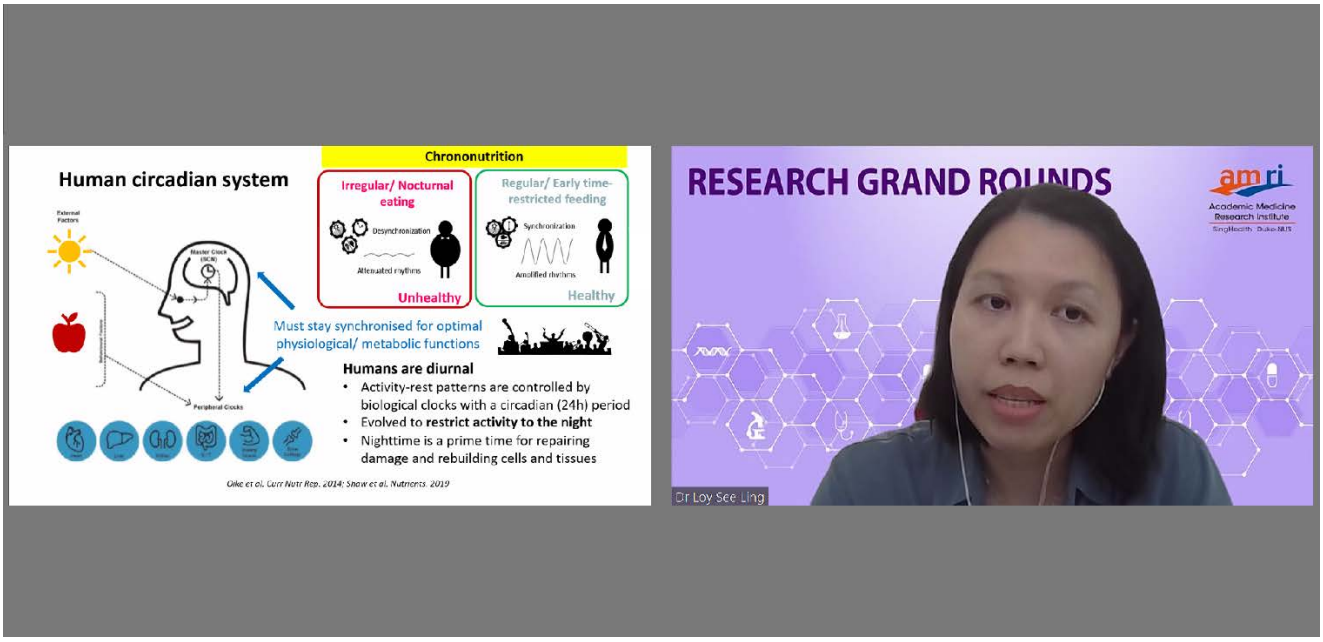
Research e-Bulletin

Maternal and Child Health Research in Singapore

In our last Research Grand Rounds (RGR) for 2023 held on 22 November, participants gained insights on SingHealth Duke-NUS Maternal and Child Health Research Institute (MCHRI) in advancing maternal and child health outcomes. Our speakers, Dr Loy See Ling (Junior Principal Investigator, Reproductive Medicine, KK Women's and Children's Hospital), Dr Yeo Joo Guan (Vice Chair (Research), SingHealth Duke-NUS Paediatrics Academic Clinical Programme) and Dr Saumya Jamuar (Director, SingHealth Duke-NUS Institute of Precision Medicine) discussed on various themes including metabolic health, genetics and immunology.

The MCHRI serves as a centre of excellence to focus and lead healthcare research and implementation initiatives in maternal and child health. Taking a life-course approach, MCHRI aims to tackle population health challenges, implement evidence-based initiatives, and cultivate a continually-learning ecosystem for researchers focusing on maternal and child health challenges.



In her introductory presentation on "The Study of Chrononutrition in Pregnancy," Dr Loy See Ling initiated the discussion by elucidating the development of an inherent 24-hour cycle in the human body, known as circadian clocks. These clocks consist of the master clock, situated in the brain, which synchronises with sunlight, and peripheral clocks dispersed throughout various organs and cells,

responsive to food timing.

When a discrepancy arises between the social clock, such as mealtime, and the biological clock, a desynchronisation between these clocks occurs, impairing the rhythmicity of clock gene expression responsible for regulating metabolic processes. This mismatch can lead to adverse health outcomes. Conversely, aligning feeding times with biological clocks enhances the rhythmicity of clock gene expression, fostering optimal metabolic outcomes. This fundamental principle constitutes the core concept of Chrononutrition.

