Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, Mar. 2, 2018 in SSC 1511 @ 12 noon

presented by:

Anonna Prioti

(Advisor: G. Harauz)

"Mapping Intramolecular Distances of the 18.5-kDa Myelin Basic Protein by Förster (Fluorescence) Resonance Energy Transfer"

Myelin Basic Protein (MBP) is an intrinsically-disordered protein that is essential for the development of myelin in the central nervous system (CNS) of higher vertebrates. The production of the myelin sheath highly depends on the classic splice isoforms of MBP. The predominant 18.5-kDa isoform of MBP in the human brain is usually used as a marker of compact myelin, which adheres together the cytoplasmic leaflets of the oligodendrocyte membrane. MBP is altered in demyelinating diseases, such as Multiple Sclerosis (MS), by changes in its "molecular barcode" of post-translational modifications. Our laboratory has previously obtained intramolecular distances between several single Cys-substituted sites throughout MBP, and a single internal Trp residue, by Förster Resonance Energy Transfer (FRET). However, my work will provide additional constraints between different segments by FRET of fluorophores attached to two different Cys-substituted residues. Our main hypothesis is that variants of MBP will adopt to a tertiary fold (paperclip or hairpin structure), when there is interaction with lipid membranes. This "tertiary fold" is more precisely defined as an average of an ensemble of conformations. Obtaining a set of distance constraints by a variety of spectroscopic approaches, including FRET, will allow us to build a three-dimensional model of this fold. The significance of this study is to enhance our understanding of MBP's topology and its various roles in the myelin sheath architecture. By analyzing the differences between MBP variants, it will help us to understand the mechanism of demyelination and may also assist in developing future treatment options for MS.