells is Safe in BALB/c Mice Toxicity Evaluation

Sze-Piaw Chin[1], Nur Izzati Mansor[1], Natasha Najwa[1], Kong Yong Then[1] & Soon Keng Cheong[2]

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2 M. Kandiah Faculty of Medicine & Health Sciences, Universiti Tunku Abdul Rahman, Selangor, Malaysia

Introduction: The safety of single dosing of human umbilical cord mesenchymal stem cells (hUCMSCs) infusion has been well documented in various animal models. However, the safety and toxicity of multiple, repeated infusions remain uncertain. Yet certain clinical conditions may require multiple and frequent dosing to achieve the benefits of hUC-MSC. This toxicity study aimed at assessing the safety of Cytopeutics® hUC-MSCs administered at multiple frequencies in healthy BALB/c mice, followed by a 14-day monitoring period.
Materials and Methods: Repeated dose toxicity was assessed in 2 groups of healthy BALB/c mice by slow bolus intravenous infusion of Cytopeutics® hUC-MSCs. The first group of mice (n=14) were injected with saline and acted as controls. The second group (n=14) received 5×10^6 cells/kg BW on days 1, 4 and 7. The dose of 5×10^6 cells/kg BW was chosen based upon the findings and efficacy study of Cytopeutics® hUC-MSCs in the Phase I/II clinical trial GVHD Study (NCT03847844). All mice were observed for 14 days to evaluate morbidity and mortality, clinical signs and clinical chemistry. At the end of the assessment period, all mice were euthanised for gross necropsy and histopathology analysis of all organs.
Results: The findings showed that multiple infusions of Cytopeutics® hUC-MSCs at 5×10^6 cells/kg BW were safe and well-tolerated in all mice. No morbidity, mortality or significant changes in clinical signs or clinical chemistry were reported during the 14-day monitoring period. A minimal 16% increment in the spleen weight and increased cellularity of the white pulp in the spleen were observed at the terminal time point in mice treated with Cytopeutics® hUC-MSCs when compared to the control group. All other organs were normal.
Discussion: All mice were not subjected to any fatalities or unusual clinical signs during the monitoring period. The administration of Cytopeutics® hUC-MSCs led to a slight increase in spleen weight and number of lymphocytes in the white pulp due to lymphocyte traffic to the spleen as a secondary lymphoid organ (SLO). This correlates with other research and suggests a physiological reaction to MSC administration. MSCs migrate to SLO and the interaction of MSCs with the spleen may account for the therapeutic immunomodulatory action on lymphocyte proliferation and activity. In conclusion, multiple infusions of Cytopeutics® hUC-MSCs at 5×10^6 cells/kg BW on days 1, 4 and 7 were safe and did not cause any adverse effects on morbidity, mortality, clinical signs or clinical chemistry in BALB/c mice.

Abstract Code: A14

Analysis of Secretome Profile in Umbilical Cord-derived Mesenchymal Stromal Cells Co-cultured with Senescent Normal Human Dermal Fibroblast

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Introduction: Cellular aging, also known as a state of irreversible growth arrest, is characterised by the gradual and irreversible loss of proliferative potential and functional capacity of cells. Fibroblasts are the most widely used model in the study of oxidative stress-induced cellular senescence and replicative cellular senescence. Mesenchymal stromal cells (MSC) are multipotent cells that can be derived from different organs and tissues and possess the ability to expand *ex vivo* and differentiate into various mesoderm-type cells. In previous studies, MSC has been shown to exert therapeutic functions through two mechanisms: differentiation and paracrine signalling. MSC can secrete bioactive factors in the culture medium to regulate local cellular responses through paracrine signalling. Thus, in our study, we evaluated the secretome profile of umbilical cord-derived mesenchymal stromal cells (UC-MSC) after exposure to senescent fibroblasts.
Materials and Methods: Normal human dermal fibroblasts (NHDF) were first treated with 200 µM hydrogen peroxide (H_2O_2) for 2 hours and allowed to recover for 5 and 7 days to develop the senescent model. The characterisation of senescent NHDF was done by a senescence-associated beta-galactosidase assay and measuring the cell proliferation rate. The senescent NHDF was then co-cultured with umbilical cord-derived mesenchymal stromal cells (UC-MSC) using the transwell system for 48 hours. The supernatant was then collected and semi-quantitative analysis of the secretome profile was carried out using chemiluminescence detection. Senescent NHDF were used as the negative control.
Results: H_2O_2-treated NHDF showed an increase in beta-galactosidase activity and a decrease in the cell proliferation rate. These findings indicated the successful generation of senescent NHDF. The secretome profile analysis of the supernatant collected from senescent NHDF after co-culture with UC-MSC showed an increase in different cytokines and growth factors which were not seen in the supernatant of untreated senescent NHDF. Among the cytokines and growth factors that were increased were Fibroblast Growth Factor-7, Platelet-derived Growth Factor, Interleukin-8 and C-X-C motif chemokine ligand family. Pathway analysis using Reactome and the KEGG Pathway Database indicated that these proteins were largely involved in cell proliferation.
Discussion: Secretome analysis showed the overexpression of proteins involved in cell proliferation in the supernatant of senescent NHDF and UC-MSC. This suggested that MSC may be able to secrete bioactive factors to ameliorate senescence in NHDF by expressing proteins that can activate cell cycle progression. Further investigations are needed to determine the functional effect of these proteins on the senescent NHDF.

