

presents the seminar series in
Cancer Biology, Biotherapy and Nanomedicine

**Engineering protein-protein interactions to
probe and rewire cell signaling**

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Date : 30 Jul 2019 (Tue)
Time : 11:00 - 12:30
Venue : YEUNG-P4703, Yeung Kin Man Academic Building

Abstract

Effective therapeutic strategies rely on our ability to interfere with cellular processes that are deregulated in human diseases. Thanks to the advance of genomic technologies in recent years, components essential for major biological pathways have been identified at the genetic level. Together they constitute signal transduction cascades relying on protein-protein interactions (PPIs) to elicit various biological functions. However, it is still poorly understood about the exact roles of individual PPI in controlling enzyme activity and complex assembly, especially in the context of diverse signaling networks. Traditional mutation-to-function studies have limitations in this regard due to unpredictable changes in protein folding and conformation, and difficulties in the identification of bona fide “separation-of-function” alleles. Hence, there is an urgent need for novel approaches that can selectively probe and investigate individual PPIs to dissect their biological roles. To tackle this problem, we have devised a structure-based combinatorial protein design and engineering strategy to develop novel protein-based PPI modulators. In the past three years, we generated inhibitors and/or activators for more than 50 E3 ligases and deubiquitinases, enzymes that determine specificity of ubiquitination and deubiquitination, respectively. With the help of these synthetic molecules, we discovered new biochemical mechanisms and new biological functions of diverse protein families in the ubiquitination system. Importantly, we have established effective delivery methods for these intracellular probes and successfully target therapeutic-relevant genes in cells and organoids.

About the Speaker

Dr. Wei Zhang is an Assistant Professor in the Department of Molecular and Cellular Biology at the University of Guelph (www.thezhanglab.com). He obtained his PhD from University of Toronto where he identified new molecular mechanisms of telomere addition to DNA breaks and the spatial organization of DNA repair. Dr. Zhang is developing combinatorial protein engineering approaches to manipulate human and viral enzymes controlling critical cell signal transduction cascades for innovative therapeutic strategies. He has received numerous awards, including the 2016 Mitacs Award for Outstanding Innovation, 2017 Cancer Research Society Scholarship for the Next Generation of Scientists, and the inaugural 2018 Donnelly Centre Research Excellence Award. To date, he has published 20 papers in high-impact journals and 3 pending patents.

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All are welcome!