Tsinghua-*Science* Workshops

Epigenetics Structure and Function

Session 11: An expansion of epigenetics: RNA methylation and nucleosomes in non-eukaryotic organisms

Thursday, October 21st, 2021 8-10 pm (GMT +08:00, Beijing)
20:00-20:45
Yang Shi, Ludwig Cancer Research, University of Oxford, UK
When RNA Modifications Meet Chromatin
20:45-21:00 Q&A

21:00-21:45
Karolin Luger, University of Colorado, Boulder, USA
Looking for histones in all the wrong places: nucleosomes in non-eukaryotic organisms
21:45-22:00 Q&A

Host

Prof. Haitao Li

Dr. Haitao Li received his doctorate degree in molecular biophysics at the Institute of Biophysics, Chinese Academy of Sciences in 2003. He then performed his postdoctoral research at Memorial Sloan-Kettering Cancer Center and was promoted to Senior Research Scientist there in 2006. Li joined the School of Medicine at Tsinghua University as a tenure-track associate professor in 2010 and became full professor with tenure in 2016. Li currently serves as associate director of the Beijing Advanced Innovation Center for Structural Biology and associate dean of the School of Medicine, Tsinghua University.

Li's research is focused on gaining molecular and mechanistic insights into epigenetic regulation impacting on health and disease. His group mainly applies structural and biochemical approaches, blended with other cellular and omic techniques to study key recognition and catalysis events involved in epigenetic regulation, and to investigate the complexity of the molecular ecosystem coupling epigenetics, metabolism and signaling. Other endeavors of the lab include structure-guided drug discovery and biointeraction-profiling tool development. Li's major contribution to science has been the elucidation of the molecular basis underlying modification-dependent histone/DNA readout and catalysis by epigenetic readers, writers and erasers, such as PHD finger, YEATS, SETD2 and ALKBH1. Dr. Li has authored more than 100 scientific publications that have received over 11,000 citations. Li is the recipient of multiple awards, including the CC Tan Life Science Innovation Award, Promega Innovation Award for Cell Biology, the Young Scholar of China Award in Cancer Research, the Wuxi PharmaTech Life Science and Chemistry Awards, Mao Yi-sheng Science and Technology Award for Beijing Youth, the HFSP Young Investigators Grant Award, and the National Science Fund for Distinguished Young Scholars of China.

Speakers

Prof. Yang Shi

Yang Shi received his PhD from New York University where he studied regulation of a multi-gene family in mice. He carried out postdoctoral research in the lab of Dr. Thomas Shenk at Princeton University where he discovered the transcription factor YY1 (Yin Yang 1 for its ability to both activate and repress transcription), which plays a critical role in many important biological processes. He began his independent research career at Harvard Medical School as an assistant professor and received tenure and full professorship in the Department of Pathology at Harvard Medical School in 2004. In 2009 he joined the Newborn Medicine Division of Boston Children's Hospital. He is currently C. H. Waddington Professor of Pediatrics and Professor of Cell Biology at Harvard Medical School. His honors include Ray Wu Award (2009), election to the American Association for the Advancement of Science (2011, AAAS Fellows), American Cancer Society Research Professor (2012) and election to the

American Academy of Arts and Sciences (2016).

His most significant and widely known scientific contribution is the discovery of the first histone demethylase LSD1, which overturned the 40-year-old dogma that histone methylation is irreversible. This groundbreaking discovery was published in Cell in 2004, and was selected by Cell as one of the 25 landmark publications over forty-year history of Cell. He also identified many additional histone demethylases, which belong to the JmjC domain-containing, dioxygenase family of enzymes. These discoveries not only provided critical novel insights into epigenetic regulation but also revealed new drug targets for cancer therapy. For instance, small molecules targeting LSD1 are now in clinical trials for AML. Excitingly, Yang's most recent work also uncovered a role for LSD1 in immune checkpoint blockage, i.e., inhibition of LSD1 can turn "cold" tumor "hot", thus enabling immune checkpoint blockage for cancers that otherwise are not responsive to immune therapy. This work laid the foundation for future combination therapies involving the use of inhibitors of epigenetic regulators such as LSD1 and checkpoint inhibitors for immune-resistant cancers.

Yang was also one of the first to describe the DNA vector-based RNAi technology, which is widely used as a means to study eukaryotic gene function. The LSD1 and the vector-based RNAi papers alone have garnered over 5,500 citations according to Google Scholar. He is also responsible for the discovery of the first reader modality that recognizes the methyl zero state on histone tails as well as a novel reader selective for a variant histone H3, which are key components in the chromatin network.

When RNA Modifications Meet Chromatin

In this presentation, I will discuss our recent efforts towards understanding the impact of RNA modifications on chromatin functions.

Prof. Karolin Luger

Dr. Luger is the Jennie-Smoly-Caruthers Endowed Chair of Biochemistry at the University of Colorado, Boulder.

Karolin Luger wants to understand the impact of chromatin architecture on genome-related processes such as gene transcription, DNA replication, and DNA repair. Luger and her team apply structural biology and biophysics tools as well as imaging, genomic, and genetic approaches to determine how chromatin is assembled and disassembled during these processes. The team also investigates the ancient origins of eukaryotic chromatin through studies of archaeal chromatin and chromatin-associated factors. Luger's work may have significance for diseases involving proteins associated with DNA repair, such as cancer.

Looking for histones in all the wrong places: nucleosomes in non-eukaryotic organisms

Invariably, all eukaryotes organize their DNA into nucleosomes, consisting of an octamer of the four core histone proteins H2A, H2B, H3, and H4, around which 147 base pairs of DNA are wrapped in two tight superhelical turns. Histone, and with them nucleosome structure, are extremely conserved throughout the eukaryotic domain of life.

With the discovery of small histone-like proteins in most known Archaea, the likely origin of histones and thus the nucleosome was identified. Most Archaea encode only one or two minimal histones that form polymers around which DNA coils in a dynamic quasi-continuous superhelix that opens and closes stochastically. Our exploration of non-eukaryotic chromatin continues with the discovery of genes encoding fused histone genes in giant viruses that infect amoeba. Our structural and functional analysis shows that these histones assemble into nucleosome-like structures, and that histones are essential for viral infectivity.