Poster Presentation

Abstract Code: A03
Effect of Cytopeutics® hUC-MSCs against Systemic Inflammation and Multiple Organ Injuries

Sze-Piaw Chin[1], Lihui Tai[1], Nurul Ashikin Mohamed Shahrehan[2], Christine Ricky[2], Audrey Fanty anak Jangan[2], Mohd Noor Syuhada Md. Halim[2], Nur Izzati Mansor[1], Natasha Najwa[1], Chui Thean Low[2] & Soon Keng Cheong[3]

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Introduction: Graft-versus-host disease (GVHD) is commonly characterised by systemic inflammation and multiple organ injuries. The immunomodulatory effects of human umbilical cord-mesenchymal stem cells (hUC-MSCs) in ameliorating acute systemic inflammation and multi-organ injury due to acute GVHD is unknown. This study aimed to investigate the efficacy of Cytopeutics® hUC-MSCs in reducing LPS-induced systemic inflammation with liver and lung injuries in BALB/c mice model.
Materials & Methods: Eighteen mice were randomly allocated into three groups: the healthy group received normal saline; the LPS-only group was induced with 5 mg/kg LPS at 0.1 mL/mouse; and the LPSCytopeutics®-hUC-MSCs group was treated with 18.5×10^6 cells/kg (human equivalent dose of 1.5×10^6 cells/kg) at 24 h post-LPS induction at 0.2 mL/mouse. Tumor necrosis factor-alpha (TNF-α), interleukin (IL)-1beta (1β), IL-6, as well as aspartate aminotransferase (AST) and alanine amino transferase (ALT) were analysed by ELISA at 24 h and day 7-post treatment. At the end of the study, all mice were euthanised by cervical dislocation and target organs were subjected to necropsy and histopathological examination.
Results: LPS at 5 mg/kg for 24 h induced extensive liver and lung injury, as evidenced by H&E staining. After treatment with hUC-MSCs, the liver injury score on day 7 was reduced to 0.40 ± 0.55 compared to the LPS-only group (1.33 ± 0.58). The observation was consistent with the reduction in AST (272.7 ± 6.1 U/L vs 398.3 ± 206.0 U/L) and ALT (57.7 ± 7.0 U/L vs 65.7 ± 18.2 U/L) levels in the hUC-MSCs group in comparison with the LPS-only group. Likewise, in the lung, the mean score of infiltrated inflammatory cells on day 7 was markedly higher in both healthy and LPS-only groups (2.33 ± 0.16), whereas the score decreased to 1.80 ± 1.30 in the hUC-MSCs treatment group. Furthermore, hUC-MSCs significantly reduced the levels of TNF-α ($p = 0.0221$) and IL-1β ($p = 0.0419$) at 24 h. IL-6 level was also reduced ($p > 0.05$). The levels of these cytokines returned to near-normal levels on day 7. Collectively, hUC-MSCs have demonstrated the capability to attenuate systemic inflammation and alleviate the severity of liver and lung injury induced by LPS.
Discussion: Treatment of 18.5 × 106 cells/kg hUC-MSCs in BALB/c mice following LPS injection led to an early resolution of acute inflammation and a subsequent reduction in lung and liver injuries. These findings provide the rationale for using hUC-MSC to improve the clinical signs of acute GVHD.

Abstract Code: A04
Immunotherapy in Cervical Cancer Treatment

Divyangana Kiran Vartak*, Than Htay Tin & Myo Oo

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Introduction: Cervical cancer ranks as the 4th most common cancer among women worldwide. It is mainly caused by human papillomavirus (HPV) types 16 and 18, which account for nearly 50% of high-grade cervical pre-cancers.
Material & Methods: The poster includes information on cervical cancer, prevention with vaccination and staging, an overview, current management and the role of immunotherapy in treating cervical cancer. Data and information were collected from important websites and journals, including PubMed, Journal of Cancer, International Reviews on Immunology, and Journal of Gynaecological Cancer.
Results: Preventing HPV infection through vaccination, screening and treating pre-cancerous lesions can effectively reduce the risk of cervical cancer and has the potential to prevent more than 90% of HPV-related cancers. However, for women who develop cervical cancer, the traditional treatments of surgery, chemotherapy and radiotherapy have limitations and complications.
Discussion: Immunotherapy, a novel treatment that harnesses the body's immune system to fight cancer, offers hope to those who have not responded well to traditional treatments or have experienced significant side effects. Immunotherapy, either alone or in combination with other systemic therapies, may provide significant benefits and improve the quality of life for women with advanced, recurrent or metastatic cervical cancer.

