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- Mother's Precious Milk: Growing Tiny Tots into Healthy Toddlers
- Rare Diseases in Malaysia: Three Decades of Progress for Genetic Medicine at the Universiti Malaya
- Transcriptomic Tailoring of Therapy for Acute Undifferentiated Leukaemia
- Snake Venomics to Clinical Diagnostics: Challenges and Opportunities

TRANSLATIONAL OMICS RESEARCH

A RESEARCH BULLETIN BY THE FACULTY OF MEDICINE, UNIVERSITI MALAYA

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Background image by Beh Hooi Chin (*3rd place winner of Research Office Photo Competition Cycle 1/2022*)

FOREWORD FROM THE DEPUTY DEAN OF RESEARCH

Selamat Sejahtera to my fellow colleagues!

I believe that 2021 ended on a better note that how it started. Everyone in the faculty of Medicine had endured the past year with great effort and courage. I hope you managed to be productive in life and at work. We should work together in achieving greater momentum to continue achieving our team and individual goals this year. One may sprint faster in the short term as an individual, but a team, that's together, tends to travel further.

The Faculty of Medicine is blessed with a good blend of talent from both clinical and science backgrounds. This unique yet distinctive environment has motivated and nurtured countless strong research collaborations in different disciplines that has placed us among the top universities.

In this issue, we are pleased to share with you the translational omics research led by our faculty members. In the cover stories, you will read about how Dr. Chong Pan Pan and team discovered and utilized mesenchymal stem cells as biological therapies for articular cartilage repair. This study has progressed to phase 1 and phase 2 clinical trials. In an article by Dr. Syaza Zafirah and team, they described the use of transcriptomic technology in an acute undifferentiated leukaemia case that led to a successful prescription of tailored personalized treatment to the case. On the other hand, Dr. Puteri and team have profiled the proteins present in human milk through proteomic approach.

Noteworthy, February 28th is the World Rare Diseases Day. While relentlessly promoting the awareness for rare diseases, Prof. Thong Meow Keong and team incorporated omics technology in their genetic research that has translated into a gene therapy for 6 patients with spinal muscular atrophy, which is a rare genetic neuromuscular condition. Dr. Tan Kae Yi employed different omics technology to unveil the complex components of snake venoms, known as venomics, which has great potential to be developed into a point-of-care device for snake bite management.

In the special highlight, Dr. Phan Chia Wei and team in Clinical Investigation Centre of University Malaya Medical Centre are working towards advancing the omics technology to 'clinical-grade' that may improve clinical outcomes beyond standard care in the hospital. On another highlight, Dr. Shamsul explained his role as partners in the South East Asian Pharmacogenomic Research Network (SEAPharm) that aims to support pharmacogenomic implementation in this region■

~I hope you find this issue inspirating and enjoy reading!~

Prof. Dr. Sanjay Rampal
Lekhraj Rampal

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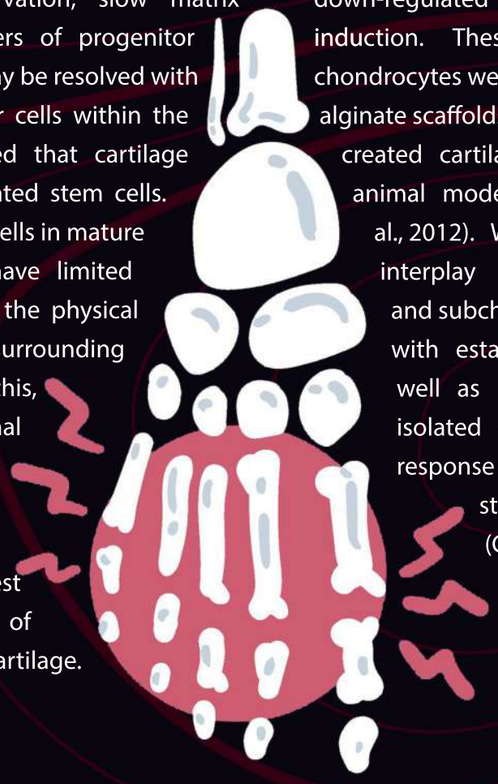
Biological Therapies for Articular Cartilage Repair:

From Basic Research to Clinical Outcome

Cartilage damage, which can potentially lead to osteoarthritis, is a leading cause of morbidity in the elderly. This is mainly due to the limited ability of cartilage to undergo self-repair following an injury resulting from the limited proliferative ability of adult chondrocytes, lack of vascularization and innervation, slow matrix turnover, and low numbers of progenitor cells. Although this issue may be resolved with the presence of progenitor cells within the tissue, it is well-established that cartilage is deficient in undifferentiated stem cells. Furthermore, the principal cells in mature cartilage (chondrocytes) have limited proliferative ability due to the physical restrictions in the surrounding environment. To overcome this, the potential of mesenchymal stem cells (MSCs) in biological therapies for cartilage regeneration has recently gained much interest in the challenging arena of repairing damaged joint cartilage.



In NOCERAL, our research focuses on isolating and expanding adult MSCs derived from bone marrow and peripheral blood, followed by inducing chondrogenic differentiation in vitro (Chong et al., 2012). The study further utilized RNA microarray to reveal up-regulated and down-regulated genes during chondrogenic induction. These MSCs and MSC-driven chondrocytes were embedded in biocompatible alginate scaffolds and transplanted into surgically created cartilage defects in knee joints of animal models (Dashtdar et al., 2011; Tay al., 2012). We have also determined the interplay of hyaline cartilage loss and subchondral bone changes in patients with established knee osteoarthritis, as well as assessed the biosynthesis of isolated osteoarthritic chondrocytes in response to varying dynamic compressive strain and loading duration (Fig. 1) (Chong et al., 2020).

