PRMT2 and RORγ expression regulate breast carcinogenesis and are associated with survival outcomes: validating new therapeutic targets

Prof George Muscat, Professor at Institute for Molecular Bioscience, The University of Queensland, Australia

Chaired by Prof Philip Ingham, Vice Dean Research and Toh Kian Chui Distinguished Professor, LKCMedicine, NTU

Date: 12 January 2016, Tuesday
Time: 10am – 11am
Venue: Matrix Building, Level 4, Exploration Theatrette (30 Biopolis Drive, Singapore 138671)

Synopsis
Breast cancer, which accounts for approximately 30 per cent of cancer in women, is the most common form of invasive cancer and cause of cancer-related death in females. Hormone dependent breast cancer has been documented for more than 100 years, and measuring the expression of two Nuclear Hormone Receptors (NRs), the estrogen and progesterone receptors (ER and PR), has underpinned disease management, treatment and prognosis. However, ER negative tumours are notoriously resistant to therapy, and are associated with poor clinical outcomes, underscoring the need to identify novel therapeutic/pharmacological targets. Though genetic alterations are involved, they do not provide a complete understanding of breast carcinogenesis.

Currently, about 15 per cent of breast cancer is associated with family history, or defined (hereditary) genetic mutations. However, recent reports indicate that a complex interplay between many other members of the NR signalling superfamily, and the epigenetic NR transcriptional co-regulators are involved in non-hereditary breast cancer. The tractable nature of the NR superfamily and epigenetic enzymes in pharmacological intervention, and the observation that all human NRs are implicated in human health and disease [accounting for 15% OF FDA approvals] provided the rationale to investigate expression of all human NRs, and (>250) transcriptional co-regulators in breast cancer cohorts, to identify novel targets.

Prof Muscat and his team identified differential expression of the NR superfamily, and NR co-regulators [including epigenomic enzymes] in neoplastic relative to normal breast. The NR (Muscat et al 2013) and co-regulator signatures (Dowhan et al 2012, Doan et al 2014 & Oh et al 2014) displayed superior discriminant, prognostic and therapeutic utility in predicting clinical outcomes in patient cohorts. This seminar will focus on the analysis of 1 epigenetic co-regulator/ enzyme (PRMT2, an arginine methyltransferase) and 1 NR, RORγ in breast cancer, and address potential functional roles/mechanism of action and clinical outcomes.