Abstract Code: A05
Fructose-Streptozotocin-Induced Diabetes: A Severe Rat Diabetic Model

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Introduction: Notorious for its high prevalence, diabetes mellitus (DM) has been a formidable rival for the healthcare system and a leading cause of mortality globally. In its most threatening form, the severe disorder manifests as uncontrollable and high fasting blood glucose (FBG) levels (> 22 mmol/L) associated with pancreatic beta cell decompensation and reduced volume. Without appropriate therapeutic advances, its prevalence and mortality rate are predicted to increase exponentially. This necessitates the development of a reliable model for the severe form of the disease. To advance diabetes research, there is a need for a cost-effective and an easily maintained animal model that corresponds to the severe stage of the disease as there is a scarcity of inexpensive ones exhibiting uncontrollable hyperglycaemia. Our aim is to corroborate the establishment of a robust and accessible rat model of severe diabetes.
Materials & Methods: 27 Sprague Dawley male rats were divided into a diabetic (DG) (n=21) and a normal control group (NC) (n=6). NC received regular drinking water while the DG received 10% fructose water ad libitum for 14 days. On the 15th day, DG received a single intraperitoneal injection of streptozotocin (40 mg/kg body weight) dissolved in citrate buffer (0.1M). NC received citrate buffer only. A week later, animals were fasted for 6 hours and their FBG levels were measured. To confirm the establishment of a severe diabetes model, a group of rats from DG (n=7) were given metformin (DM) dissolved in reverse osmosis water orally (300 mg/kg body weight) for 28 days, while a diabetic control group (DC) (n=7) and NC received the vehicle only. Body weight, and food and water intake were measured daily. Cage-side observation was conducted and FBG levels were monitored weekly.
Results: The induction had a success rate of 94%. A week after the induction, the DG had a mean FBG of 25.4 mmol/L, severe weight loss, fatigue, polyuria, polyphagia, and polydipsia compared to the normal control ($p<0.0001$). Over the 28 days, all the signs persisted even in the metformin-receiving group. The mortality rate was 28.6% in the DC group, and 14.3% in the DM group.
Discussion: Fructose drinking and a single dose of streptozotocin can induce severe diabetes characterised mainly by persistent hyperglycaemia that is uncontrollable despite administration of metformin. This animal model provides an accessible tool for studying unmanageable hyperglycaemia and evaluating potential therapeutic interventions.

Abstract Code: A06
Public Health Implications of Widespread Use of Cell Therapies for Aging

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Introduction: Growing old, although a natural part of life, brings forth numerous challenges that affect individual health and global healthcare systems. Recent developments in cell therapies shine a beacon of hope for potentially mitigating the impacts of aging, potentially enhancing life quality for older individuals. However, the broader public health consequences of such therapies still require comprehensive understanding. Our study aimed to delve deeper into the public health implications that might emerge from Aim: Our study is rooted in understanding the real-world implications that could unfold from the large-scale adoption of cell therapies for aging. We sought to comprehend how such therapies might shape health outcomes, the challenges and feasibility of large-scale execution, and the ethical, societal, and economic repercussions attached to it.
Materials & Methods: We adopted a people-centric, mixed-method approach for our research. We dove deep into the sea of existing literature on cell therapies for aging, prioritising the understanding of personal experiences, perceptions, and traditional research methodologies. Simultaneously, we conducted comprehensive, semi-structured interviews with a broad spectrum of individuals such as healthcare providers, public health professionals, and ethicists. The primary aim of these interviews was to unravel the human stories and ethical dimensions woven into the fabric of cell therapy practices. Moreover, we embarked on a journey of health economic modelling to illuminate potential economic impacts on public health. This model was meticulously designed around human-led data and subjective experiences, ensuring that the results stayed true to the realities of economic and health resource distributions.
Results: Cell therapies for aging show promise in enhancing health outcomes. Still, our research revealed that their application on a larger canvas could invite significant ethical, societal, and economic challenges. These include the steep price tag attached to the therapy, worries regarding fair access, and the probability of increased life expectancy without an equivalent increase in healthy living years. The human stories collected from the interviews emphasised the urgent need for a sturdy regulatory structure to safeguard the ethical use of these therapies.
Discussion & Conclusion: As we stand on the cusp of significant advancements in cell therapy, it's critical to focus on its broader public health implications. Our research reaffirms the need for in-depth interdisciplinary dialogue, informed policy-making, and thorough evaluations of cost-effectiveness. To ensure cell therapies for aging are deployed in the most beneficial way, we must strike a balance between scientific potential and societal implications. In this manner, we can realise the full public health potential while keeping potential risks at bay.

Abstract Code: A07

Cell Therapies for Aging: Impact on Surgical Interventions and Patient Outcomes in the Elderly

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Introduction: Aging is an inevitable part of life that brings along a plethora of health-related challenges, often impacting the overall wellness of individuals. Among these challenges, the adverse effects of aging become highly apparent during surgical procedures where elderly patients typically experience longer recovery periods, increased complication rates, and reduced post-operative quality of life. However, with the advent of cell therapies, there's an emerging potential to significantly improve healthcare for our aging population and possibly mitigate the negative impacts of aging on surgical outcomes. The objective of this research is to delve into the potential influences of cell therapies on surgical interventions and patient outcomes in the aging population. The study emphasizes understanding the benefits of integrating cell therapies into surgical procedures, particularly whether it enhances recovery, curtails complications, and uplifts the overall wellness of elderly patients.

Materials & Methods: Our study adopted a mixed-method approach that incorporated a comprehensive review of existing literature on cell therapies for aging, specifically in surgical contexts. Alongside this, we conducted in-depth interviews with surgeons and healthcare professionals experienced in treating elderly patients and/or utilizing cell therapies. Lastly, we analysed case studies of elderly patients who had undergone surgical interventions with the integration of cell therapies.

