CANCER SCIENCE INSTITUTE OF SINGAPORE

SEMINAR ANNOUNCEMENT

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Mutational landscape of Monomorphic Epitheliotropic Intestinal T-cell Lymphoma

Date: Tuesday, 14 June 2016
Time: 10.30am - 11.30am
Venue: L1 Auditorium, Clinical Research Centre (10 Medical Drive, Singapore 117597)
Host: Prof Daniel Tenen

Abstract:

Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL, also known as type II enteropathy-associated T-cell lymphoma) is an aggressive intestinal disease with poor prognosis and its molecular alterations have not been comprehensively characterized. We performed whole-exome sequencing of four EITL tumor-normal pairs, followed by amplicon deep sequencing of 42 tumor samples and discovered frequent alterations of the JAK-STAT and G protein-coupled receptor (GPCR) signaling pathways in a large portion of samples. Specifically, Mutations of STAT5B (63% of cases), JAK3 (35%), GNAI2 (24%) and CREBBP are noted, with the majority occurring at known activating hotspots in key functional domains. Moreover, STAT5B locus carried copy-neutral loss of heterozygosity resulting in the duplication of the mutant copy, suggesting the importance of mutant STAT5B dosage for the development of this disease. Dysregulation of the JAK-STAT and GPCR pathways was also supported by gene expression profiling and further verified in patient tumor samples. In vitro overexpression of GNAI2 mutants led to upregulation of pERK1/2, a member of MEK-ERK pathway. Notably, inhibitors of both JAK-STAT and MEK-ERK pathways effectively reduced viability of patient-derived primary EITL cells, indicating potential therapeutic strategies for this neoplasm with no effective treatment currently available.

Biography:

Dr Tan Soo Yong obtained his medical qualifications from the National University of Singapore and thereafter underwent postgraduate training in Forensic Pathology and Histopathology in Singapore and in the University of Sheffield, United Kingdom. Qualifying in both forensic and histopathology, he is a Fellow of the Royal College of Pathologists (UK) and a Diplomate of the Society of Apothecaries of London. Dr Tan obtained his PhD from Oxford University, working in the field of haematopathology. His current research interest is in the pathology of NK/T cell lymphoma and Type II Enteropathy-associated T-cell lymphoma (Type II EATL). For his work on the pathology of Type II EATL, he has been elected as a member of the International Lymphoma Study Group (ILSG) and a member of the team responsible for updating the WHO Classification of haematolymphoid neoplasms. Dr Tan sits on the Editorial Board of two pathology journals (Journal of Clinical Pathology, Biobanking and Biopreservation). He is currently Associate Professor in the National University of Singapore Yong Loo Lin School of Medicine, a Senior Consultant and Clinician Investigator in the Department of Pathology, National University Hospital. Dr Tan holds multiple concurrent appointments as Senior Consultant to the Ministry of Health Singapore, Visiting Consultant to the National Skin Centre and National Cancer Centre Singapore, Head of the Advanced Molecular Pathology Laboratory (AMPL) and Senior Principal Investigator at the Institute of Cell and Molecular Biology (IMCB).