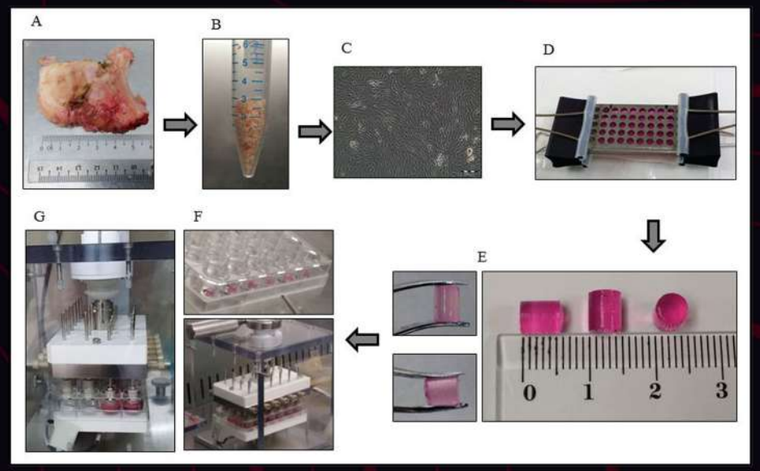


Figure 1: Dynamic compression of chondrocytes embedded in the scaffold. (A) Osteoarthritis proximal tibial cuts were collected during total knee replacement surgery. (B) Fine pieces of cartilage tissue. (C) Culture of chondrocytes cells in a 2D environment. (D) Mould of agarose seeded chondrocytes cells scaffold. (E) The size of each scaffold was 5mm x 5mm (diameter x height). (F, G) Bioreactor for the dynamic compression of the chondrocytes-embedded scaffold.

The promising finding arising from these animal and human studies has now been translated into clinical service involving suitable screened patients with grade I and II knee osteoarthritis to undergo repair through platelet-derived extracellular vesicles (PEV) treatment. The autologous PEV was processed in the Good Manufacturing Practice (GMP) laboratory (Fig. 2), and the intra-articular injection was performed at the orthopaedic clinic. Our prospective cohort showed patients who received PEV exhibited the most improvement among other control groups. Currently, we are undertaking Phase I & II randomised controlled clinical trials to determine the safety and efficacy of intra-articular injection of combined autologous peripheral blood-derived MSCs (PB-MSC) with PEV in the treatment of knee osteoarthritis. It is hoped that PEV+PB-MSC can serve as a biological therapy for articular cartilage regeneration in the future ■

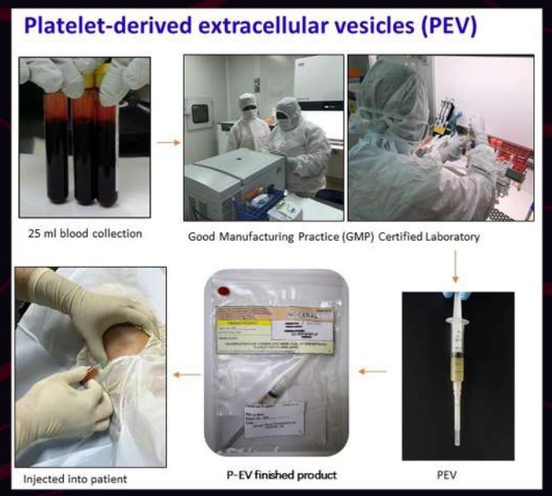


Figure 2: Isolation and intra-articular injection of platelet-derived extracellular vesicles (PEV).

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1. Chong, P. P., Panjavarnam, P., Ahmad, W., Chan, C. K., Abbas, A. A., Merican, A. M., Pingguan-Murphy, B., & Kamarul, T. (2020, Oct). Mechanical compression controls the biosynthesis of human osteoarthritic chondrocytes in vitro. Clin Biomech (Bristol, Avon), 79, 105178.

2. Chong, P. P., Selvaratnam, L., Abbas, A. A., & Kamarul, T. (2012, Apr). Human peripheral blood derived mesenchymal stem cells demonstrate similar characteristics and chondrogenic differentiation potential to bone marrow derived mesenchymal stem cells. J Orthop Res, 30(4), 634-642.

3. Dashtdar, H., Rothan, H. A., Tay, T., Ahmad, R. E., Ali, R., Tay, L. X., Chong, P. P., & Kamarul, T. (2011, Sep). A preliminary study comparing the use of allogenic chondrogenic pre-differentiated and undifferentiated mesenchymal stem cells for the repair of full thickness articular cartilage defects in rabbits. J Orthop Res, 29(9), 1336-1342.

4. Tay, L. X., Ahmad, R. E., Dashtdar, H., Tay, K. W., Masjuddin, T., Ab-Rahim, S., Chong, P. P., Selvaratnam, L., & Kamarul, T. (2012, Jan). Treatment outcomes of alginate-embedded allogenic mesenchymal stem cells versus autologous chondrocytes for the repair of focal articular cartilage defects in a rabbit model. Am J Sports Med, 40(1), 83-90.

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TRANSCRIPTOMIC TAILORING OF THERAPY FOR ACUTE UNDIFFERENTIATED LEUKAEMIA

A 7-year old boy was presented with a 2-week history of fever and easy bruising. Clinical examination of the boy revealed normal facies, pallor and mild hepatosplenomegaly. His bone marrow aspirate showed 80% infiltration by lymphoid-looking blasts. On flow cytometric examination, the immature cells expressed CD45(dim), low side scatter, CD34 (heterogeneous), CD133, CD7, HLA-DR and CD117(dim) with partial expression of CD90, CD64(dim), cCD79a(dim) and CD2 (Fig. 1). Myeloid, monocyte, megakaryocyte, erythroid and other T-cell associated markers were absent. These findings were consistent with a diagnosis of acute undifferentiated leukaemia (AUL). PCR-based screening for common leukaemia-associated oncogene fusion transcripts did not yield any positive results.