Results: It looks like cell therapies, if done right, could actually make a big difference in the way elderly patients recover after surgery. They could bounce back quicker, have fewer issues afterwards, and overall just feel better. But here's the catch: the kind of cell therapy used and the exact surgical procedure performed seem to influence these improvements.

Discussion: The use of cell therapies in surgical procedures shows a significant transformation in healthcare outcomes for our aging population. Despite this promising outcome, it's clear that further in-depth exploration is needed to uncover best practices for seamlessly integrating these therapies into surgical procedures. This study underlines the need for relentless innovation, well-informed policymaking, and cross-disciplinary collaboration to optimise surgical care for aging populations. The findings act as a call to action for more comprehensive investigations into the specific mechanisms and strategies that will most effectively leverage cell therapies in surgical interventions.

Abstract Code: A08
Implementing CAR-T Therapy: A Surgeon's Perspective

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Introduction: With the advent of Chimeric Antigen Receptor T-cell (CAR-T) therapy, a new frontier in cancer treatment has been opened. Despite its considerable promise in combating certain types of cancer, the complexities and challenges involved in integrating such advanced therapies into surgical practice demand careful exploration. This paper aimed to share unique insights into the practical implementation of CAR-T therapy from a surgical perspective. It strives to illuminate the potential and challenges of this novel therapy, with the intent to inspire informed practices and stimulate further research.
Materials & Methods: We undertook a comprehensive review of existing literature on CAR-T therapy in surgical contexts, complemented by a series of case studies. The case studies detail our experiences incorporating CAR-T therapy into surgical procedures, focusing on patient outcomes and the issues encountered during the practical application of this treatment.
Results: Our findings underscore that while CAR-T therapy offers enhanced survival rates and improved patient outcomes, the transition to its implementation presents significant challenges. Key issues include patient selection, managing potential side effects, and the necessity of coordinating multidisciplinary care.
Discussion: The incorporation of CAR-T therapy in surgical oncology necessitates a paradigm shift in surgical practice. To fully harness the benefits of CAR-T therapy, there is a need for robust training programs for surgical teams, a detailed understanding of the therapy, and a patient-centric approach. Our study emphasizes the importance of continued investigation into CAR-T therapy's practical implications, aiming to facilitate its more efficient and effective integration into surgical practice.

Abstract Code: A09
Cardiac Complications Post-COVID-19 Vaccination – An Interim Report of a Systematic Review

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Introduction: Cardiac complications following COVID-19 vaccination, the most widely recognised of which is myocarditis, are rare occurrences. This systematic review aimed to identify reported cardiac complications post-vaccination and determine factors associated with undesirable outcomes.
Materials & Methods: The review was registered with PROSPERO (CRD42022310861) and followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. Three electronic databases were searched using specific strategies. Inclusion criteria involved adult cases aged 18-65 years with detailed descriptions of cardiac complications, while cases with a history of COVID-19 infection were excluded. Univariate and multivariate analyses were performed to identify associations between undesirable outcomes and various demographic, lifestyle (such as smoking, drug use, and alcohol consumption), underlying illness, and vaccine-related factors (vaccine type and number of vaccine doses).
Results: 906 articles were initially found; 106 articles comprising data from 178 patients were identified for analysis after content evaluation. The study found that the most commonly observed complications were inflammatory heart conditions, accounting for 89.9% of all reported cardiac complications. Other cardiac complications were uncommon and included, in decreasing order, ischemic heart disease (3.9%), cardiomyopathy (3.9%), cardiac arrhythmias (1.7%), and myocardial injury (0.6%). Patients with myocarditis accounted for a large proportion (n=123, 69.1%) of the inflammatory cardiac conditions, the majority of whom were males who comprised 83.3% of all myocarditis cases. Overall, the myocarditis patients were relatively young with an average age of 30.8±11.6 years (mean ± SD). The clinical course was uneventful in most cases (n=107, 77.5%). However, 19 patients (13.86%) had an acute disease course and four cases were fatal (2.9%); information for eight cases (5.8%) was insufficient to determine the disease course or complications. Univariate analysis revealed that undesirable outcomes of inflammatory cardiac complications were associated with female gender.
Discussion & Conclusion: The findings confirm that myocarditis is the most frequent cardiac complication following COVID-19 vaccination. An unexpected observation was the association between female gender and a higher risk of undesirable outcomes of myocarditis in the background of the male predominance of this condition. This finding requires further validation and if validated, fundamental investigations to uncover its pathophysiological basis. This interim review report highlights inflammatory disorders, particularly myocarditis, as the most common cardiac complication post-COVID-19 vaccination, with the majority being uncomplicated. Further research is necessary to enhance our understanding and prevent these complications.