Chrononutrition, an emerging discipline, emphasises not just the quantity and content of food but also underscores the importance of timing for overall well-being. Unfortunately, food timing is often overlooked in discussions about basic nutrition.

Dr Loy also highlighted a specific maternal chrononutrition study which reveals two distinct patterns: one group consumed more calories during the day, while the other consumed more at night. Examining the glycaemic outcomes in pregnant women who ate at night, higher fasting plasma glucose was noted in those practicing night eating during the second trimester.

To determine the possibility of an inverse causal relationship between maternal night eating and hyperglycaemia, Dr Loy conducted a longitudinal study. Her findings indicated that maternal night eating observed at early pregnancy was related to continuously higher glucose throughout 24 hours especially during the post-midnight period, higher fasting and 1-hour glucose levels, as well as lower beta-cell function at later pregnancy. She highlighted that the co-existence of both high glucose and low beta-cell function is worrying as this condition could predispose women to a higher risk of Type 2 diabetes development after delivery. She further showed that maternal night eating was linked to preterm birth and significant postpartum weight retention.

In her concluding statements, Dr Loy acknowledged that the field of maternal chrononutrition is in its early stages and many questions remain to be addressed. There is an ongoing effort to incorporate meal timing screening and intervention as part of the new model-of-care. The instrument utilised is currently deployed in the HELMS cohort at KKH through a mobile app. Based on women's adherence to meal timing and food intake, relevant nudges will be sent to their phone app, offering tips and recommendations to address such behaviours.

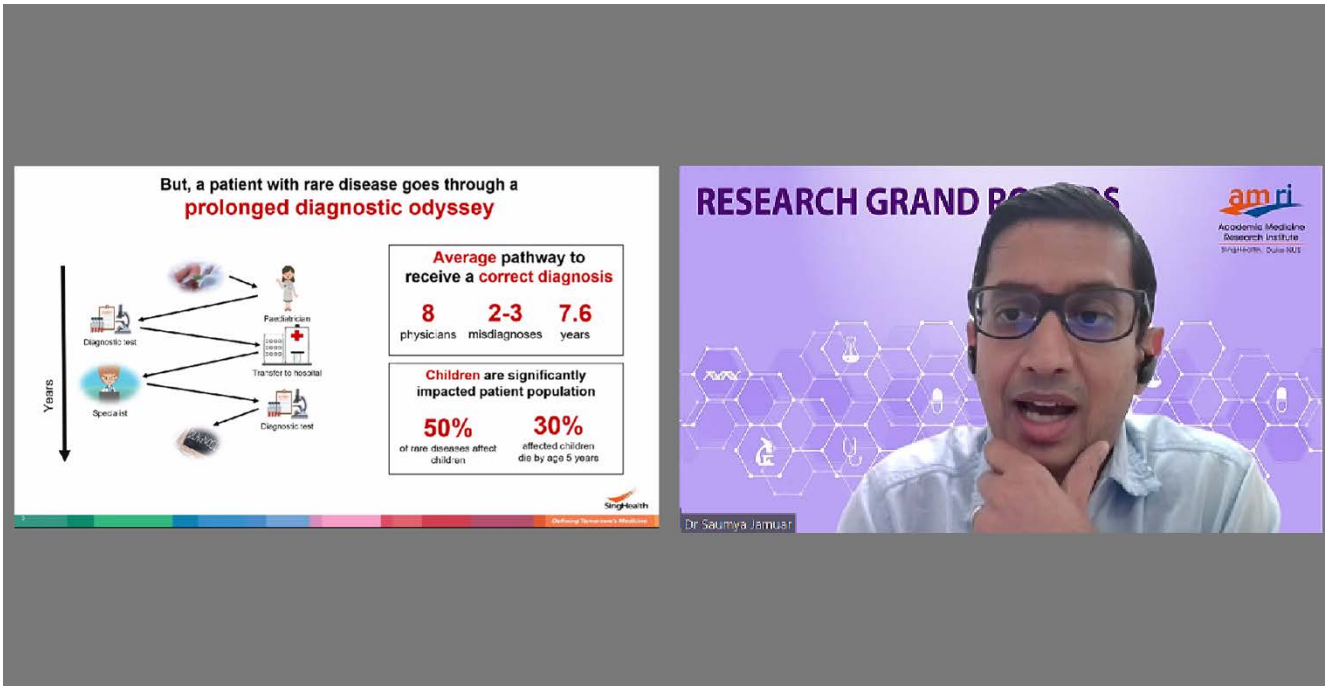
Next, Dr Yeo Joo Guan began by sharing the unmet needs in Systemic Lupus Erythematosus (SLE), a complex and heterogeneous systemic autoimmune disease. The unmet needs include a lack of understanding of the immunopathogenic complexity and diversity within the umbrella diagnosis of lupus. Additionally, the absence of mechanistically based stratification hinders complete therapeutic targeting and understanding of the disease. Furthermore, the lack of differentiation between childhood and adult-onset lupus often leads to the extrapolation of treatments from adult studies to children without direct evidence of benefits.

