



BiophysTO Lunchtime Seminar Series

Date

Thursday, February 23, 2017
12:00 pm (noon)

Location

McLennan Physical Laboratories,
Room MP606, 255 Huron Street

Streaming

Seminar live streamed to
DV3129 @ UTM

**Pizza & refreshments
provided**

Dr. Roman Melnyk

The Hospital for Sick Children
Molecular Structure & Function Program

How Bacterial Toxins Deliver Proteins Across Membranes and into Cells

Protein translocases, found in all kingdoms of life, facilitate the transport of proteins across biological membranes. How these membrane-embedded translocases recognize and transport their heterogeneous and structurally unwieldy protein substrates across membranes is poorly understood. A major aim of our research is to elucidate how bacterial toxins that carry their own protein translocation machinery deliver toxic enzymes into mammalian cells. After hijacking a host receptor for cell-surface binding, many bacterial toxins, including anthrax toxin, diphtheria toxin and *C. difficile* toxins, are internalized into acidified endosomes whereupon marginally hydrophobic segments emerge and insert into the host membrane to create a transmembrane pore, which is thought to serve as a conduit for associated toxic enzymes to reach the cytosol. Using a combination of electrophysiology, biophysics and cell biology, we have elucidated how segments destined for the membrane are 'hidden' within the soluble pre-pore and how they subsequently assemble into functional pores that enable translocation of enzymes into cells. Further, we demonstrate the ability of one toxin translocase to deliver large and potentially folded proteins across membranes – features that allow for the possibility of repurposing toxins as vectors for targeted intracellular delivery of therapeutic cargo into cells.

Host: Dr. Walid A. Houry



**Seminar
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