Abstract Code: A10
Approaching Patients Presented with Bone Tumours

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Introduction: Due to their diversity and extensive details, bone tumours are one of the most difficult orthopaedic topics for both undergraduate students and doctors. All the references present this subject thoroughly and based on the type. The goal is to determine the best course of action rather than to identify the specific type of bone tumours.
Materials and Methods: Via an algorithm system, this poster demonstrates the approach of those patients depending on their clinical picture and initial plain X-ray. The clinical picture of benign bone tumour patients is milder than malignant tumours. On the other hand, the radiological signs of bone tumours can fairly distinguish between benign and malignant bone tumours. The presence of well-defined borders, a narrow zone of transition, bony expansion, and trabeculations without periosteal reaction or soft-tissue extension are imaging indicators that the tumour is benign as opposed to malignant. This algorithm system uses Enneking`s classification of benign bone tumours (Latent, Active, and Aggressive) for categorising the patients into three classes. Patients who presented with aggressive benign bone tumour features must be considered malignant until proven otherwise.
Recommendations: We recommend using this guideline as a simple framework for clinicians and students in addressing the complexities of managing bone tumours.

Abstract Code: A12

Genetically Engineered Human Umbilical Cord-derived Mesenchymal Stromal Cells Expressing Human Interleukin-12 Inhibit Growth of Lung Adenocarcinoma Cells *In Vitro*

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Introduction: Interleukin-12 (IL-12) is a crucial immunomodulatory cytokine known for its antitumour effects. Nonetheless, the systemic administration of IL-12 at therapeutic dosage leads to serious toxicity in cancer patients due to the induction of an extremely high systemic level of interferon-γ. Mesenchymal stromal cells are promising cellular vehicles for cancer therapy. They are highly amenable to transduction by viral vectors to express and deliver exogenous proteins to tumour sites due to their tumour-homing ability. In this study, we genetically engineered human umbilical cord-derived mesenchymal stromal cells (hUCMSC) using an adenoviral vector to express hIL-12 and examined their effect on lung adenocarcinoma cells.
Materials and Methods: The hIL-12 gene was first cloned into linearised pAdenoX-ZsGreen1 using Adeno-XTMAdenoviral System 3. The linearised recombinant adenoviral plasmid was then packaged into a recombinant adenovirus using HEK293 cells and further amplified and purified. Viral titers were determined and multiplicity of infection (MOI) 10 was selected to infect hUCMSC in generation of hUCMSC expressing hIL-12 (hUCMSC-IL12). The hUCMSC-12 ($1x10^4$ cells/well) were co-cultured with H1975 lung adenocarcinoma cells ($1x10^3$/well) in a 24-well transwell system for 5 days. Cell viability of H1975 was assessed using the CCK-8 assay, with untransduced hUCMSC serving as a negative control. A similar co-culture assay was repeated again using MRC-5 human lung fibroblast cells. The supernatant in the co-culture assay was collected for quantification of hIL-12 levels using ELISA.
Results: On the fifth day of co-culture with hUCMSC-IL12, H1975 cell viability significantly reduced to 66.8%. In contrast, H1975 co-cultured with untransduced hUCMSCs did not result in any significant difference in cell viability (91.6%). Similarly, the viability of MRC-5 human lung fibroblast cells was also not affected after 5 days of co-culture with hUCMSC-IL12 (114.0%). Lastly, the hIL-12 protein expressed by hUCMSC-IL12 increased from 1.2µg/ml on day 3 to 2.2µg/ml on day 5.
Discussion & Conclusion: Based on our results, hUCMSC-IL12 exhibited a growth inhibition effect on lung adenocarcinoma cells without adversely affecting the viability of normal human lung fibroblast cells. Hence, genetically engineered hUCMSC expressing hIL-12 using the adenoviral vector can be potentially utilised as cellular vehicles in cancer therapy to overcome the systemic toxicity of IL-12.

Abstract Code: A13

Social Demographics and Vaccine-Related Perceptions on the Intention for COVID-19 Vaccine Booster among the Elderly Residing in Long-Term Care (LTC) Homes in Klang Valley

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Introduction: COVID-19 vaccine booster is an effective measure to boost the declining immunity of vaccine recipients, thereby protecting these recipients from severe disease. The elderly comprises a target group for boosters due to their weakened immune systems and higher risk of underlying chronic diseases. Despite this, only 5.8% of the elderly in Malaysia have taken the second booster as of 13th October 2022. Hence, this study aimed to identify the prevalence of vaccine booster hesitancy (VBH) and its associated factors among the elderly residing in long-term care (LTC) homes in the Klang Valley.
Materials & Methods: A cross-sectional analytical study was conducted from 28th November to 8th December 2022. Universal sampling was employed to select the LTC homes in the Klang Valley as well as the participants. A questionnaire was designed and validated to assess the sociodemographic factors and vaccine-related perceptions on vaccine booster hesitancy. The survey was carried out through face-to-face interviews with 158 LTC home residents aged ⩾ 60. The chi-square test and binary logistic regression were used for data analysis.
Results: We observed a high prevalence (42.4%) of VBH among the participants; indeed, 40.5% indicated that they were unlikely/very unlikely to receive an annual booster dose. Among the significant factors positively associated with VBH are female gender (OR: 1.42, 95% CI: 1.01-3.89), history of side effects from past COVID-19 vaccinations (OR: 2.18, 95% CI: 1.14-4.20), fear of side effects following a booster dose (OR: 15.37-16.36), and low trust in vaccines (OR: 5.09, 95% CI: 2.17-11.90), medical experts (OR: 5.47, 95% CI: 2.41-12.40), mass media (OR: 2.31, 95% CI: 1.16-4.59) and the government (OR: 5.78, 95% CI: 2.81-11.92) respectively.
Discussion: The results emphasise that targeted health promotion activities are a necessary tool in disseminating reliable sources of information to the public to prevent them from developing unwarranted fears and negative perceptions towards the vaccine booster.

