BIOPHYSICAL ANALYSES OF DISEASE-RELATED PROTEINS: TDP-43, GELSOLIN AND CRYSTALLIN. **Josephine Esposto**[1], Robert J. Huber[2], Sanela Martic*[1,3] [1]Environmental and Life Sciences Program, Trent University, Peterborough, ON; [2]Department of Biology, Trent University, Peterborough, ON; [3]Department of Forensic Science, Environmental and Life Sciences Program, Material Science Program, Water Quality Center, Trent University, Peterborough, ON K9L 0G2. (josephineesposto@trentu.ca)

The accumulation of misfolded proteins in the form of aggregates is linked to several diseases of the nervous system such as ALS, AD, PD, and prion diseases. The biophysical techniques, such as spectroscopy, microscopy etc. are ideally suited for study of aggregation and its inhibition [1]. Herein, we report on the analysis of proteins involved in ALS, amyloidosis, and cataract formation. Turbidity absorbance and Thioflavin T fluorescence spectroscopy, as well as transmission electron microscopy were used to characterize the protein structures [1,2]. The role of single-point amino acid mutations on the aggregation propensities was also evaluated. In addition, the inhibition of protein and peptides aggregates was achieved using small organic molecules and large antibodies. Overall, the data show that the aggregation process is unique to a protein which in turn can be targeted toward identification of viable therapeutics against neurodegenerative diseases.

[1] Ahmad M, Esposto J, Golec C, Wu C, Martic-Milne S. Aggregation of gelsolin wild-type and G167K/R, N184K, and D187N/Y mutant peptides and inhibition. Mol Cell Biochem. 2021 Jun;476(6):2393-2408.
[2] Esposto JC, Martic S. Phosphorylated TAR DNA-binding protein-43: Aggregation and antibody-based inhibition. Biochim Biophys Acta Mol Basis Dis. 2021 Dec 1;1867(12):166234.