He commenced therapy with prednisolone based on lymphoid blast morphology but exhibited a poor response, with Day-8 marrow aspirate showing presence of 45% blasts. A decision was made to utilize high-throughput RNA sequencing to understand the blast biology and personalize therapy. This led to the discovery of a deleterious mutation in the PTPN11 gene (c.215C>T; p.A72V), which is commonly found in juvenile myelomonocytic leukaemia (JMML). Additionally, the patient's bone marrow cells were found to cluster close to JMML when projected on a t-distributed stochastic neighbour embedding (t-SNE) projection of a gene expression data set of diagnostic childhood leukaemia blasts (Fig. 2). Of note, germline mutations of PTPN11 gene are associated with constitutional Noonan syndrome but this entity was excluded in this patient by demonstration of wild-type sequence using his buccal epithelial cells.

Based on the transcriptomic analysis findings, he was prescribed azacitidine monotherapy using a conventional treatment schedule for JMML (Niemeyer, 2021). He achieved marrow morphological remission after a 1-week course of azacitidine. Following a second block of azacitidine, he underwent myeloablative chemotherapy and matched-sibling donor blood stem cell transplantation (HSCT). At two years of follow-up, he remains in remission from his underlying disease. Notably, mutation analysis of his bone marrow cells at Days +180 and Day +365 post-HSCT revealed only wild type PTPN11.

Acute undifferentiated leukaemia (AUL) is a very rare type of blood cancer that is biologically distinct from acute lymphoblastic or myeloid leukaemia. Paediatric AUL is challenging to treat, as there is no established therapy and generally confers a poor prognosis. Transcriptomic characterization has allowed for better understanding of underlying cancer cell biology and has helped determine the best-tailored therapy for our patient.

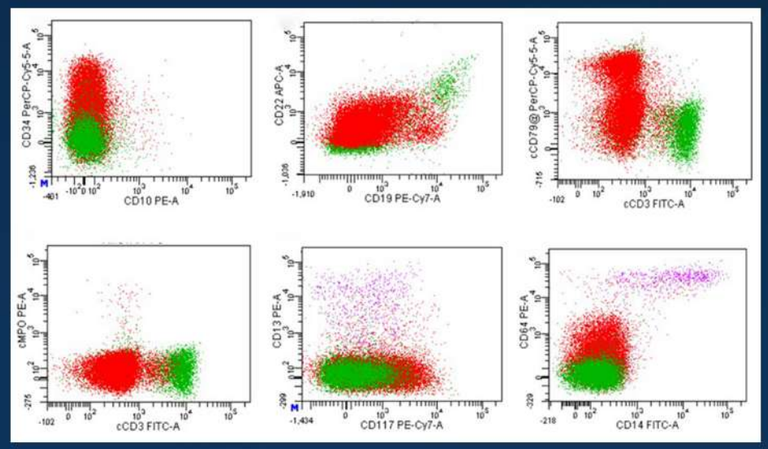
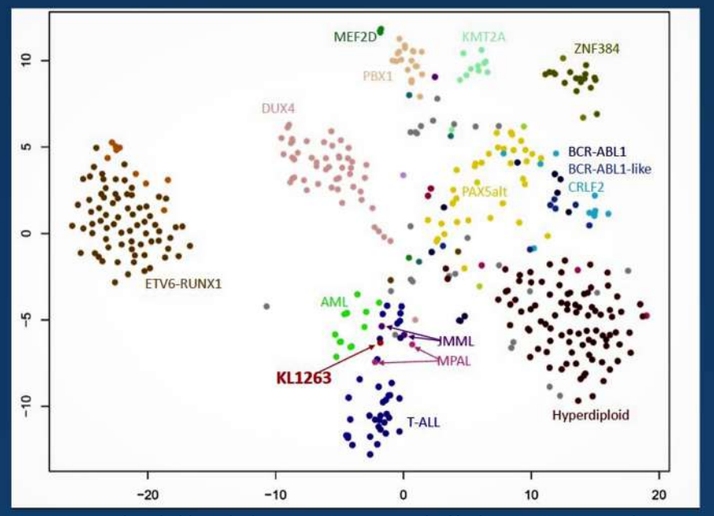


Figure 1 (right): Flow cytometric analysis of the patient's bone marrow sample. The blast cells are highlighted in red, lymphocytes in green and monocytes in purple. The blast cells express CD34 (heterogeneous), CD117(dim), cCD79a (dim) and are negative for lymphoid markers i.e. CD10, CD19, CD22 and cCD3 as well as myeloid markers i.e. cMPO, CD13, CD64 and CD14.

Figure 2 (below): Gene expression t-SNE plot of diagnostic samples from subjects in the Malaysia-Singapore ALL2010 study. The patient's blasts (KL1263) clustered between AML and T-ALL, with the JMML and MPAL cases clustered nearby.



Key: ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; JMML, juvenile myelomonocytic leukaemia; MPAL, mixed-phenotypic acute leukaemia. (Figure courtesy of Dr Li Zhenhua and Prof Allen Yeoh, National University of Singapore).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Mother's Precious Milk: Growing Tiny Tots into Healthy Toddlers

Human milk is a living fluid that undergoes significant changes throughout the entire breastfeeding period, and it is considered as the gold standard of infant nutrition. The content of human milk is uniquely tailored; its composition changes throughout the day and night, the months, and the years, to meet the child's nutritional and immunoprotective needs for an optimal growth. The time between birth and two years old has been acknowledged as the critical window for child development. This will create a foundation for good health and well-being during adolescence and adulthood. The WHO and UNICEF recommend exclusive breastfeeding for the first 6 months of life and for breastfeeding to remain in place for two years and beyond with additional complementary foods.