Abstract Code: A15

Enhancing Vaccine-Preventable Disease Surveillance in Pakistan: Assessing the Impact of Typhoid Conjugate Vaccines on Incidence and Prevalence

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Introduction: Typhoid fever is a vaccine-preventable illness that poses a substantial public health burden in Pakistan. Typhoid conjugate vaccines (TCVs), recently developed, provide potential ways to successfully tackle these illnesses. Strong surveillance systems are necessary to track the effect of these vaccinations on illness incidence and prevalence, which is essential for determining their effectiveness. By analysing the effect of TCVs on the incidence and prevalence of targeted diseases, this study sought to improve the surveillance of diseases that can be prevented by vaccination in Pakistan. We want to comprehend the efficiency of these vaccinations in lowering the burden of vaccine-preventable illnesses in areas where they have been introduced thorough investigation.

Materials & Methods: Data from national and regional monitoring systems for vaccine-preventable illnesses, including typhoid fever, were used in a retrospective observational analysis. Disease incidence and prevalence patterns were compared before and after the introduction of TCVs throughout a specific time period. The study concentrated on areas where these vaccinations were integrated into the national immunisation programme.

Results: Our examination of data from vaccine-preventable illness monitoring found overwhelming evidence of the effectiveness of TCVs. There was a considerable decrease in the incidence of targeted illnesses in areas where these vaccinations were deployed. Following the introduction of TCVs, there was a statistically significant reduction in confirmed cases of typhoid fever ($p<0.001$). Furthermore, the prevalence of other vaccine-preventable illnesses, such as pneumococcal infections and influenza, fell by 25% ($p<0.05$) and 30% ($p<0.01$), respectively, following the introduction of new-generation vaccinations.

Discussion: The outcomes of this study highlight the necessity of extensive vaccine-preventable illness surveillance in determining the effectiveness of TCVs. The large decrease in illness incidence and prevalence, which is backed by rigorous statistical data, demonstrates the potential of these vaccinations to lower the burden of vaccine-preventable diseases and enhance public health outcomes in Pakistan.

Abstract Code: A18
Reprogramming of Double-Hit Diffuse Large B-cell Lymphoma Cells Line into Induced Pluripotent Stem Cells

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Introduction: Studies have demonstrated the success of reprogramming cancer cells into induced pluripotent stem cells (iPSCs). However, not all cancer cells are amenable to reprogramming. The underlying mechanisms limiting the reprogramming of cancer cells are largely unknown. This study demonstrated the resistance of the double-hit diffuse large B-cell lymphoma (DH-DLBCL) cell line to cellular reprogramming using Sendai virus (SeV)-mediated gene transduction.
Materials & Methods: The CytoTune-iPS 2.0 Sendai Reprogramming Kit was used for the reprogramming. It contains four SeV-based reprogramming vectors: hOCT4, hKOS, hc-Myc and hKlf4, which consist of the four transcription factors for efficient reprogramming. The DH-DLBCL cell line (CRL-3382) was purchased from American Type Culture Collection (ATCC). CRL-3382 was reprogrammed using the kit according to the feeder-dependent protocol. Mouse embryonic fibroblasts (MEF) were used as feeder layers. The transduced cell RNA was extracted using trizol reagent and bleach gel electrophoresis was performed to evaluate the extraction efficacy. The resulting RNA was converted into cDNA using RevertAid First Strand cDNA Synthesis Kit, and PowerUp SYBR Green Master Mix for PCR. PCR was performed with gene-specific primers Sendai SeV, Sendai Sox 2, Sendai Klf 4 and Sendai c-Myc to evaluate the transduction efficacy of CRL-3382.
Results: The DH-DLBCL cells continued to proliferate with no iPSC-like colonies observed after 30 days post-transduction. The bleach gel electrophoresis showed the RNA was successfully extracted and glyceraldehyde-3-phosphate dehydrogenase (GAPDH), a housekeeping gene, was used as comparison of gene expression data. Evaluation of genes transduction efficacy by PCR showed positive expression of the KOS and Sendai SeV genes. The other c-Myc and Klf4 genes expression was not demonstrated by PCR.
Discussion: CRL-3382 has the oncogenes c-Myc and BCL-2. The results indicate that the SeV successfully delivers the KOS-transcription factors into CRL-3382. The detection of Sendai SeV expression in the PCR proved that the virus was successfully transduced into the cells. However, no iPSC-like colonies were formed. Different approaches were attempted to improve the reprogramming efficacy, such as lowering the cell density for transduction and lowering the seeding density. However, all of the attempts failed to yield iPSC-like colonies. Resistance of cancer cells to reprogramming capacity has been reported but the underlying mechanisms limiting its efficiency remain elusive. Previous studies have reported presence of genes that could be obstacles in cancer cell reprogramming such as EZH1, PRMT6 and MXD1. Further study is needed to evaluate if the two oncogenes c-Myc and BCL-2 are hindering the reprogramming of our cell line.

