Institute of Medical Biology

Genome Institute of Singapore

Seminar Announcement

- All Are Welcome -

Speaker: **Dr Thomas Preiss**
The John Curtin School of Medical Research, ANU Australia

Title: **Mechanisms and patterns of eukaryotic post-transcriptional gene control**

Date : **16 Nov 2011 (Wednesday)**

Time : **2pm – 3pm**

Venue: **IMB Seminar Room, Neuros Level 6, Biopolis**

Co-Hosts: **Dr Prabha Sampath** (Tel: 64070171, email: prabha.sampath@imb.a-star.edu.sg) **&**
Dr Edwin Cheung (Tel: 68088184, email: cheungcwe@gis.a-star.edu.sg)

Abstract of the Seminar:

Part I: Global analyses suggested that miRNAs predominantly act through decreasing mRNA stability. Cells commonly co-express several mRNA isoforms, which differ in their regulatory UTRs. We tested multiple mRNA targeted by let-7 in HeLa cells and initially found that translational regulation appears modest when measuring the composite polysome profile of all extant isoforms of a given mRNA. In contrast, we saw clear effects at the level of translation initiation for multiple examples when selectively profiling mRNA isoforms carrying the 5' or 3' UTRs that were actually permissive to miRNA action. These results reaffirm the importance of translational control as part of the miRNA mechanism in animal cells.

Part II: Regulated processing can give rise to many miRNA variants. Next-generation sequencing of murine cardiomyocyte miRNAs revealed appreciable expression of 403 miRNAs. Arm bias broadly agreed with annotation, although 44 miR * were unexpectedly abundant; conversely, 33 -5p/-3p annotated hairpins were asymmetrically expressed. 105 miRNAs showed marked 5' isomiR expression. We demonstrated differential mRNA targeting by two prevalent 5' isomiRs of miR-133a. We further saw expression of 5 novel miR*, 46 unusual variants and 147 novel candidate miRNAs. Knowledge of this unexpected miRNA sequence diversity will underpin research into cardiac function, disease and therapy.

Part III: The modified base 5-methylcytosine (m^5C) is well known in DNA. We have resolved m^5C patterns in the human transcriptome. We coupled bisulfite conversion of RNA with next-generation sequencing. We were able to identify the majority of previously known m^5C sites in tRNAs and discovered ~200 novel sites in tRNAs as well as thousands of sites in mRNAs and non-coding RNAs. We verified a subset by bisulfite allelic sequencing and found that most sites were dependent on the methyltransferase NSUN2. Our data suggests a broader role of this m^5C in the function of cellular RNA.

About the Speaker:

Thomas Preiss is a molecular biologist determining the mechanisms and transcriptome-wide patterns of eukaryotic mRNA translation as one of life's core processes and its regulation by RNA-binding proteins and non-coding RNA as a means of controlling gene activity.

From 1995-2002 Thomas Preiss was a postdoctoral scientist at the EMBL in Germany. His work from that time lent support to the 'closed-loop' model of translation initiation, which posits that for efficient initiation, the cap structure and poly(A) tail have to be brought in close proximity through protein-mediated bridging interactions. Since 2002 he has led his own group in Australia, first at the Victor Chang Cardiac Research Institute in Sydney, and since 2011 he is Professor of RNA Biology at The John Curtin School of Medical Research / The Australian National University in Canberra. They uncovered a correlative network linking tail length to other mRNA characteristics and cellular processes in yeast. The lab also investigate the miRNA mechanism in mammalian cells and discovered that miRNAs target key components of the mRNA closed-loop during translation initiation: they block functions of the cap structure as well as the poly(A) tail.

A current focus is the functional analysis of eukaryotic transcriptomes by next generation sequencing with an emphasis on miRNA and mRNA processing diversity, understanding the translation process by footprinting translation complexes along mRNA, and the detection of RNA modifications such as 5-methylcytosine. In collaborative work, Thomas Preiss extends these basic science objectives into medical research areas such as heart disease, neurological disorders and cancer.