Breastfeeding beyond infancy, also known as long-term breastfeeding, is not a common practice in Malaysia. The Malaysian National Health Morbidity Survey in 2016 reported the prevalence of exclusive breastfeeding was 47.1%, while continued breastfeeding among children aged 20–23 months old was only 39.4% [1]. Many are unaware of the losses incurred due to inadequate breastfeeding. A study conducted on the cost of not breastfeeding in Malaysia in 2019 reported 110 death cases among children under 5 years and 458 maternal deaths from cancers and diabetes which can be prevented yearly by breastfeeding. The spending on medical costs could also be reduced by RM27.8 million per year [2]. Such a situation occurs due to a lack of awareness and knowledge of the importance of adequate breastfeeding.

Figure 1: Monthly knowledge sharing webinars with BreastFeeding Counselor Networking Programme (BCNP)

The breastfeeding process requires a strong and continuous commitment, especially among working mothers. As mothers themselves, Dr. Puteri and her team were motivated to explore the dynamic changes in human milk composition in long-term breastfeeding. In the quest to ensure children get the best benefit of mother's milk, they profile and identify the components found in human milk and decipher their bioactive, protective and functional roles. Their study, funded by the UM's IIRG programme [3], utilizes proteomics methodology to analyse human milk samples collected throughout 24 months of lactation period. Certain proteins are found to be regulated differently in the early and late stages of breastfeeding. These proteins are involved in various biological processes, mainly immune response and cellular metabolism, in a time-dependent manner which aligns with the development of infants' and children's growth processes. Apart from this, the team is also interested in discovering the metabolites in human milk and their relationship with circadian rhythms in infant growth. By sharing outcomes of the research with the community, Dr. Puteri hopes to instil awareness on the benefits of human milk and support mothers in long-term breastfeeding practice. To manifest this mission, she actively shares information with the public through sessions held by the Breastfeeding Counsellor's Associations and presents papers locally and internationally.

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Department of Molecular Medicine

1. Institute for Public Health (IPH) 2016. National Health and Morbidity Survey 2016 (NHMS 2016): Maternal and Child Health. Vol. I: Methodology and General Findings, 2016.
2. https://www.aliveandthrive.org/en/resources/cost-of-not-breastfeeding-advocacy-brief-series
3. UM Impact-oriented Interdisciplinary Research Programme: Breast Milk Sharing in Ethnically Diverse Malaysia" under the subprogramme IIRG032B-2019 "Investigating The Dynamic Changes in Human Milk Protein Composition of Malaysian Mothers at Different Stages of Lactation"

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Figure 2 and 3: Community engagement at the "The Gift of Love" event organised by The Breastfeeding Advocacy Network (TBAN) in conjunction with World Breastfeeding Week 2019. Booth for research promotion and information dissemination to the public.

Rare Diseases in Malaysia:

Three Decades of Progress for Genetic Medicine at the Universiti Malaya

February 28th 2022 was World Rare Disease Day. Since 1995, the Genetic Medicine Unit of the Department of Paediatrics Universiti Malaya (UM) led in the research of rare diseases and genomic diagnoses of various undiagnosed syndromes. These efforts enabled personalised medicine culminating in the first successful gene therapy treatment for spinal muscular atrophy in Malaysia.

The World Health Organization (WHO) defines a rare disease as any disease which affects a small percentage of the general population. Rare Disease Group Europe (EURORDIS) defines rare diseases (RD) as conditions affecting 5 in 10,000 of the general population while in Malaysia, it is a disease with a prevalence of 1 in 4,000 of the general population (http://www.mrds.org.my). Although each RD is individually rare, collectively they number over 7000 types and the RD community makes up 5-8% of the population. RDs may happen to anyone regardless of race, gender, age, or socioeconomic background and 80% of RDs are genetic in origin. Sadly, 30% of patients with RD passed away by the age of 5 years (1). About 9% or 45,000,000 people in Southeast Asia are afflicted by RDs. The survivors with RDs often need long term medical care as a result of these chronic diseases. RDs are non-communicable diseases but due to the lack of a RD registry, there is little data on their epidemiology in Malaysia. The UN General Assembly in 2021 approved a resolution on addressing the challenges of persons living with a rare disease and their families. Yet, patients with RDs face stigmatization and arduous "diagnostic odysseys" - delayed treatment due to late diagnosis, low awareness by members of the public and healthcare professionals, limited access to genetic services and reduced access to life-saving medicines (2).

Recognizing the need for research on RD, the first dedicated Genetic Medicine unit in Malaysia was established in UM in 1995 and scored many "firsts": first to treat lysosomal diseases (Gaucher, Pompe disease and mucopolysaccharidosis type VI) with enzyme replacement therapy; first to train genetic counselors to enable board-certification in 2003; first to establish a RD support group; first public hospital to start newborn screening program for RDs and to offer next-generation sequencing for undiagnosed malformation syndromes.

Figure 1: First gene therapy in Malaysia for spinal muscular atrophy (2020)

Figure 2: Celebration of World Rare Disease Day in UMMC on February 28th

Extensive research and collaborations with national and international institutions were conducted on RDs which many were hitherto unknown in the Malaysian population. These included the use of software development for pedigree drawing (Gold Medal ITEC), artificial intelligence in facial dysmorphology and craniofacial conditions, use of "Omics" technology in the delineation of new syndromes, clinical drug trials for genetic therapeutics and policy development for RDs in Malaysia. Gene therapy was successfully used in Southeast Asia for the first time in 2020 for 6 UMMC patients with spinal muscular atrophy, a rare genetic neuromuscular condition.