Abstract Code: A19

Generation and Characterisation of an iPS Cell Line Derived from Peripheral Blood Mononuclear Cells of a Di(a+) Blood Donor for the Purpose of Producing Antibody-screening Red Cells

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Introduction: Red blood cells (RBC) express various antigens that can elicit a humoral immune response. Antibodies against the RBC antigens can cause haemolytic transfusion reactions and haemolytic disease of the foetus and newborn. Antibody screening (ABS) for these RBC antigens is therefore essential during pretransfusion testing and antenatal screening. ABS is usually performed using red cell panels that are developed from red cells procured from selected donors with the specific antigen combination. This approach lacks sustainability as it can be challenging to recruit donors with the desired antigen combination, especially within the Asian population whereby the spectrum of clinically significant antibodies is wider. For example, anti-Mia and anti-Dia are antibodies that are found commonly among Asians but rare among the Caucasian population. Thus, the use of induced pluripotent stem cells (iPSC) to generate RBCs expressing these antigens is proposed to circumvent this issue as iPSC can provide a consistent source of erythrocytes.

Materials & Methods: Peripheral blood mononuclear cells (PBMC) were isolated by density gradient centrifugation from a blood donor expressing Dia. The cells were then culture-expanded to form erythroid precursors in an erythroid expansion medium, and subsequently reprogrammed into iPSC using the Epi5 Episomal Reprogramming Kit. Pluripotency was characterised by immunofluorescence staining against Oct4, Sox2, Nanog and Tra-1-81. Embryoid body (EB) formation was performed to assess the trilineage differentiation potential. Quantitative RT-PCR was performed on the EB and iPSC to detect markers of the three germ layers and pluripotency markers, respectively. The H9 human embryonic stem cell line was used as a positive control for the assays.

Results: The iPSC colonies were observed on day 20 post-transfection. The colonies were positive on immunofluorescence staining for all the pluripotency markers studied. The generated iPSCs expressed the pluripotent genes as confirmed on qRT-PCR, with 0.30-fold for Oct4; 0.12-fold for Sox2; 0.16-fold for Nanog, as compared to the embryonic stem cell line, H9. EBs were shown to form on differentiation day 1.

Discussion: We have demonstrated the successful generation of an iPS cell line from erythroid precursors derived from the PBMC of a blood donor expressing the Dia antigen. This iPSC line will potentially serve as a source for consistent production of Dia+ reagent cells for ABS panels.

Abstract Code: A20
Role of Physiotherapy in Regenerative medicine and Stem Cell Therapy

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Introduction: Regenerative medicine is an interdisciplinary innovative field of medicine that applies principles of engineering and life sciences to promote tissue regeneration. It includes the injection of stem cells or progenitor cells, immunomodulation therapy and tissue engineering in the injured part. Stem cell therapy promotes the repair response of inflamed, dysfunctional and injured tissue using stem cells and their derivatives. The treatment is designed to heal injuries and reduce pain. It can be used in the treatment of arthritis, cancer, endometriosis, injuries to ligaments, tendons, cartilage, or bone. Physiotherapy deals with restoring body movement and function after injury, illness and disability. Physiotherapy management given to patients undergoing stem cell therapy has been reported to enhance the overall recovery time and quality of life. Physiotherapy treatment strategies include aerobic programming, resistance exercises, and functional training in order to alleviate debilitating symptoms of fatigue and pain, and deconditioning is used along with the therapy. Conditions like cancer, spinal cord injuries and tendon injuries have recovered well with a better patient outcome. Strength training intervention has been shown to enhance early recovery and improve muscle strength and functional ability as well.
Materials & Methods: A general review of the latest studies using Google, Pubmed and medical journals highlights the role of physiotherapy in various patients undergoing regenerative medicine and stem cell therapy.
Results: Most of the studies support the use of physiotherapy strategies along with the stem cell therapy. Exercise for tendonitis, rotator cuff injury, multiple sclerosis in combination with regenerative therapy has helped patients achieve better clinical outcomes.
Discussion & Conclusion: Physiotherapy in combination with regenerative medicine and stem cell therapy can aid in restoring, maintaining and improving mobility, function and wellbeing and relieve the condition faster so that patients can resume an active, pain-free life. Physiotherapy has been shown to play a vital role in the early rehabilitation of patients undergoing stem cell therapy. Though there is no specific modification in the rehab protocol, it still aids in the faster and complete recovery of the patients.

Abstract Code: A21

Differentiation of hiPSCs and hESCs into Haematopoietic Stem and Progenitor Cells Thru Haemogenic Endothelia Formation