To gain a comprehensive understanding of lupus, Dr Yeo detailed a study conducted by his team, comparing the immunome of adult-onset SLE and childhood-onset SLE (cSLE) to healthy individuals. Mass cytometry was employed to capture a multitude of variables at high resolution followed by the use of machine learning analysis to understand the disease immune architecture.

He elaborated further on the SLE immunome, revealing multiple derangements in different immune subsets not only between healthy individuals and lupus patients but also showing distinct age differences. His findings indicated that there were commonalities in the immune cellular composition as well as distinct differences between cSLE and adult-onset SLE. Particularly in adult-onset SLE, there was a reduction in CTLA4 expression in non-regulatory T cells which may result in a reduction of the cellular activation threshold.

Dr Yeo emphasised the potential utility of the multi-dimensional approach. This approach allows for

strategic differentiation between individuals with healthy and lupus conditions, presenting opportunities for diagnostic purposes and further development.



Dr Saumya Jamuar, our final speaker, began by addressing the prolonged diagnostic odyssey experienced by patients with rare diseases. He advocated for a life-course approach, starting with mapping the patient journey in the genetics clinic. He acknowledged the existence of pain points and bottlenecks at various steps in the process.

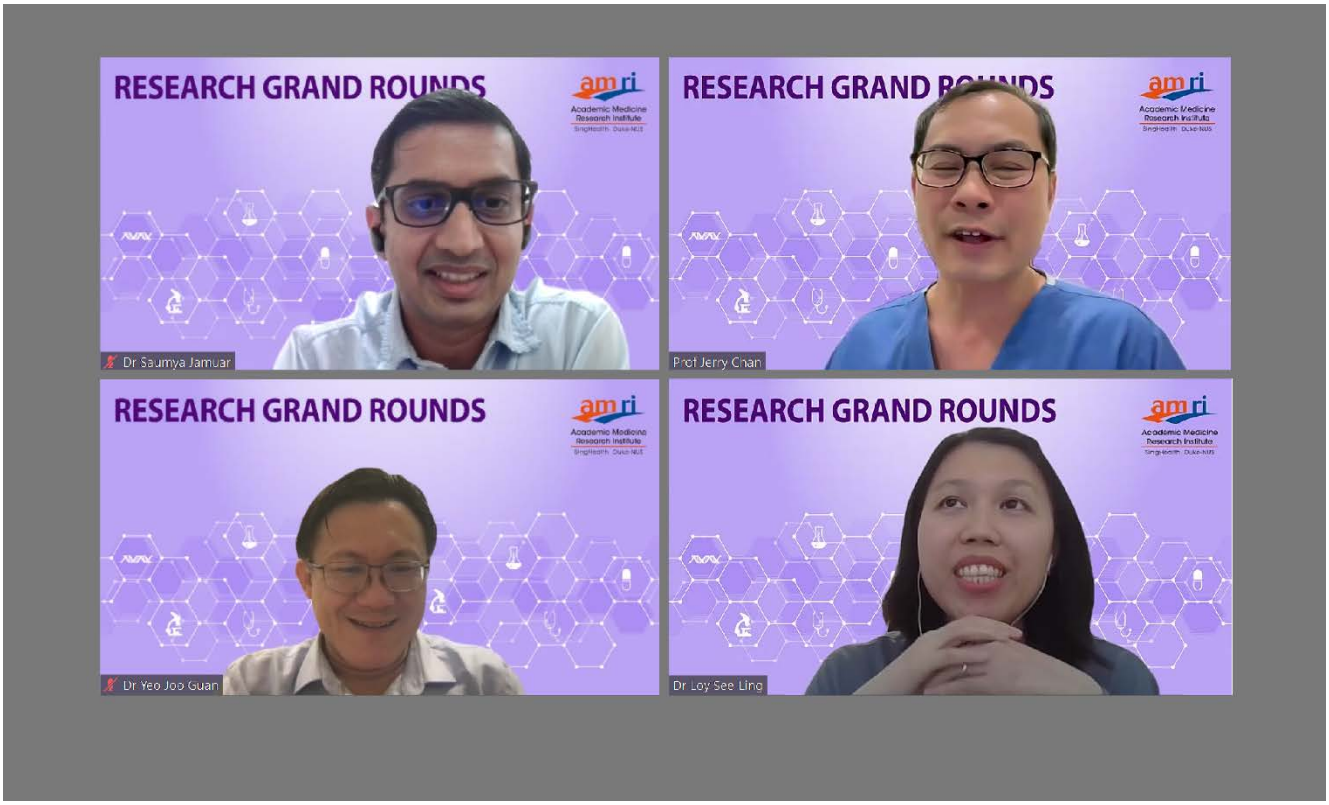
Dr Saumya highlighted the pain point of genetic testing, citing limited labs and prolonged wait times of months to years for results. In response, the initiative 'Bringing Research Innovations for the Diagnosis of Genetic Diseases in Singapore (BRIDGES)' was launched. This initiative leveraged cutting-edge genomic technologies in collaboration with research institutes to directly benefit patients and enhance health outcomes. This work has now been successfully translated to a clinical test for critically ill children, achieving a diagnostic yield of 54%, with a median results turnaround time reduced to 10 working days.

