Universitat Pompeu Fabra Barcelona | Master in Bioinformatics for Health Sciences

Master project 2024-2025

Personal Information

Supervisor	Mara Dierssen & Rosa Martinez
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Group	Cellular & Systems Neurobiology, Theoretical Regulatory Biology

Project

Computational systems biology

Project Title:

dosage-sensitivity in neurological disorders

Keywords:

phospho-proteomics, protein-protein interaction network, non-monotonicity, systems biology

Summary:

This project will combine the analysis of phospho-proteomic data with dynamical systems modelling in order to clarify the dosage-sensitivity associated with Dyrk1A . Dyrk1A is a pleiotropic kinase key to neurological conditions, including the cognitive disability associated with Down syndrome, and neurodegenerative disorders like Alzheimer's disease. Dyrk1A is dosage-sensitive: when one copy of the Dyrk1A gene is missing, or the gene is triplicated, similar phenotypes arise both at the functional level, as well as at the level of abnormalities of neuronal morphology. Given these observations, previous work has hypothesized that the dosage-sensitivity of Dyrk1A could be mediated by N-WASP, a key regulator of dendrite branching. This project aims to test this hypothesis. To this end, the student will analyse phosphoproteomics data collected by the Dierssen lab in brain tissues with 1, 2 or 3 Dyrk1A copies, aiming to identify a phosphorylation network around Dyrk1A and NWASP. Subsequently, mechanistic mathematical modelling with Ordinary Differential Equations will be performed to test whether the identified interactions could underlie the dosage-sensitivity of Dyrk1A. The student will be jointly supervised by members of the Dierssen group regarding the analysis of the data, and Rosa Martinez-Corral regarding the modelling part.

References:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10793573/ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6873902/
https://www.sciencedirect.com/science/article/abs/pii/S0969996113002295?via%3Dihub
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https://www.sciencedirect.com/science/article/abs/pii/S0969996105000665?via%3Dihub
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9800213/ https://journals.biologists.com/jcs/article/125/1/67/32223/Dyrk1A-negatively-regulates-the-actin-cytoskeleton

Expected skills:

Some background in -omics data analysis as well as mechanistic models with ordinary differential equations.

Possibility of funding:

To be discussed

Possible continuity with PhD:

To be discussed

Comments:

We are located at the PRBB and Fundacio Pasqual Maragall Building in Barcelona. Hybrid work model acceptable, with in-person time especially devoted to meetings and discussion.