Internship Proposal

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Project Title:
Regulation of neurogenesis and neuronal reprograming by Ascl1

Level:

Master Student

Project Summary:

Most of our neurons were generated from multipotent neural stem cells during embryonic development, a process called neurogenesis. Proneural transcription factors such as Ascl1 function as master regulators of neurogenesis, being both required and sufficient for activating a neuronal differentiation program in neural stem cells. Reminiscent to its role in neurogenesis, Ascl1 is the transcription factor most often used in protocols whereby somatic cells are directly reprogrammed into “neurons”. Direct cell-fate conversion of astrocytes into neurons is becoming a promising strategy to tackle pathologies associated with neuronal loss.

We study the regulatory logic of neurogenesis by focusing on how this is governed by Ascl1. We aim at identifying which genes are activated by Ascl1, and the molecular mechanisms that regulate its activity during embryonic development. We also use this knowledge to improve neuronal reprogramming, using an astrocyte-to-neuron fate conversion paradigm.

Work to be developed by the student:

We use the mouse embryo as an experimental model, complemented by cellular models of neurogenesis and neuronal reprogramming. Members of our lab usually acquire extensive expertise in molecular biology, and a variety of techniques used in gene expression analysis. Our work has also a strong component of genomics (both wet-lab and bioinformatics based).

References:

Soares MAF, Soares DS, Teixeira V, Heskol A, Bressan RB, Pollard SM, Oliveira RA, Castro DS. Hierarchical reactivation of transcription during mitosis-to-G1 transition by Brn2 and Ascl1 in neural stem cells. Genes Dev. 2021 Jul 1;35(13-14):1020-1034. doi: 10.1101/gad.348174.120. Epub 2021 Jun 24.

Vasconcelos FF, Sessa A, Laranjeira C, Raposo AASF, Teixeira T, Hagey DW, Tomaz DM, Muhr J, Broccoli V, Castro DS. MyT1 counteracts the neural progenitor program to promote vertebrate neurogenesis. Cell Reports. 2016. Oct 4;17(2):469-483

Vasconcelos FF, Castro DS. Transcriptional control of vertebrate neurogenesis by the proneural factor Ascl1. Front Cell Neurosci. 2014. Dec 2;8:412

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