

Group Name: Molecular mechanisms of neuronal identity

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Title of the MRP:

How neurons know who they are and stay that way

Summary of the MRP:

The complexity of the nervous system relies fundamentally on the great diversity of its basic units, the neurons. The identity of specific cell types in the nervous system is defined early in development by unique transcriptional programs that are actively maintained throughout life. Changes in neuronal identity, such as gene expression or epigenetic modifications, are crucial for the plasticity of the nervous system. These changes can influence synaptic connectivity and neuronal function, contributing to learning and adaptation. Disruption of these mechanisms underlies major neurological diseases, such as Alzheimer's and Parkinson's.

In previous work, we have found that CUT homeobox genes are required for pan-neuronal gene expression and neuronal function (Leyva-Díaz and Hobert, 2022; Leyva-Díaz *et al.*, 2025). We use genome-wide approaches, including single-cell RNA-seq, together with classical genetics to identify these regulators. This project aims to uncover additional transcriptional regulators that maintain neuronal identity in *C. elegans*, a powerful genetic model.

Specific Aims:

1. Effect on pan-neuronal gene expression:
 - Analysis of single mutant candidates: *lsy-2/MZF1* and *ces-1/SCRT1*.
 - Genetic interaction studies: combinatorial mutants
2. Behavioral analysis of neuronal function:
 - Locomotion assays: crawling (tracking) and swimming
 - Synaptic transmission assays: sensitivity to aldicarb

The project is ideal for students interested in neurobiology, gene regulation, and modern genomic techniques. The student will gain valuable experience in genetics, confocal microscopy, and behavioral neuroscience.

If you are curious about how neurons define who they are, and how this relates to brain health, we invite you to join us and explore the transcriptional logic of the nervous system.

Methods and technology involved in the MRP:

- Bioinformatic analysis of ChIP-seq and single-cell RNA-seq data
- Confocal microscopy for the analysis of fluorescent reporters
- CRISPR/Cas9 genome editing
- In vivo quantification of gene expression
- *C. elegans* behavioral assays (locomotion tracking, swimming, aldicarb)
- Genetic interaction studies

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