HONG KONG RNA CLUB

香港城市大學
City University of Hong Kong

Hybrid Seminar

16 Jan 2025 (Thur) / HKT 16:30-17:30

Venue: City University of Hong Kong
Yeung Kin Man Acad Building
(AC1), B5-311

****Registration required: click here****

Distinguished Speaker:

Prof. Hsueh-Ping (Catherine) Chu

Associate Professor
Institute of Molecular and Cellular Biology
National Taiwan University

A non-coding RNA TERRA regulates genomic G-quadruplexes

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A non-coding RNA TERRA regulates genomic G-quadruplexes

Prof. Hsueh-Ping (Catherine) Chu

Associate Professor

Institute of Molecular and Cellular Biology

National Taiwan University

Abstract

The genome consists of non-B form DNA structures such as G-quadruplexes (G4), which are stacked guanine tetrads and are involved in regulation of transcription activity by recruiting transcription factors. TERRA, a telomeric repeat-containing RNA, is capable of folding into an RNA G-quadruplex and interacting with chromatin remodeler ATRX. TERRA ablation causes gene expression changes in mammalian cells; however, how this non-coding RNA regulates chromatin status is largely unknown. Here we uncover that TERRA regulates the DNA G-quadruplex (G4) structures and ATRX occupancy near transcription start sites *in vivo*.

We investigated the function of TERRA RNA in modulating chromatin status on a genome-wide scale, and performed ATAC-seq and ChIP-seq for ATRX, H3K9me3, and G4 after TERRA depletion in mouse embryonic stem cells. We found that TERRA depletion leads to increased ATRX occupancy on repetitive sequences and subtelomeric regions. Strikingly, ATRX ectopically binds to transcription start sites (TSS) in TERRA knockdown cells. Such elevation of ATRX loading at transcription start sites is accompanied by the reduction of DNA G4 structures and gene repression. Loss of ATRX alleviates the effect of gene repression caused by TERRA depletion. Immunostaining analyses demonstrate that knockdown of TERRA diminishes DNA G4 signals, whereas silencing ATRX elevates G4 formation. These results suggest that TERRA prevents ATRX from binding to chromatin and maintains DNA G4 around transcription start sites. We propose that TERRA RNA sequesters G4 binding proteins and sustains DNA G4. In this talk, I will present the findings that provide insights into the mechanism of how a non-coding TERRA regulates genomic G-quadruplexes.

Biography

Hsueh-Ping (Catherine) Chu is an Associate Professor in the Institute of Molecular and Cellular Biology at National Taiwan University. She obtained her Ph.D. in Biomedical Sciences from Rutgers University in 2009 and worked as postdoctoral fellow at the Harvard Medical School and Mass General Hospital. She has won the Taiwan Outstanding Women in Science award in 2024. She is now working on the functions of non-coding RNAs and developed methods to study

the interactomes of non-coding RNA. She also studies the roles of TERRA in epigenetic regulation, telomere maintenance, ageing and human diseases. Her works were published in *Nature Protocols*, *Nucleic Acids Research*, and *Nature Communications*.