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Modeling the Nervous System in Development and Disease Using Pluripotent Stem Cells

Position

Lecturer, Sackler Faculty of Medicine

Research

Our lab makes use of *human embryonic stem cells* in order to elucidate developmental programs in the human nervous system, with particular interest in *neural stem cells* (NSCs).

The NSC ontogeny dogma predicts that early developing NSCs are highly potent and can yield all nervous system cell types, but they rapidly lose this potential as development proceeds. Because NSCs behave similarly in culture, they are almost useless for studying differentiation to most neuronal cell types – a major impediment for understanding basic development and application to regenerative medicine.

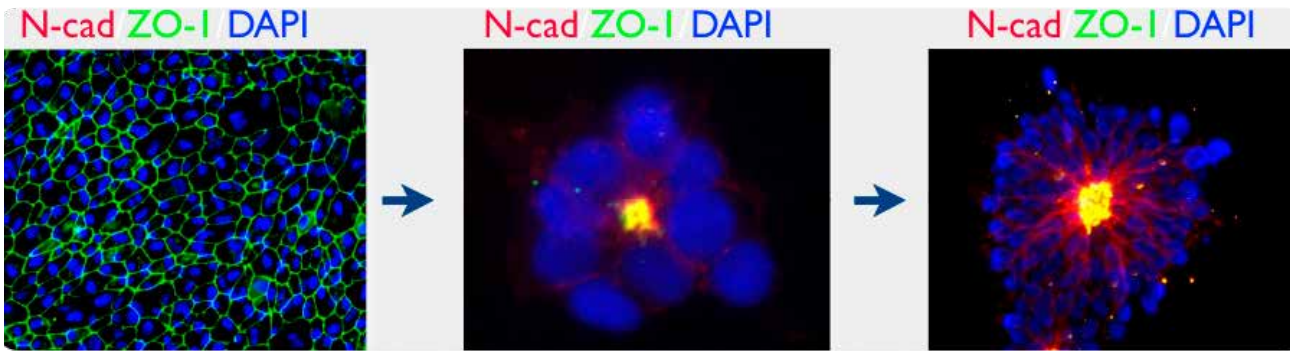
Our main goal is to learn the biology of early neural stem cells in the lab in order to develop strategies for standardizing their growth in culture without loss of differentiation potential. Such continuously self renewing cells will serve as a *gold standard NSCs* for studying nervous system development and disease, making cells for therapy and discovering novel drugs.

We use a variety of techniques in mouse and human embryonic stem cells and NSCs cells including transgenics (genetic labeling), viral expression of coding genes and microRNAs, classic stem cell assays, FACS-sorting and stem cell differentiation, and two-photon/confocal live cell imaging.

Publications

Lipchina I, **Elkabetz Y**, Hafner M, Sheridan R, Mihailovic A, Tuschl T, Sander C, Studer L, Betel D. Genome-wide identification of microRNA targets in human ES cells reveals a role for miR-302 in modulating BMP response. *Genes Dev.* 2011; 25:2173-86.

Lafaille FG, Pessach IM, Zhang SY, Ciancanelli MJ, Herman M, Abhyankar A, Ying SW, Keros S, Goldstein PA, Mostoslavsky G, Ordovas-Montanes J, Jouanguy E, Plancoulaine S, Tu E, **Elkabetz Y**, Al-Muhsen S, Tardieu M, Schlaeger TM, Daley GQ, Abel L, Casanova JL, Studer L, Notarangelo LD. Impaired intrinsic immunity to HSV-1 in human iPSC-derived TLR3-deficient CNS cells. 2012. *Nature* 2012; 491:769-73.



Human embryonic stem cells (Left panel) differentiate into NSCs (Middle and tight panels), which organize in a shape of rosettes. Neural rosettes have strong tight and adherens junctions, and are the earliest and most potent NSCs.