PRESS RELEASE

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Checking out the Boundaries: Milestone in Lipidomics Achieved

Ring trial enables establishment of ceramide reference values

Singapore, 10 October 2024 - Results of the first phase of a Ceramide Ring Trial have just been published in the renowned journal *Nature Communications*, representing a significant landmark in the field of lipidomics. This achievement, involving researchers at the **Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine)** and scientific teams from all over the world, represents a groundbreaking advance in the establishment of reference values for ceramides, plasma lipids involved in cardiovascular disease risk prediction. The ring trial was initiated and coordinated by SLING, the Singapore Lipidomics Incubator, and performed under the umbrella of the International Lipidomics Society (ILS).

Lipidomics – the large-scale study of pathways and networks of cellular lipids in biological systems – aims to understand the roles of lipids in health and disease by analysing their structures, functions, and interactions in cells. Understanding the upper and lower concentration boundaries of lipids is essential for scientific progress and the clinical translation of lipidomics. To do this, the Ceramide Ring Trial was the first step in assessing technical reproducibility across a global network of laboratories.

It all started with a meeting in Singapore

In a ring trial, multiple laboratories independently analyse the same samples using similar or different methods to compare their results. It helps in assessing the reliability and consistency of measurements across different labs, improving standardisation and quality control in scientific testing.

“It all started with a meeting at NUS between scientists from the major laboratories in the field that agreed that the comparability between lipidomic studies is a major issue,” says Professor Markus Wenk, **Dean, College of Health and Life Sciences at Hamad Bin Khalifa University** and **Visiting Toh Chin Chye Professor in the Department of Biochemistry at NUS Medicine,** who initiated this project and is the senior corresponding author on the published study. After seven years of collaborative efforts, the results from 34 participating laboratories across 19 countries have been summarized in a study published in Nature Communications. To reduce complexity, the Ceramide Ring Trial focused on human plasma and aimed to investigate concentration levels and their variabilities of four distinct endogenous ceramides. These lipids play a role in multiple pathologies and have been associated as biomarkers in cardiovascular diseases. Participants of the trial utilized their own preferred analytical method and/or a standardized protocol to quantify ceramides in a human plasma reference material (NIST SRM1950 (used as standard for metabolites in human plasma, provided by the National Institutes of Standards and Technology, NIST) and three additional human plasma reference materials as examples of human diseases such as

diabetes, by using specially formulated mixtures of ceramide synthetic standards (from Avanti Polar Lipids) for absolute quantitation.

“This was a true community effort, where most of the labs in the lipidomics field, a private company and the National Institute of Standards and Technology in the United States joined forces with a clear goal in mind. We obtained relevant results for the research community and we benefitted from the expertise of all the groups involved, " explains **Assistant Professor Federico Torta from the Department of Biochemistry and the Precision Medicine Translational Research Programme at NUS Medicine and Cardiovascular & Metabolic Disorders research programme at Duke-NUS Medical School.**

“The results obtained from different laboratories using different methods and instrumentations were well comparable, better than we initially anticipated,” adds Bo Burla, a senior researcher from the Life Sciences Institute at NUS. “Using specific synthetic standard for absolute quantitation was key to reduce variability and improve accuracy, allowing us to reach consensus in the concentrations of the analytes of interest. This study is the largest and most targeted public inter-laboratory and cross-platform ring trial for distinct ceramides in human plasma and sets a new benchmark for future harmonisation of lipidomics research and beyond”.

For more information, please visit the International Lipidomics Society website: https://lipidomicssociety.org.

Publication in Nature Communications: Federico Torta, Nils Hoffmann, Bo Burla, Irina Alecu, Makoto Arita, Takeshi Bamba, Steffany A. L. Bennett, Justine Bertrand-Michel, Britta Brügger, Mónica P. Cala, Dolores Camacho-Muñoz, Antonio Checa, Michael Chen, Michaela Chocholoušková, Michelle Cinel, Emeline Chu-Van, Benoit Colsch, Cristina Coman, Lisa Connell, Bebiana DaCosta Sousa, Alex M. Dickens, Maria Fedorova, Finnur Freyr Eiríksson, Hector Gallart-Ayala, Mohan Ghorasaini, Martin Giera, Xue Li Guan, Mark Haid, Thomas Hankemeier, Amy Harms, Marcus Höring, Michal Holčapek, Thorsten Hornemann, Chunxiu Hu, Andreas J. Hülsmeier, Kevin Huynh, Christina M. Jones, Julijana Ivanisevic, Yoshihiro Izumi, Harald C. Köfeler, Sin Man Lam, Mike Lange, Jong Cheol Lee, Gerhard Liebisch, Katrice Lippa, Andrea F. Lopez-Clavijo, Malena Manzi, Manuela R. Martinefski, Raviswamy G. H. Math, Satyajit Mayor, Peter J. Meikle, María Eugenia Monge, Myeong Hee Moon, Sneha Muralidharan, Anna Nicolaou, Thao Nguyen-Tran, Valerie B. O’Donnell, Matej Orešič, Arvind Ramanathan, Fabien Riols, Daisuke Saigusa, Tracey B. Schock, Heidi Schwartz-Zimmermann, Guanghou Shui, Madhulika Singh, Masatomo Takahashi, Margrét Thorsteinsdóttir, Noriyuki Tomiyasu, Anthony Tournadre, Hiroshi Tsugawa, Victoria Tyrrell, Grace van der Gugten, Michael O. Wakelam, Craig E. Wheelock, Denise Wolrab, Guowang Xu, Tianrun Xu, John A. Bowden, Kim Ekroos, Robert Ahrends & Markus R. Wenk. Concordant inter-laboratory derived concentrations of ceramides in human plasma reference materials via authentic standards

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About National University of Singapore (NUS)

The National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education, research and entrepreneurship, with a focus on Asian perspectives and expertise. We have 16 colleges, faculties and schools across three campuses in Singapore, with more than 40,000 students from 100 countries enriching our vibrant and diverse campus community. We have also established more than 20 NUS Overseas Colleges entrepreneurial hubs around the world.

Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, research centres of excellence, corporate labs and more than 30 university-level research institutes focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research and cybersecurity.

For more information on NUS, please visit nus.edu.sg.

About the NUS Yong Loo Lin School of Medicine (NUS Medicine)

The NUS Yong Loo Lin School of Medicine is Singapore's first and largest medical school. Our enduring mission centres on nurturing highly competent, values-driven and inspired healthcare professionals to transform the practice of medicine and improve health around the world.

Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,000 graduates have passed through our doors. In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives. The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is one of the leading medical schools in Asia and ranks among the best in the world (Times Higher Education World University Rankings 2024 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2024).

For more information about NUS Medicine, please visit https://medicine.nus.edu.sg/.