UNIVERSITY of GUELPH

COLLEGE of BIOLOGICAL SCIENCE

DEPARTMENT OF MOLECULAR AND CELLULAR BIOLOGY

PhD student positions in structural biology

Positions available: Two fully funded **PhD student positions** are available immediately in the Vahidi Lab at the Department of Molecular and Cellular Biology, University of Guelph [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 and regulatory particles?
- What is the role of allostery in the machinery that tags substrates for proteasomal 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.

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"" *PNAS. 117*, 5895-5906 (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" *PNAS 115*, E6447-E6456 (2018).
3. S. Vahidi, Y. Bi, S. D. Dunn, and L. Konermann, "Load-dependent destabilization of the γ-rotor shaft in F_OF_1 ATP synthase revealed by H/D-exchange mass spectrometry" *PNAS 113,* 2412-2417 (2016).

Qualifications:

-Must hold a MSc focused on protein structure:function, biochemistry, biophysics, or related field.
-A strong background in protein NMR and/or protein mass spectrometry is preferred.
-Passion for science and discovery, curiosity, and commitment.

How to apply:

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

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