BiophysTO Lunchtime Seminar Series

Date
Thursday, May 2 2019
12:00 – 1:00 pm

Location
McLennan Physical Laboratories
Room MP606
60 St. George Street

Pizza and refreshments will be provided

Dr. Kate Lee

Department of Biochemistry
University of Toronto

How Cells Control Protein Aggregation under Stress

Cellular space is compartmentalized into numerous organelles that concentrate specific sets of molecules at distinct locations. In addition to membrane-bound organelles, cells contain various membrane-less organelles that assemble through liquid phase separation. Our lab uses quantitative live imaging and biochemical approaches to understand how membrane-less organelles are regulated in cells. Our recent work focuses on an organelle called stress granules (SGs) that form in response to proteotoxic stresses. SGs concentrate many proteins that are associated with neurodegenerative diseases, Amyotrophic Lateral Sclerosis and Frontotemporal Dementia, and a number of these proteins form rigid aggregates that are thought to drive neuron death. How these protein aggregates arise is not well understood. We found that one such SG protein, Fused in Sarcoma (FUS), phase separates to form dynamic, liquid-like compartments in cells and in a test tube, mediated by its low-complexity (LC) domain. However, liquid FUS droplets with mutations in the LC domain converted over time into solid protein aggregates, suggesting that pathological protein aggregates may arise from aberrant transition of liquid organelles. Our recent data indicate that cells use multiple mechanisms to prevent this liquid-to-solid phase transition from occurring. Moreover, our studies using human neurons differentiated from induced pluripotent stem cells provide insight into how losing these mechanisms drive neurodegeneration. By leveraging these findings, our goal is to identify strategies to improve neuron health and function.

Host: Dr. Walid A. Houry

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