

## Graduate and undergraduate student positions in Biochemistry

**Positions available:** Several fully funded **graduate** (PhD and MSc) and **undergraduate** student positions are available in the Vahidi Lab at the Department of Molecular and Cellular Biology, University of Guelph for Summer and Fall of 2020. [vahidilab.ca]

**Research projects:** The Vahidi Lab uses state-of-the-art methods to investigate the structure, function, and dynamics of large biomolecular machines in order to solve problems of biological and clinical importance. A key focus of the group is on the protein degradation machinery that helps to maintain proper level of proteins (protein homeostasis) in *Mycobacterium tuberculosis*, the causative agent of TB, the world's single largest infectious killer. *M. tuberculosis* relies heavily on robust proteasome function to survive the immune system of the host, rendering this mega-Dalton sized system an attractive drug target in the pharmaceutical industry. The projects address the following questions:

- What is the assembly mechanism of the *M. tuberculosis* proteasome core particle and its regulatory particles?
- What is the role of allostery and long-range interactions in the machinery that tags substrates for proteasomal degradation?
- How are substrates selected for tagging and degradation?
- What is the molecular basis of antibiotics that operate on the proteasome?

Most of the research will be based on the use of modern biomolecular electrospray mass spectrometry (ESI-MS) (e.g. H/D exchange, covalent labeling, native MS, BioID, etc.) and high-field NMR spectroscopy (e.g. methyl-TROSY). These powerful methods are highly complementary and allow us to tackle challenging problems within our own group. Because of the dominant role that these two methods play in biological and chemical research, trainees from our lab will be well-positioned in the job market after graduation.

### **Relevant publications:**

1. S. Vahidi, Z. A. Ripstein, J. B. Juravsky, E. Rennella, A. L. Goldberg, A. K. Mittermaier, J. L. Rubinstein, and L. E. Kay, "An allosteric switch regulates *Mycobacterium tuberculosis* ClpP1P2 protease function as established by cryo-EM and methyl-TROSY NMR" *Proc. Natl. Acad. Sci. U.S.A.* In Press, DOI: 10.1073/pnas.1921630117 (2020).
2. S. Vahidi, Z. A. Ripstein, M. Bonomi, T. Yuwen, M. F. Mabanglo, J. B. Juravsky, K. Rizzolo, A. Velyvis, W. A. Houry, M. Vendruscolo, J. L. Rubinstein, and L. E. Kay, "Reversible inhibition of the ClpP protease via an N-terminal conformational switch" *Proc. Natl. Acad. Sci. U.S.A.* **115**, E6447-E6456 (2018).
3. S. Vahidi, Y. Bi, S. D. Dunn, and L. Konermann, "Load-dependent destabilization of the  $\gamma$ -rotor shaft in F<sub>o</sub>F<sub>1</sub> ATP synthase revealed by H/D-exchange mass spectrometry" *Proc. Natl. Acad. Sci. U.S.A.* **113**, 2412-2417 (2016).

### **Qualifications:**

- Passion for science and discovery, curiosity, and commitment.
- Background in biochemistry, biophysics, molecular biology, microbiology, bioanalytical chemistry, or related field.
- Excellent communication, problem solving, troubleshooting skills.

### **How to apply:**

Please send a brief cover letter, your CV, and a recent transcript to (svahidi@uoguelph.ca).