Position Description:

Two Graduate Student (PhD or MSc) positions are available immediately in the Zhang Laboratory at the Department of Molecular and Cellular Biology, University of Guelph.

Research Project:

The Zhang Lab uses structure-based combinatorial protein engineering technology to create synthetic intracellular probes modulating protein-protein interactions to accelerate understanding of biology and to facilitate development of novel therapeutics (see "**Representative Publications**").

The recent clinical success of PARP inhibitors (e.g. Olaparib and Rucaparib) in treating ovarian cancer patients with *BRCA1* or *BRCA2* mutations highlights the importance of "synthetic lethality" concept when exploring DNA damage response (DDR) protein deficiencies for cancer therapy. While we learned a great deal about the signal transduction network in DDR in the past decade, there is a paucity of efficient platforms to develop probes that can modulate DDR protein function in cells to validate drug targets and to develop therapeutic leads. The successful candidate will be able to use protein rational design and engineering approaches to develop inhibitors of selective protein-protein interactions that are critical for DDR. These synthetic molecules will be used to probe DNA damage checkpoint signaling pathways for elusive molecular mechanisms. We will deliver these protein-based inhibitors to induce "synthetic lethality" in cancer cells by disrupting signaling pathways that cancer cells rely on to survive due to specific mutation background or under stress/treatment conditions.

Representative Publications:

1. Gabrielsen M, Buetow L, Nakasone MA, Ahmed SF, Sibbet GJ, Smith BO, **Zhang W***, Sidhu SS*, Huang DT*. (2017) A general strategy for discovery of inhibitors and activators of RING and U-box E3 ligases with ubiquitin variants. ***Molecular Cell*** 68, 456-470. (*Corresponding authors)
2. **Zhang W**, Bailey-Elkin BA, Knaap RCM, Khare B, Dalebout TJ, Johnson G, van Kasteren PB, McLeish N, Gu J, He W, Kikkert M, Mark BL, Sidhu SS. (2017) Potent and selective inhibition of pathogenic viruses by engineered ubiquitin variants. ***PLoS Pathogens*** 13(5): e1006372.
3. **Zhang W**, Wu KP, Sartori MA, Kamadurai HB, Ordureau A, Jiang C, Mercredi PY, Murchie R, Hu J, Persaud A, Mukherjee M, Li N, Doye A, Walker JR, Sheng Y, Hao Z, Li Y, Brown KR, Lemichez E, Chen J, Tong Y, Harper JW, Moffat J, Rotin D, Schulman BA, Sidhu SS. (2016) System-wide modulation of HECT E3 ligases with selective ubiquitin variant probes. ***Molecular Cell*** 62, 121-36.

Qualifications:

- Background in Molecular Biology, Biochemistry, Genetics or related discipline
- At least 1-year lab experience in protein biochemistry, molecule biology or mammalian cell biology
- Excellent organization, time management, and communication (oral and written) skills
- Problem solving and analytical abilities for experimental design
- Self-motivated, detail oriented, and with satisfactory work performance and attendance record

Application process:

Please send cover letter, CV, and transcript to Dr. Wei Zhang (weizhang@uoguelph.ca). Feel free to contact Dr. Zhang to inquire about details of the potential research projects.