Tsinghua-*Science* Workshops

Epigenetics Structure and Function

Session 10: Structural and functional work on DNA methylation and its regulation

Thursday, September 23rd, 2021 8-10 pm (GMT +08:00, Beijing)
20:00-20:45
Dinshaw Patel, Memorial Sloan-Kettering Cancer Center, USA
Structural Biology of DNA Methyltransferases
20:45-21:00 Q&A

21:00-21:45
Bing Zhu, Institute of Biophysics, Chinese Academy of Sciences, China
Epigenetics: from inheritance to memory
21:45-22:00 Q&A

Host

Prof. Haitao Li

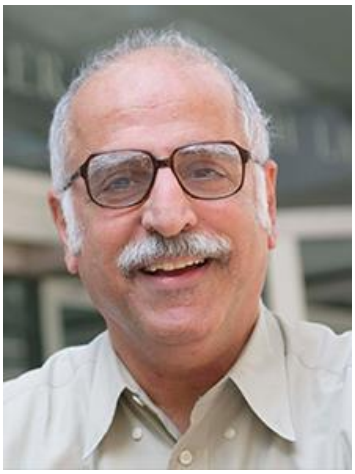
Dr. Haitao Li received his doctorate degree in molecular biophysics at the Institute of Biophysics, Chinese Academy of Sciences in 2003. He then performed his postdoctoral research at Memorial Sloan-Kettering Cancer Center and was promoted to Senior Research Scientist there in 2006. Li joined the School 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. Dinshaw Patel



I received my PhD in Chemistry from New York University (NYU) in 1968 for research in the photochemistry. I decided next to shift the emphasis of my research to the life sciences and hence completed postdoctoral training (one year) in Biochemistry at NYU School of Medicine followed by postdoctoral training (two years) in Biophysics at AT&T Bell Laboratories. I was next promoted to permanent Member of Technical Staff at Bell Labs and spent the next 15 years undertaking NMR-based studies of the structure and dynamics of cyclic peptides, proteins and nucleic acids. I moved to Columbia University Medical School in 2004 as a tenured Professor of Biochemistry and Molecular Biophysics where my group spent the next 8 years doing NMR-based research on DNA mismatches, bulges and junctions, on DNA triplexes and G-quadruplexes, and drug-DNA complexes. I was recruited in 1992 as a tenured Member to the Cellular Biochemistry and Biophysics Program at the Memorial Sloan-Kettering Cancer Center to set up a Structural Biology component to the program. My group's research during the 1990s focused on NMR-based studies of covalent chiral carcinogen-DNA adducts,

and complexes of antibiotics and peptides with natural and *in vitro* selected RNA targets.

My laboratory began to increasingly use x-ray crystallography starting around 2000 with the emphasis initially on RNA-mediated gene regulation, with subsequent extension to histone-mark and DNA-mark mediated epigenetic regulation, to lipid transfer proteins, and more recently to nucleic acid pattern recognition receptors and CRISPR-Cas surveillance complexes. We have complemented our structural efforts with functional studies undertaken by collaborators to deduce mechanistic insights into the biological systems of interest. Starting in 2019, my group has increasingly used cryoEM to study macromolecular structure, recognition and regulation.

Dr. Patel has published 540+ papers and reviews. His h-index (Google Scholar) is 126.

Web site: http://www.mskcc.org/mskcc/html/10829.cfm

Structural Biology of DNA Methyltransferases

The lecture will cover the structural biology of DNA methyltransferases (DNMTases). Topics will include DNMT1, a mammalian maintenance DNMTase and its partner UHRF1, DNMT3, a mammalian de novo DNMTase, and DNMT5, a fungal maintenance DNMTase whose activation is controlled by a SNF2 ATPase. If time permits, aspects of RNA-dependent DNA methylation in plants will also be discussed. The focus will be both on the apo-enzymes and their DNA complexes and the principles underlying methylation at the cytosine 5 position.

Prof. Bing Zhu

Bing Zhu, Ph.D., is investigator and deputy director of the Institute of Biophysics, Chinese Academy of Sciences. Dr. Zhu received his Ph.D. in molecular genetics from the Shanghai Institute of Plant Physiology, Chinese Academy of Sciences in 1999. Following his postdoctoral studies on DNA demethylation and co-transcriptional chromatin modifications at the Friedrich Miescher Institute, Switzerland, and at the Howard Hughes Medical Institute, he joined the National Institute of

Biological Sciences, Beijing, as a faculty. He joined the Institute of Biophysics, Chinese Academy of Sciences as an investigator in 2014. He greatly contributed in revealing mechanisms governing mitotic inheritance of chromatin modifications. He clarified the nucleosome partition pattern during DNA replication. He discovered the first chromatin modifying enzyme that senses nucleosome density. More recently, he advanced our knowledge in mechanisms regulating the de novo establishment of DNA methylation, DNA methylation maintenance, signal induced selective demethylation and its role in transcriptional memory. Dr. Zhu is an internationally recognized scientist, who was awarded as an International Early Career Scientist Howard Hughes Medical Institute in 2012. Dr. Zhu currently serves as a member of the Board of Reviewing Editors of Science magazine.

Epigenetics: from inheritance to memory

The epigenetic systems help to fulfil two basic challenges of multicellular organisms: proliferation and differentiation. Epigenetic plasticity allows cells to differentiate, whereas epigenetic inheritance and maintenance help to maintain cell fate in proliferating cells and postmitotic cells. Among epigenetic modifications, DNA methylation is maintained with the highest fidelity, yet its maintenance remains to be imperfect and the DNA methylome deteriorates during aging and tumorigenesis. In this seminar, I will highlight our recent discoveries regarding mechanisms governing DNA methylation inheritance, selective demethylation, and transcriptional memory. I will also report our unpublished study regarding an interesting mechanism regulating cell differentiation, which we termed as reining.