UNVEILING THE ROLE OF INTRINSICALLY DISORDERED MOTIFS IN P97-P47 COMPLEX USING SOLUTION NMR SPECTROSCOPY. **Rui Huang,** University of Guelph, Guelph, ON, Canada. (rhuang08@uoguelph.ca)

Cellular activities reply on proper functioning of a myriad of large biomolecular complexes. To understand the mechanisms by which these molecular machines work, it is crucial to obtain structural information as well as detailed characterization of their conformational dynamics. Here we present our structural study characterizing the dynamic complex formed between p47 and a 320-kDa p97 construct using solution Nuclear Magnetic Resonance (NMR) Spectroscopy. p97 is a highly conserved and abundant cytosolic enzyme in the AAA+ superfamily (ATPases associated with diverse cellular activities). It plays an indispensable role in protein homeostasis and is involved in a variety of diverse cellular processes ranging from proteasomal and lysosomal degradation to membrane fusion and cell cycle regulation. Elevated expression of p97 has been reported in a number of different cancer types and is correlated with cancer aggressiveness and therapeutic resistance, making p97 a promising therapeutic target. p97 interacts with more than 30 adaptor proteins which recruit p97 to various specific cellular functions, one of which, named p47, directs p97 function to the remodelling of cellular membranes. We discovered multiple previously unidentified linear motifs residing in the intrinsically disordered linker region of p47 that play important structural and functional roles in the complex. We characterized the intra-molecular and the inter-molecular interactions involving these motifs, and demonstrated how these interactions are regulated by the nucleotide state of p97 and dictate the overall dynamics and functionality of the complex. Our results highlight the important roles that intrinsically disordered regions (IDRs) play in regulating the structure and function of large molecular assemblies.