Addressing another pain point, Dr Saumya discussed the challenge of capturing clinical signs and utilising data from medical history. He emphasised that it's not easy to extract relevant information. However, he recommends leveraging artificial intelligence (AI) and a natural language processor (NLP) with human-in-the-loop design to improve the rare disease diagnostic odyssey. This approach

can help analyse clinical notes, extract pertinent information, and convert it into standardised clinical notes.

Finally, he highlighted another pain point, focusing on identifying at-risk families with genetic diseases. He contrasted this with the current standard of genetic screening in Singapore which focuses primarily on Thalassemia. His team, in response, developed a customised carrier screening panel for couples who may be at risk of other severe recessive genetic diseases after understanding the genome profile of the local Singaporean population.

During the Q&A segment, the attendees actively and enthusiastically participated, posing a wide range of questions related to Chrononutrition, SLE and rare disease genetics. The engaging discussion provided valuable insights and delved deeper into the understanding of maternal and child health research in Singapore.



Prof Jerry Chan facilitated the Q&A session, with several key takeaways:

- Meal timing appears consistent throughout pregnancy. When considering seasonal variations, studies suggest a higher risk of depression and mental state disruptions due to the dysregulated biological clock in winter. However, further research is needed to

understand how meal timing changes across seasons and its consequential impact on health outcomes in pregnant population.

- The use of available high-dimensional technology enables researchers to gain a better understanding of complex diseases. However, many initial results remain descriptive. While specific immune subsets are identifiable, their interactions with other cells are still unknown. Further functional-related studies are needed to delve into the mechanisms of these cells.
- Given the acceleration of technologies, there is hope that new therapies can be developed in the next 5 to 10 years once children with rare disease are diagnosed. However, it is notable that many barriers such as funding and regulatory exist.

We would like to thank Dr Loy, Dr Yeo, Dr Saumya and Prof Chan for sharing their perspectives on Maternal and Child Health Research in Singapore. If you have further enquiries or are interested to collaborate with our presenters, feel free to write to:

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- Dr Yeo Joo Guan (gmsyeo@duke-nus.edu.sg), or
- Dr Saumya Jamuar (saumyashekhar.jamuar@duke-nus.edu.sg), or
- Prof Jerry Chan (jerrychan@duke-nus.edu.sg).

About Research Grand Rounds (RGR)

Held every two months over lunchtime, RGR showcases the achievements of researchers from the SingHealth Duke-NUS Academic Medical Centre (AMC), serving as a knowledge exchange and community engagement platform.

About Academic Medicine Research Institute (AMRI)

The SingHealth Duke-NUS Academic Medical Centre (AMC) is driven by 3 key pillars: clinical delivery, education and research; with the aim to discover new treatments and enhanced diagnostic tools to improve care for our patients. As one of the largest academic healthcare cluster in Singapore, basic scientists and clinical researchers within the AMC work together to address disease areas that most affect our population. Academic Medicine Research Institute (AMRI) is the AMC's one-stop research enabler that provides support in administration and scientific techniques to the research community in the AMC. These research support functions reside within SingHealth and its member institutions, and Duke-NUS Medical School.

For more information, visit https://www.singhealthdukenus.com.sg/research or scan QR code to explore our AMC Research website!

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