Unlike the Ministry of Health Malaysia which was allocated an annual budget of over RM20 million for RD, university teaching hospitals were not given any drug budgets to treat RD. This will have an adverse impact on the teaching of RDs in medical schools. Universities must be included as part of the National Strategic Framework for RD and be given appropriate allocations to treat patients and obtain resources to train genetic counselors, clinical geneticists and doctors skilled in diagnosing and treating RD early. This will enable Malaysia to achieve the 2030 UN Sustainable Developmental Goals where no one is to be left behind in personalized and genomic medicine (3,4) ■

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1. Thong MK, Azlina A-A, Todd L, Vaisnavi MR. White Paper: Rare Diseases in Malaysia. Published by IDEAS (Institute for Democracy and Economic Affairs) (2019) ISBN:978-967-16674-3-9. http://www.ideas.org.my/wp-content/uploads/2019/12/RD_WhitePaper_V5.pdf
2. Thong MK, See-Toh Y, Hassan J, Ali J. Medical genetics in developing countries in the Asia-Pacific region: challenges and opportunities. Genet Med. 2018 Oct;20(10):1114-1121. doi: 10.1038/s41436-018-0135-0.
3. Thong MK. Achieving the targets of sustainable development goals (2030 agenda) for congenital disorders in Asia: Bottlenecks and interventions. Am J Med Genet C Semin Med Genet. 2019 Jun;181(2):254-261. doi: 10.1002/ajmg.c.31690
4. Jamal RA, Looi LM, Mohd Nor N, Thong MK, Teo SH, et al. Academy of Sciences Malaysia "Position Paper on Precision Medicine Initiative in Malaysia" (2020) ISBN No. e978-983-2915-55-3.https://www.akademisains.gov.my/asm-publication/precision-medicine-initiative-in-malaysia/

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Snake Venomics to Clinical Diagnostics:

Challenges and Opportunities

Imagine yourself being bitten by a venomous snake and might not be receiving the appropriate treatment! Isn't it worrying? Each year, venomous snakebites cost the lives of countless people and leave many more with permanent disfigurement and disability, particularly in Asia's tropics and subtropics(1). Snakebite envenomation has topped the priority list of neglected tropical diseases (NTD) since its inclusion by the World Health Organization (WHO) in 2017(2), however, the global efforts to resolve this tragic situation remain inadequate, even until today.

Clinical management of snakebite patients relies on the identification of biting snakes in selecting the "right" treatment. In the case of envenoming, the appropriate antivenom must be given promptly to the patients to increase the survival rate. However, in clinical settings, the selection of antivenom is often dependent on the decision of clinical personnel based on the patient's description of the biting snakes and the toxic symptoms developed. Admittedly, it is peculiar, but this is mainly because a validated snakebite diagnostic test for determining the best course of treatment, remains unavailable until today.

Although a timely diagnosis of snakebite envenoming is essential, the development of a validated diagnostic device is more complicated than we could imagine. This is why, except for Australia, a clinical diagnostic device for snakebite remains unavailable worldwide. The main reason for this is the diversity of venomous snakes, as each of them has its complex toxin cocktail (venom) that makes the accurate diagnosis of biting snakes challenging.

In the Faculty of Medicine, our research team has spent years employing -omics technologies such as proteomics and transcriptomics to unveil the complex snake venoms, as well as exploring their pharmacological and immunological properties. The discovery would enable the identification of causative toxins as therapy targets, while also revealing unique toxins that can be used as a target analyte for clinical diagnostics of snakebite.

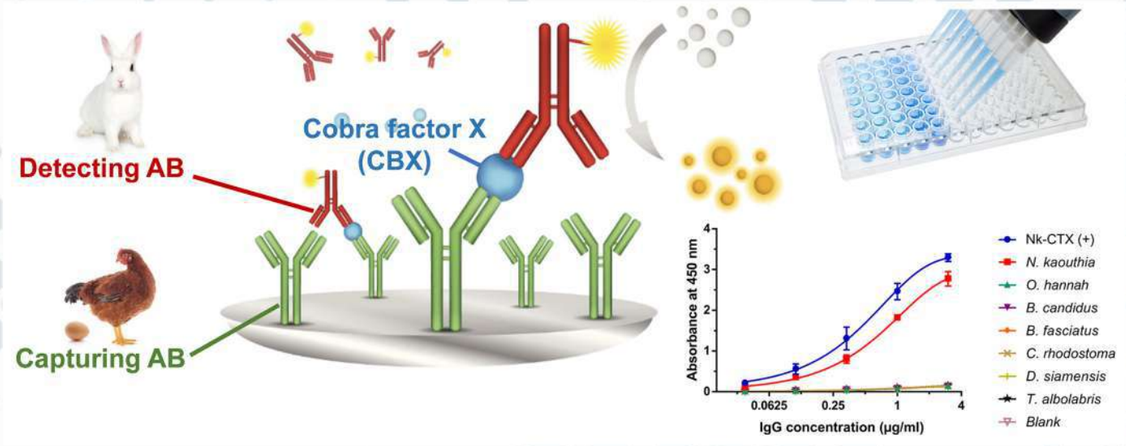

Figure 1: Direct double-antibody sandwich ELISA showed selective immunodetection of cobra venoms among different venoms tested.

We recently showed that the antibodies produced from a unique toxin discovered through proteomics could serve as potential for diagnosis of cobra bite (Figure 1). We suggest that these antibodies not only provide quick identification for cobra bites but also allow clinical monitoring of cobra bite patients. It is seen as an opportunity to translate fundamental knowledge to bedside applications through the development of the point-of-care device and the aim is in line with WHO's strategic goals to improve the clinical management and outcomes of snakebite envenoming. The works currently undertaken are challenging, not only from the scientific perspective but also in terms of the need for various collaborative efforts from different parties to enable a successful translation in snakebite management. However, we believe that the outcome of our study will contribute towards WHO's vision to halve the number of deaths and disabilities due to snakebite by 2030(3).

