HKUST-Yale University Joint Symposium of Life Science and Quantitative biology

Lecture Theater - F	**15 Dec 2018 (Sat)**	**10:00-17:00**

Organizers: Professors Ning LI, Robert Qi, Guang Zhu Can Yang, Weichuan Yu (HKUST) and Hongyu Zhao (Yale)

Morning session

10:30 am -11 :20am **Prof. Tony Koleske** , **"Progress in understanding schizophrenia, will new genes lead to new treatments?"**

Departments of Molecular Biophysics and Biochemistry and Neuroscience, Yale University
Ph.D. 1993, Whitehead Institute/MIT – mentor Richard Young; Postdoc 1994-1998, MIT – mentor David Baltimore; Faculty 1998-present, Yale University

Dr. Koleske will provide a general introduction to schizophrenia, and its impact on those afflicted, and on society. He will discuss evidence that schizophrenia results from a combination of genetic and environmental factors and the mechanisms by which they are thought to act. Dr. Koleske will discuss his laboratory' s research focusing on a key risk gene for schizophrenia, TRIO, and how alterations in its function impact brain development and behavior in a mouse model. Finally, he will provide perspective on how treatments might be developed to target new schizophrenia risk genes that are emerging.

Levy, A.D., Xiao, X. Devi Sudarsana, S.P., Bennett, A.M., Greer, C.A., Howe, J.R., Machida, K., and **Koleske, A.J.** Noonan syndrome-associated phosphatase SHP2 dephosphorylates GluN2B Y1252 and alters GluN2B-associated binding proteins to regulate NMDA receptor function. Cell Rep,24(6):1523-1535.
Omar, M.H., Kerrisk Campbell, M., Xiao, X. Zhong, Q., Brunken, W.J., Miner, J.H., Greer, C.A., and **Koleske, A.J.** (2017) CNS neurons deposit laminin α5 to stabilize synapses. Cell Rep. 21(5):1281-1292

11:30 am - 12:00 pm **Professor Robert Qi** , Division of Life Science

"Regulation of microtubule growth initiation at microtubule-organizing centers"

The spatial and temporal organization of the microtubule cytoskeleton requires γ-tubulin ring complexes (γTuRCs), which initiate microtubule growth and mediate microtubule attachment at microtubule-organizing centers, such as centrosomes and the Golgi complex. By using a wide range of approaches, we investigate the nature and assembly dynamics of γTuRCs and to understand γTuRC association with its regulators. One of the identified regulators is CDK5RAP2, a widely expressed protein whose mutations cause autosomal recessive primary microcephaly. The molecular description of γTuRCs and functional determination of its associated proteins allowed us to progress on understanding the control mechanisms of microtubule nucleation and array organization.

12 noon – 1:50 pm Lunch (Hosted by Professor Yu, weichuan)

Afternoon session

2:00 to 2:45 pm **Professor Christian Tschudi**, **"Establishing a road map of the developmental program leading to infectivity in African trypanosomes"**

Christian Tschudi is the John Rodman Paul Professor of Epidemiology and Director of Graduate Studies at the Yale School of Public Health and earned an A.B. in microbiology and a Ph.D. in biochemistry from the University of Basel in Switzerland.

He currently co-directs an NIH-sponsored Global Infectious Disease Training Program (D43) in translational research training on leishmaniasis & emerging infectious diseases and is the co-director of the China Scholarship Council-Yale World Scholars Program in Public Health. Dr. Tschudi is an expert on neglected tropical diseases, as evidenced by editorial board and study section appointments and a Burroughs Wellcome Award. He is currently the organizer of the international conference on kinetoplastid molecular cell biology. Dr. Tschudi' s studies focus on the biology of trypanosomes the causative agents of devastating diseases in Africa and South America with special emphasis on one of the fundamental steps in the life of a pathogen, namely the acquisition of infectivity.

