NANYANG TECHNOLOGICAL UNIVERSITY
SINGAPORE

School of Biological Sciences
College of Science

Seminar Announcement

ZBTB48 is both a vertebrate telomere-binding protein and a transcriptional activator

Date: 19 August 2019
Time: 2.30 p.m.
Venue: Classroom 4, SBS
Hosted By: A/P Koh Cheng Gee

Speaker:
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Telomeres constitute the ends of linear chromosomes and together with the shelterin complex form a structure essential for genome maintenance and stability. Due to the end replication problem and active end processing, telomeres shorten with every cell division, ultimately leading to cellular senescence. Cancer cells would eventually share this fate. However, they (re-)activate mechanisms to defy telomere shortening that are in part orchestrated by telomere-binding proteins. In addition to the constitutive binding of the shelterin complex, other direct, yet more transient interactions are mediated by the CST complex and HOT1, while subtelomeric variant repeats are recognized by NR2C/F transcription factors. Recently, we systematically investigated telomere-binding proteins in 16 vertebrate species using label-free quantitative mass-spectrometry based proteomics, creating a phylointeractomics map of telomeres and identified ZBTB48 as a novel telomere-associated factor throughout the vertebrate lineage. Here, we show that ZBTB48 binds directly both to telomeric as well as to subtelomeric variant repeat sequences *in vitro* and *in vivo*. ZBTB48 is found at telomeres of human cancer cells regardless of the mode of telomere maintenance and it acts as a negative regulator of telomere length. In addition to its telomeric function, we demonstrate through a combination of RNAseq, ChIPseq and quantitative label-free expression proteomics experiments that ZBTB48 acts as a transcriptional activator on a small set of target genes, including mitochondrial fission process 1 (MTFP1). This discovery places ZBTB48 at the interface of telomere length regulation, transcriptional control and mitochondrial metabolism. We are currently exploring the mechanism behind ZBTB48's role at telomeres and as a transcriptional activator through various mass spectrometry-based interactomics approaches.