For more details, please contact kytan_kae@um.edu.my. For more information, please visit www.vetoxlab.com.

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1. Gutiérrez, et al. (2017). Snakebite envenoming. Nature reviews Disease primers, 3(1), 1-21.
2. Chippaux, J. P. (2017). Snakebite envenomation turns again into a neglected tropical disease!. Journal of Venomous Animals and Toxins including Tropical Diseases, 23(1), 1-2.
3. Williams, et al. (2019). Strategy for a globally coordinated response to a priority neglected tropical disease: Snakebite envenoming. PLoS neglected tropical diseases, 13(2), e0007059.

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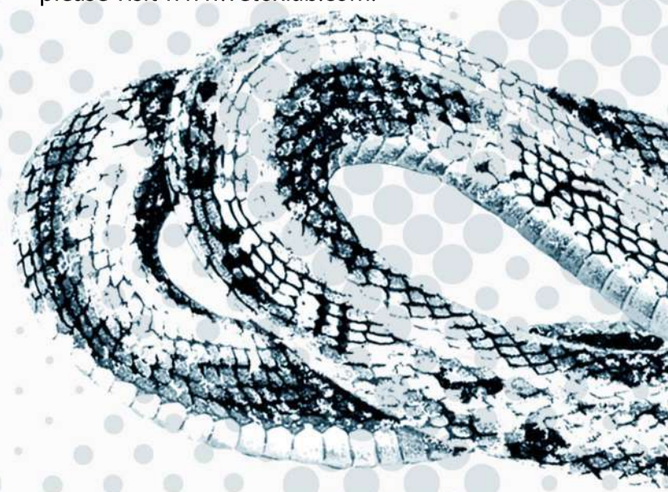
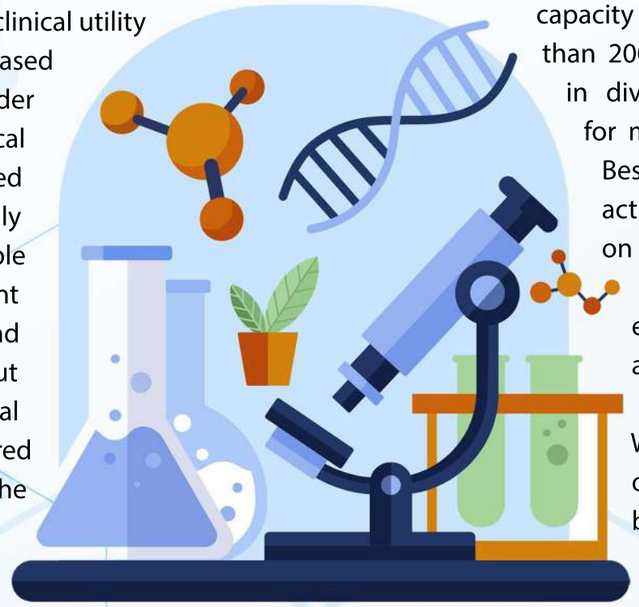


The Role of Clinical Trial in Translating Clinical Utility of Omics Technology

Translational research represents a systematic approach of conducting research that begins with basic sciences, and its transition into practical applications to improve human well-being. Clinical trial settings, particularly Phase I studies, which transition from preclinical (animal studies) to human investigation, are excellent examples of translational aspects of drug discovery.

Today, the field of omics is fast evolving. Clinical management is already being shaped by omics, particularly in the field of clinical cancer, which has seen the most adoption of omics approaches. Precision medicine comes to mind when we think of omics. The perception is somewhat true as genomics has allowed for more personalized therapy. Precision medicine centers on choosing (immuno)therapies and chemotherapeutic drugs based on tumour molecular profiling and the patient's genetic background.

In order for an omics technology to advance to a "clinical-grade" omics assay, numerous criteria must be met, including a robust-designed clinical trial. The omics-based prediction that algorithmically determines the optimal treatment regime should be valid, reproducible, and determined in an unbiased manner. Most importantly, the goal of an omics clinical trial should be to gather data to support the clinical utility of the omics-based technology under investigation. Clinical utility is demonstrated when a test not only delivers a considerable benefit to a patient above and beyond standard care, but also improves clinical outcomes as compared to not performing the test.



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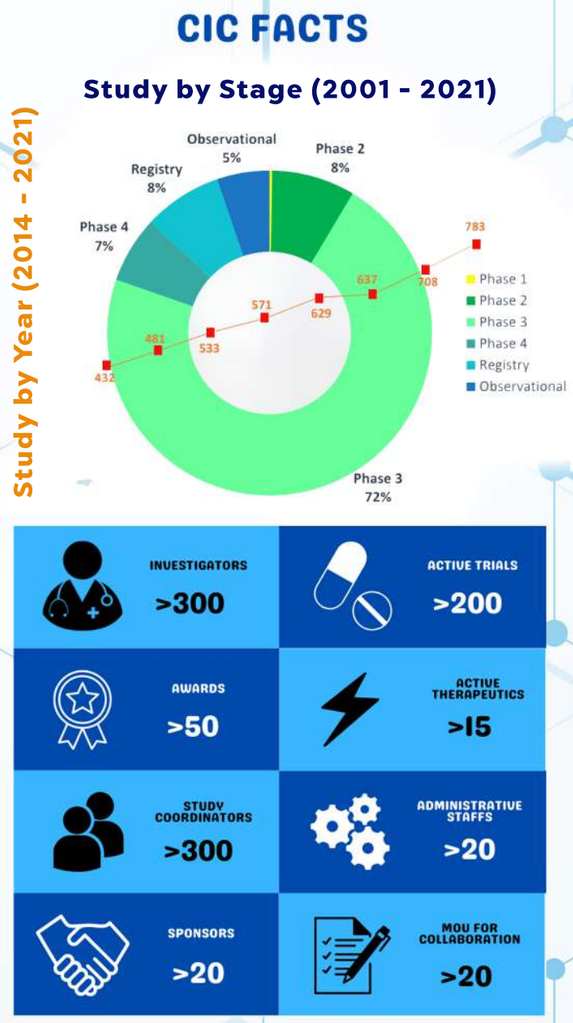
Omics technology is often dependable on big data, artificial intelligence, and machine learning. Such integrated omics technology must be carefully considered because it will be used to determine treatment decisions in the future. Therefore, understanding of ethical, legal, and regulatory requirements is essential to various stakeholders under the framework of a clinical trial, e.g. the trial sponsor, principal investigator, institutional review board, statisticians, and scientists, in which their roles must be carefully defined and addressed.