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Introduction: Haematopoietic stem cells (HSCs) are one of the important candidates for cell-based therapy due to their capability of differentiating into functional haematopoietic cells. HSC can be derived from pluripotent stem cells such as embryonic stem cells. Human induced pluripotent stem cells (hiPSCs) have been explored as an alternative cell source for HSC generation as the use of human embryonic stem cells (hESCs) raises ethical controversy. Notably, the formation of intermediate haemogenic endothelia (HE), the specialised endothelial cells with haematopoietic potentials, is a crucial step for haematopoietic differentiation processes. In this study, we aimed to compare the differentiation capacities of hiPSCs and hESCs into HE as well as those of haematopoietic stem and progenitor cells (HSPCs).
Materials & Methods: iPSCs derived from human dermal fibroblasts (hNHDF-iPSC) and hESC lines (hUES9), were differentiated using STEMdiff™ Hematopoietic Kit into heterogeneous cultures for 12 days. The identities of the differentiated cells were then characterised with HE-related markers (CD31, CD34, CD144 and CD43) and HSC markers (CD34, CD43 and CD45).
Results: Before differentiation, hNHDF-iPSC showed significantly higher expression of TRA-1-81 ($p = 0.04$), SSEA4 ($p = 0.03$) and TRA-1-60 ($p = 0.04$) as compared to hUES9. After 12-day differentiation, the hNHDF-iPSC-derived differentiated adherent cells expressed significantly higher HE-related markers [CD144 ($p < 0.001$) and CD43 ($p = 0.04$), and CD34+CD144+ ($17.0 \pm 0.8\%$ vs $5.2 \pm 0.3\%$, $p < 0.001$)]. A regression test showed that the expression of CD34+CD144+ HE cells was significantly affected by the expression of pluripotency markers [SSEA4 ($p = 0.023$) and TRA-1-60 ($p = 0.024$)]. Interestingly, the HSPC production from hNHDF-iPSC was significantly higher than from hUES9 ($39.2 \pm 3.3\%$ vs $54.0 \pm 1.4\%$, $p = 0.008$). Regression test indicated that the expression of HSPCs may be affected by the CD34+CD144+ population ($p = 0.008$). Immunophenotyping analysis showed HSPCs are heterogeneous cultures consisting of two daughter populations: early haematopoietic progenitor (EHPs) with CD34+CD43+CD45- and haematopoietic stem cells (HSCs) with CD34+CD43+CD45+ expression. No significant differences were found between the production of EHPs ($37.2 \pm 3.2\%$ vs $25.4 \pm 2.7\%$, $p = 0.10$) and HSCs ($16.8 \pm 2.0\%$ vs $13.9 \pm 4.1\%$, $p = 0.97$) from hNHDF-iPSC and hUES9.
Discussion: In conclusion, our study showed that hiPSCs possess comparable differentiation capacities as hESCs in deriving HSCs and HSPCs which could be a potential source for cell therapy. The hiPSC, which consisted of a more homogenous population of pluripotent cells, may have greater differentiation capacities to produce functional HE with haematopoietic potential as compared to hUES9.

THE ORGANISING COMMITTEE WOULD LIKE TO THANK THE FOLLOWING FOR THEIR GENEROUS SUPPORT AND CONTRIBUTIONS:

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premier stem cell bank

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Established in 2002, CryoCord is one of the largest and most comprehensive private stem cell facilities in the Southeast Asia, specialising in long-term human stem cell, tissue cryopreservation and research.

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Cell-Based Research & Treatment

Company Overview

RESEARCH & DEVELOPMENT

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IIFA has confirmed that extracting cells from the umbilical cord to be used for the medical treatments is **HALAL ACCORDING TO SHARIA**.

Endorsement by His Excellency Prof. Koutoub Moustapha Sano, Secretary General of the International Islamic Fiqh Academy (IIFA) to Cytopeutics.

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PRE-CLINICAL STUDIES

- Safety, toxicity & tumorigenicity
- Biodistribution
- Osteoarthritis (OA)
- Stroke
- Systemic inflammation

Ongoing Studies:

- Diabetes mellitus
- Vernal keratoconjunctivitis (VKC)
- Elixir Multicellular Immune Therapy (EMIT) in colorectal cancer

CLINICAL STUDIES

- BM-MSC in severe ischemic cardiomyopathy
- BM-MSC in stroke
- BM-MSC in osteoarthritis
- BM-MSC in critical limb ischemia
- UC-MSC in healthy volunteer

Ongoing studies (UC-MSC):

- Graft versus host disease (GvHD)
- Stroke
- Osteoarthritis & cartilage injury
- Non-healing wounds

OUR COLLABORATORS

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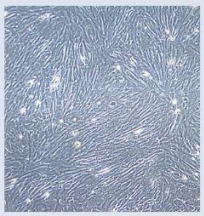
MALAYSIAN GENOMICS RESOURCE CENTRE BERHAD

STEM CELL THERAPY

MESENCHYMAL STEM CELLS (MSC)



EXOSOMES

EXXO LABS

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- Osteoarthritis
- Diabetes
- Knee injury
- Lung disease
- Stroke
- Neurodegenerative diseases

Next Gen Stem Cells

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Treatment potential of exosomes therapy:

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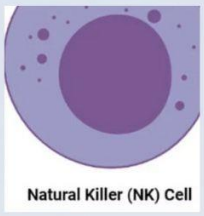
- Autoimmune disorders
- Scalp and hair
- Skin

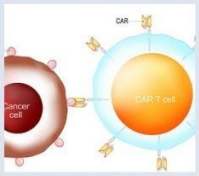
CANCER IMMUNOTHERAPY

NATURAL KILLER (NK) CELLS



Natural Killer (NK) Cell

CAR T-CELLS



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- Autologous NK Cells : for prevention, immune enhancement and wellness.
- Allogenic NK Cells: For treatment of cancer.

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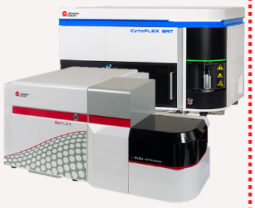

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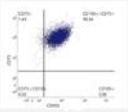

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