Internship Proposal

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Project Title:
Biochemical dissection of astrocyte-mediated synapse assembly

Level:

Master Student

Project Summary:

Astrocytes are a major cell type in the brain. Work by our group has shown that astrocytes are essential for the formation of synapses (points of contact between neurons) in the brain. It appears that astrocytes are specialized to build different types of synapses, including those between either excitatory or inhibitory neurons. Failure of proper synapse formation is thought to lead to impairments in information processing, which causes important neuropsychiatric diseases, such as schizophrenia and autism spectrum.

We want to identify astrocyte secreted factors that differentially modulate synapse assembly. We will use cultured astrocytes expressing a novel biotin ligase localized to the endoplasmic reticulum, enabling us to biotinylate secreted proteins, allowing isolation and subsequent identification using mass-spectrometry. Proteins of interest will then be recombinantly expressed in bacteria, purified and applied to cultured neurons to assess synaptogenic potential.

Work to be developed by the student:

Tissue culture, viral vector transduction, biochemical assays (including pull-downs and mass-spectrometry), protein expression and purification, fluorescence microscopy.

References:

Holt, M.G. (2023). Astrocyte heterogeneity and interactions with local neural circuits. Essays in Biochemistry. Online ahead of publication.

Pestana, F.P., Edwards-Faret, G., Belgard, T.G., Martirosyan, A., Holt, M.G. (2020). No longer underappreciated: the emerging concept of astrocyte heterogeneity in neuroscience. Brain Sci. 10:E168.

Batiuk, M.Y., Martirosyan, A., Wahis, J., de Vin, F., Marneffe, C., Kusserow, C., Koeppen, J., Viana, J.F., Oliveira, J.F., Voet, T., Ponting, C.P., Belgard, T.C., Holt, M.G. (2020). Unraveling region-specific astrocyte subtypes at single cell resolution. Nat. Commun. Mar 5;11(1):1220. doi: 10.1038/s41467-019-14198-8.

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