As a research centre dedicated to facilitate the conduct of safe and credible clinical research in drug and medical devices, Clinical Investigation Centre (CIC) in the University Malaya Medical Centre (UMMC) serves as a point of contact for an integrated network of experienced clinical investigators, as well as a large pool of research subjects. The centre is equipped with trained personnel and sophisticated infrastructure, providing a capacity of conducting more than 200 active trials currently in diverse therapeutic areas for multicentric clinical trials. Besides, the centre also actively teaches and trains on subjects like ethics and Good Clinical Practice to ensure the scientific authenticity and quality of our clinical trials. With the integration of omics technology, it is believed that CIC will continually serve as a centre of excellence for clinical trials.■



For further reading:
1. Akademi Sains Malaysia (2018). Precision Medicine Initiative in Malaysia.
2. McShane LM, et al (2013) Criteria for the use of omics-based predictors in clinical trials. Nature. 2013, 502: 317-320.

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Experts push for pharmacogenomics research collaboration among South East Asian countries

Pharmacogenomics (PGx) is increasingly being recognized as a potential tool to improve efficacy and safety of drug therapy by ensuring patients get the right drug, at the right dose and at the right time. To strengthen PGx research among the South East Asian (SEA) countries, a PGx working group called South East Asian Pharmacogenomics Research Network (SEAPharm) was established in 2012 with the ultimate goal to support PGx implementation in the region.

In February 2018, the "100 Pharmacogenes" project kick off meeting was initiated at Mahidol University, Bangkok. A researcher from Universiti Malaya, Dr Shamsul Mohd Zain was honored to join forces in this project as one of the SEAPharm active members representing Malaysia. The project brings together experts not only from South East Asian countries but also Greece, Japan and the United Arab Emirates.

Thanks to the successful SEAPharm meeting held in Singapore in August 2018, an expanded research collaboration between participating SEA countries was formed focusing on the "Re-sequencing Project of 1,000 Southeast Asian Individuals Using the 100 Pharmacogenes". The aim of this project is to identify genetic variations of 100 pharmacogenes associated with adverse drug reactions (ADRs). ADRs can cause a significant impact on morbidity and mortality, which can lead to a major economic burden.

This vital information would assist in developing a pharmacogenomics guideline and clinical practice in the future, and improve the safety and efficacy of pharmacotherapy for SEA individuals by implementing clinical pharmacogenomics services; the "low-hanging fruit" in genomic medicine, at a very low cost and helping to reduce unnecessary healthcare costs from inefficient or inappropriate drug therapies. The full realization of the project's vision is still many years away but could happen when strategic partnerships are in place and the project is well executed.

Under the big umbrella of "100 Pharmacogenes" project, lies six subprojects namely (1) pharmacogenes variations in various populations in SEA; (2) PGx of severe adverse drug reactions (SCARs); (3) PGx of drug-induced liver injuries (DILI); (4) cost effectiveness analysis of pharmacogenes variant screening in Southeast Asians; (5) PGx in clinical pharmacy practice; and (6) pharmacogenes assay development in the clinical setting. Eventually, the fruit of this research collaboration will lead to the setting up of a database of 100 pharmacogenes in SEA and that is made accessible to the SEAPharm members. Furthermore, output from this project could also help in determining the pattern of genetic variations among the Southeast Asian populations, and correlate the genetic information with the drug response and ADRs to assist clinical decision-making process.

Figure 1: In February 2018, the "100 Pharmacogenes" project kick off meeting was initiated at Mahidol University, Bangkok.

In 2021, this collaboration has produced enormous data on SEA pharmacogenes variations with two reports successfully published. While this will facilitate the sharing and/or pooling of ADR data among member countries, the reliability and quality of these data must be preserved and properly stored. Although there are some delays due to COVID-19, subproject (1) is nearing its completion. The other subprojects are expected to be finished within three to five years. Researchers and clinicians who are working in SCARs and DILI are welcome to collaborate ■

Shamsul Mohd Zain
Department of Pharmacology

Background vector adapted from freepik (www.freepik.com)

AWARDS & ACHIEVEMENTS

1 **Honorary Fellow of the Philippine Society of Colon and Rectal Surgeons & Porfirio M.Recio Memorial Lecturer 2022**

Professor Dr. April Camilla Roslani (Department of Surgery)

2 **The Fullbright Malaysian Scholar Program**

Professor Dr. Yvonne Lim Ai Lian (Department of Parasitology)

3 **L'Oréal-UNESCO Fellowship for Women in Science Award**

Associate Professor Dr. Cindy Teh Shuan Ju (Department of Medical Microbiology)

