BiophysTO Lunchtime Seminar Series

Date
Thursday, Jan 12, 2023
12:00 – 1:00 pm

Location
McLennan Physical Laboratories, 60 St George street.
Room: MP606

Dr. Voula Kanelis

Department of Chemistry, University of Toronto;
Department of Cell and Systems Biology, University of Toronto;
Department of Chemical and Physical Sciences, University of Toronto Mississauga

Structural studies define regulatory features in ATP binding cassette transporters

ATP binding cassette (ABC) proteins generally couple the energy from the hydrolysis of ATP to the active transport of solutes across cellular membranes. While all ABC proteins contain a core structure of two transmembrane domains (TMD1, TMD2) and two nucleotide binding domains (NBD1, NBD2), many ABC proteins contain additional domains. For example, some members of the C subfamily of ABC (ABCC) proteins, such as the multidrug resistant protein 1 (MRP1), contain an N-terminal transmembrane domain (TMD0) and L0 linker that regulate transport activity and cellular trafficking, and mediate protein-protein interactions. ABCC proteins also contain intrinsically disordered regions, such as the regulatory (R) region that connects NBD1 to TMD2, that are phosphorylated. Additional regulation of ABC transporters is provided by proteolytic processing, and/or oligomerization.

We have conducted electron cryo-microscopy (cryo-EM) studies of the yeast cadmium factor 1 protein (Ycf1p), a homologue of MRP1, in its proteolytically processed form. Surprisingly, proteolytic digestion of a luminal loop in TMD1 promotes the formation of a dimeric form of the protein, which is formed by both protein-protein and protein-lipid interactions. Further, the phosphorylation state and the ATPase activity of the monomeric and dimeric Ycf1p species differ. NMR and other solution-based studies of the Ycf1p R region suggest that different phosphorylation states alter the conformation of the R region. Because Ycf1p is a close homologue of human MRP1 and is also similar to other human MRPs, our Ycf1p structural studies reveal the molecular features of other dimeric ABCC transporters.

Host: Dr. Walid A. Houry

Seminar Sponsors

UTSG
Biochemistry Physics Chemistry