**MIT-Palestine UROP project**

Project title:

**Homology modeling and functional impact of a novel missense variant in the N-terminus of the TECPR2 protein.**

Palestine Faculty

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**Overview**

Autophagy is an evolutionary conserved catabolic pathway in eukaryotic cells responsible for lysosomal degradation of cytoplasmic proteins and aged organelles. TECPR2 is implicated in the autophagy pathway. Biallelic missense and loss of function variants in the TECPR2 gene are reported to cause neurodevelopmental disorder associated with recurrent episodes of acute respiratory dysregulation and decompensation commonly associated with mild concurrent illnesses. Exome sequencing in two patients transient and reversible encephalopathy with respiratory rhythm dysregulation revealed a novel homozygous missense variant NM\_014844.5: c.745G>A shared among the two affected individuals, that leads to the substitution of a conserved glycine to arginine (p.Gly249Arg). In this UROP-project, we aim to perform secondary and tertiary protein structure analysis for the N-terminus of the TECPR2 in the wild type and in the (p.Gly249Arg) mutant, using available online pipelines and modelling tools. Although crystallographic experiments to study the TECPR2 protein domains are not yet performed, comparative studies suggested that both the C-terminus and N-terminus parts of the TECPR2 are highly conserved across species. Modelling studies suggested that the N-terminus of the TECPR2 protein contains 7 bladed β-propeller fold (WD-40) repeat domains, and the C-terminus contains 6 TECPR-repeats forming a double β-propeller motif. We would like to confirm the functional impact of the (p.Gly249Arg) variant on the proposed models, in order to better characterize the functional consequence of this variant.

Start date: Summer 2021

End date: Autumn 2021

Estimated hours per week: 10-15

Application deadline: to be determined.

Required student skillset: The project is for students with strong background in Molecular Biology, Biochemistry, Molecular Genetics. Some Computational Modeling experience is preferred.

Requested budget: None on MIT side

How can the J-WEL project help? Advance Computational Modelling skills among Palestinian students’ graduates.

Contacts: Reham Khalaf-Nazzal, MIT colleague.