One of the fundamental steps in the life of a pathogen is the acquisition of infectivity. In the case of African trypanosomes, this occurs in the tsetse fly. Although the intricate nature of trypanosome development in the fly has been recognized for more than a century, the molecular mechanisms are still mysterious, due to experimental challenges of studying parasites in the fly. By overexpressing a single RNA-binding protein (RBP6) in non-infectious trypanosomes, we recapitulated *in vitro* the events leading to acquisition of infectivity in tsetse. The *in vitro* process opens numerous research avenues that will further our understanding how the pathogen becomes infectious and, further down the road, will provide an opening for new intervention strategies.

Kolev, N.G., Ramey-Butler, K., Cross, G.A., Ullu, E., and **Tschudi, C.** Developmental progression to infectivity in *Trypanosoma brucei* triggered by an RNA-binding protein. Science (2012), 338(6112), 1352-1353.

Christiano, R., Kolev, N.G., Shi, H., Ullu, E., Walther, T.C., **Tschudi, C**. The proteome and transcriptome of the infectious metacyclic form of *Trypanosoma brucei* define quiescent cells primed for mammalian invasion. Mol. Microbiol. (2017), 106, 74-92.

3:00 to 3:45 pm **Professor Zhu, Guang**, Division of Life Science

"Mechanistic Study of Human DNA Replication Proteins that Regulate Cell Proliferation and Differentiation"

Proper organ development requires the precise regulation of both the total number of cells (cell proliferation) and the types of cells (cell differentiation). During cell proliferation, Cdt1 mediated loading of DNA helicase (Mcm2-7) to replication origins is required for DNA replication. And Hox gene activation is necessary for embryonic cell differentiation. It has been shown that these two processes are linked through the cell cycle-regulator Geminin and the homeodomain-containing transcription factors Hox. To understand the molecular mechanism involved, we determined the solution structures of Geminin-Hox, Orc6-DNA, G-quadruplex and Cdt1-Mcm6 complexes by nuclear magnetic resonance (NMR) spectroscopy and conducted biochemical study to delineate the structural basis of this mutual regulation. In addition, we are interested in structure-functional study of G-quadruplex of DNA and RNA in human DNA replication initiation and related diseases. Our biochemical and structural study showed that human Cdc6 binds G4 DNA directly supporting a role for G4 DNA in the recruitment of Pre-RC to replication origins.

[1] B. Zhou et al. *Sci. Rep.*, **2015**, 5, 16673 [2] J.P. Lee et al. *Peptide Science*, **2015**, 21, 593-8

[3] B. Zhou et al. *Proc. Natl. Acad. Sci. U S A.* **2012**, 109 23 8931-8936; [4] C.D. Liu et al. *Nucleic Acids Res*. **2012**, 40, 3208-17; [5] L.H. Chen et al. *J Biol. Chem*. **2012**, 287, 26104–26114
[6] C.D. Liu et al. *Chem. Sci*: **2018**, 10.1039/C8SC03813A ; [7] B. Zhou et al. *Sci. Rep*. **2018**, 8:2366

4:00 to 4:50 pm **Professor Wang, Jiguang,** Division of Life Science

"Investigation of tumor evolution informs precision cancer medicine"

Recent progression of cancer genome projects has uncovered the mutational landscapes of many cancers, but how cancer cell evolves with and without therapy is still unclear. Scientists believe one major reason of treatment failure is the temporal-spatial dynamics of cancer cells. Actually, cancer cells are constantly evolving, with different groups of cells accumulating distinctive mutations. As the search for more effective cancer diagnostics and therapies continues, remained key questions include a) how to interpret intratumor heterogeneity (ITH); b) how to understand the tumors change over time and how to predict the impact of ITH on tumor progression; and c) how to disentangle the order in which mutations occur. Being able to predict how a tumor will behave based on signs seen early in the course of disease could enable the development of new diagnostics that could better inform treatment planning.

6:00 - 9:00 pm **Dinner (hosted by Dean)**
