NUS National University of Singapore | Department of Anatomy
Yong Loo Lin School of Medicine

NUHS National University Health System

ORAL PQE

The role of ADARs-interacting RNA Helicases in shaping the RNA editome in cancer

Adenosine-to-inosine (A-to-I) RNA edco- or post-transcriptional process catalysed by the adenosine deaminase acting on iting is a RNA (ADAR) family of proteins, contributing towards transcriptome diversity. In the past decade, we and others have reported aberrant A-to-I RNA editing profiles are implicated in cancers. Albeit changes in expression and activity of ADAR genes are thought to have been responsible for the dysregulated RNA editome in diseases, they are not always correlated, indicating the involvement of secondary regulators. Our very recent studies have identified that RNA helicases, a highly-conserved class of enzymes that modulate RNA structures, RNA-RNA and RNA-protein interactions in an ATP-dependent fashion, interact with ADARs and may work towards reshaping the A-to-I RNA editome in cancer. In this project, I validated the binding of ADARs to three candidate RNA helicases DDX21, DHX30 and DDX17 in EC109, an esophageal squamous cell carcinoma (ESCC) cell line. Further, an unbiased transcriptome-wide RNA editing analyses of RNA helicase-depleted cells was performed wherein DDX21 and DHX30 were uncovered as novel bidirectional regulators of A-to-I RNA editing; whilst DDX17 was shown to behave more like an A-to-I editing enhancer. Strikingly, all three helicases tend to regulate distinct clusters of editing sites. Functionally, silencing DDX21, DHX30 or DDX17 dramatically inhibits tumorigenic capabilities of EC109 cells. Moving forward, my research focus will be placed on understanding precise mechanisms by which different bidirectional regulators (eg. DDX21, DHX9 and DHX30) reshape A-to-I editome either via structurally remodelling ADAR substrates, affecting ADAR homodimerization or by altering the ADARs-dsRNA binding affinity, and to further understand how this contributes to cancer progression.

Monday
8 July 2019
2pm – 3.30pm
Seminar Room, MD10
Level 2, Anatomy Museum

Priyankaa Pitcheshwar

Graduate Student
Anatomy, NUS Medicine

Address enquiries Dr Hu Qidong at 66013730 or Ms Nuramalina Binte Abdul Ghani at 65163200. All are welcome.