4 **Inaugural Women's Institute of Management (WIM) Tan Sri Dato' Napsiah Omar Women Leaders Award 2022 (Category: Education)**

Professor Dato' Dr. Adeeba Kamarulzaman (Department of Medicine)

5 **Conferred the title of "Professor Emeritus" during the 61st Universiti Malaya Convocation Ceremony**

Professor Emeritus Ng Kwan Hoong (Department of Biomedical Imaging)

6 **Asia Pacific Medical Education Conference 2022 (APMEC 2022)**

Young Scholar Merit Award

Chan Chee Ken (MBBS Stage 3.3), Lam Thian Yin (MBBS Stage 3.3), Dr. Kanesh Kumaran Seevalingam (Department of Surgery), Associate Professor Dr. Retnagowri Rajandram (Department of Surgery), Associate Professor Dr. Shanggar Kuppusamy (Department of Surgery)

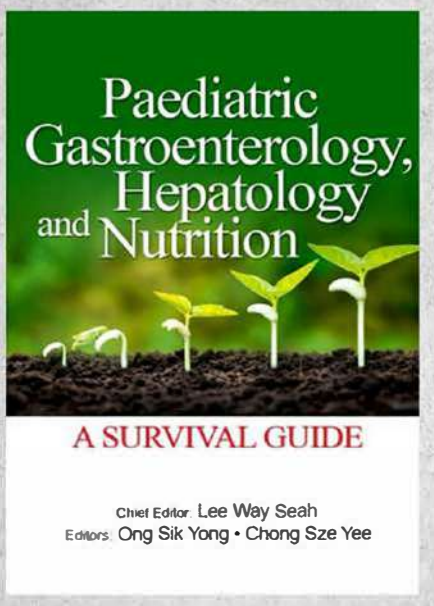
7 **Malaysia Technology Expo (MTE 2022) - International Innovation Awards**

Gold Award Winner

Project leader: Dr. Wong Kah Hui (Department of Anatomy, Faculty of Medicine, UM)
Team members: Ms. Lew Sze Yuen (Department of Anatomy), Dr. Lim Siew Huah (Department of Chemistry, Faculty of Science, UM)
Madam Cheng Poh Guat (CEO, Ganofarm R&D Sdn Bhd), Assistant Professor Dr. Lim Lee Wei (The University of Hong Kong)

Silver Award Winner

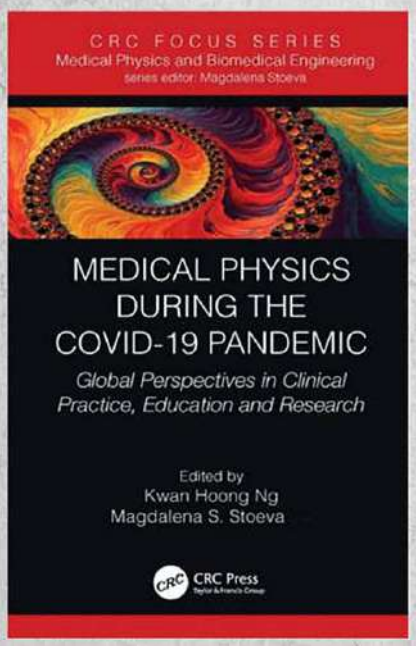
Project leader: Prof. Dr. Moy Foong Ming (Department of Social and Preventive Medicine, Faculty of Medicine, UM)
Team Members: Professor Dr. Loo Chu Kiong (Department of Artificial Intelligence, Faculty of Computer Science and Information Technology, UM), Dr. Fadzilah Hanum bt Mohd Mydin (Department of Primary Care, Faculty of Medicine, UM)



Paediatric Gastroenterology, Hepatology and Nutrition: a Survival Guide

Chief Editor: Lee Way Seah
Publisher: University Malaya Press
ISBN: 978-967-488-179-9

Concise and well-crystallised, this book is written by a group of well-trained practising paediatric gastroenterologists in Malaysia. Collectively, they have many years of clinical experience and their opinions are well regarded in Malaysia. This is an up-to-date approach to various common problems in gastroenterology, hepatology and nutrition in children and will serve as an invaluable guide for all practising physicians dealing with children. It is a 'must read' guide for postgraduate students and paediatric trainees preparing for clinical professional examinations.



Medical Physics During the COVID-19 Pandemic

Editor from UM: Ng Kwan Hoong
Publisher: Taylor & Francis Group
ISBN: 978-100-314-438-0

Spreading to every corner of the Earth, the COVID-19 virus has had an unparalleled impact on all aspects of our lives. This book explores in detail how the COVID-19 pandemic has affected clinical practice, education, and research in medical physics, and how colleagues on the frontline dealt with this unpredictable and unprecedented pandemic. It tackles key questions such as: How did medical physicists first respond to the situation? What innovative strategies were taken and how effective were they? How are medical physicists preparing for the future?

There will be a focus on the different experiences of regional medical physicists and the responses and outlooks in clinical practice, education, and research in the affected continents, Asia-Pacific, the Middle East, Europe, Africa and North and Latin America. With over 91 contributors from 39 countries, this unique resource contains key perspectives from teams from each territory to ensure a global range of accounts.

The collective opinion and wisdom from the major medical physics journal editors-in-chief are also explored, alongside how the pandemic has affected the quantity and quality of publications. Voices of early-career researchers and students of medical physics will be included, with narratives of their experiences coping with life during the pandemic. Lastly, communicating leadership in times of adversity is highlighted.

This book will be a historic account of the impact of the COVID-19 virus on the field of medical physics. It will be an ideal reference for medical physicists, medical physics trainees and students, hospital administrators, regulators, and healthcare professionals allied with medical physics.

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