Selected Projects/Profiles

STaR Award - Stuart Cook (NHCS and Duke-NUS)

Professor Stuart Cook’s research uses state-of-the-art approaches to discover genes that cause heart and artery diseases, which are the commonest cause of death and disability worldwide. This is achieved by integrating advanced cardiac imaging with genomic data to derive unbiased and novel insights into human disease. This is possible thanks to the huge advances in human genetics in the post Human Genome Project era and, more recently, the availability of ultra high throughput sequencing technologies, such as those at Duke-NUS. Success in this area relies not just on technology but also on close attention to the human condition and a detailed understanding of patients. This is what defines the Clinician Scientist and enables them to work at the interface between science and medicine as they endeavor to translate basic discoveries into healthcare improvements.

The overall aim of Prof Cook’s research is to identify new ways of preventing, diagnosing, stratifying and treating patients with cardiovascular disease. In Singapore there are a number of areas where this research could have an impact on local healthcare. One of the new programs this team will be running at the National Heart Centre Singapore will investigate why some people’s hearts go into abnormal rhythms that can cause them to have strokes. The team hopes to find new ways to predict and prevent heart rhythm problems with the ultimate goal of preventing strokes. Prof Cook also has an interest in sudden cardiac death that can happen at any age and is devastating for the families of affected individuals. Working with industrial partners and using cutting-edge genetics and data analysis tools he hopes, in time, to develop research into clinical diagnostic tools to screen people in Singapore and prevent sudden cardiac death. A final area that is part of this research is healthy cardiovascular ageing, which is particularly important given the ageing populations around the world, and in Singapore. In all these areas it is critical to study the local population in health and disease. The team aims to recruit interested patients and volunteers into research studies to make these goals a reality.

Over the last five years, Prof Cook and his team have identified a number of new genes for heart disease and published their findings in premier scientific journals
that include Nature and Nature Genetics. This year, the team published a paper in the New England Journal of Medicine with collaborators and close colleagues from Harvard University, USA. In this study, the team identified that mutations in Titin, the biggest human gene, cause heart muscle weakness. This is a major step forward in the understanding of heart muscle disease and tests have already been developed to screen for this gene in individuals with a family history of heart failure.

Professor Cook is a Distinguished Clinician Scientist, Senior Consultant in Clinical and Molecular Cardiology and Senior Research Advisor with the Department of Cardiology at the National Heart Centre Singapore. He also has a primary academic appointment as Professor at the Duke-NUS Graduate School Singapore, in their Cardiovascular and Metabolic Diseases Research Program, where he has established a laboratory.

**STaR Award - Karl Tryggvason (Duke-NUS)**

Professor Karl Tryggvason has been a Professor in the Department of Medical Biochemistry and Biophysics at Karolinska Institutet in Stockholm since 1994 where he has had a distinguished career. Understanding the role of basement membrane proteins in normal physiology and disease has been a major research interest. In particular, his laboratory has made major contributions in understanding the molecular features of the filtration barrier in the kidney. Through this work, he determined the causes of human kidney diseases such as congenital nephropathy of the Finnish type and Alport's syndrome. Moreover, his findings opened a new and burgeoning field of research around the role of the glomerular epithelial cell or podocyte in human glomerular diseases.

Professor Tryggvason’s work has also led to understanding the molecular basis of other non-renal basement membrane diseases such as junctional epidermolysis bullosa and congenital muscular dystrophy. More recently, his laboratory has developed methodologies for synthesizing laminins, a family of basement membrane proteins, and has shown that these proteins can be used to control stem cell growth and differentiation.
At Duke-NUS, Professor Tryggvason plans to build a program focused on understanding the causative mechanisms of diabetic nephropathy, the leading cause of end-stage kidney disease in Singapore.

Professor Tryggvason has published more than 380 research articles. He is a member of the Swedish Royal Academy of Sciences, Vice-Chairman of the Nobel Assembly at Karolinska Institutet, and he has received a number of international awards, mainly for his kidney research, including the American Society of Nephrology Homer Smith Award and Louis Jeantet and Anders Jahre awards. Professor Tryggvason is also the founder of four companies, including NephroGenex, Inc. (USA) that has developed a drug for diabetic kidney disease.

**Transition Award - Jimmy Lee (IMH, Duke-NUS)**

Schizophrenia affects one in a hundred persons and is one of the leading causes of disability in Singapore and around the world. In clinical practice today, psychiatrists rely on reliable accounts and behavioural observations to make a diagnosis and monitor improvements following treatments. These observations and reports can be difficult to obtain, and result in delays in treatment. There is a need for more reliable and objective tools to assist psychiatrists in delivering and monitoring care. Dr Lee’s early work has demonstrated the potential of blood-based biomarkers in identifying individuals with schizophrenia. In this study, his team attempted to reproduce the same results from earlier studies in a larger sample. The team is also looking to evaluate the ability of these blood-based biomarkers in predicting clinical outcomes, especially with regard to selection of suitable therapeutic regimen.

If the objectives of the study are fulfilled, this study team would have identified a truly novel peripheral biomarker for psychosis. This will be a significant advancement in the management of psychosis as a biomarker will provide much needed objectivity when it comes to evaluating disease response and making an informed decision in developing treatment plans.

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