

Neural Stem Cells and Neural Progenitors

Nov. 11 2019

Altman J.: the first evidence for new dentate granule cells in postnatal rat hippocampus (1965)

Cori Cepko: discovered multipotency of neural progenitors in retina (1987)

Sally Temple: described neural progenitors and stem cells (1989)

Brent Reynolds and Samuel Weiss: generation of neurons from isolated neurosphere-forming cells (1992)

Fred Gage: discovered the human brain produces new nerve cells in adulthood (1998)

Hongjun Song: revealed self-renewing and multipotent adult neural stem cells in the hippocampus (2011)

Neural stem cells

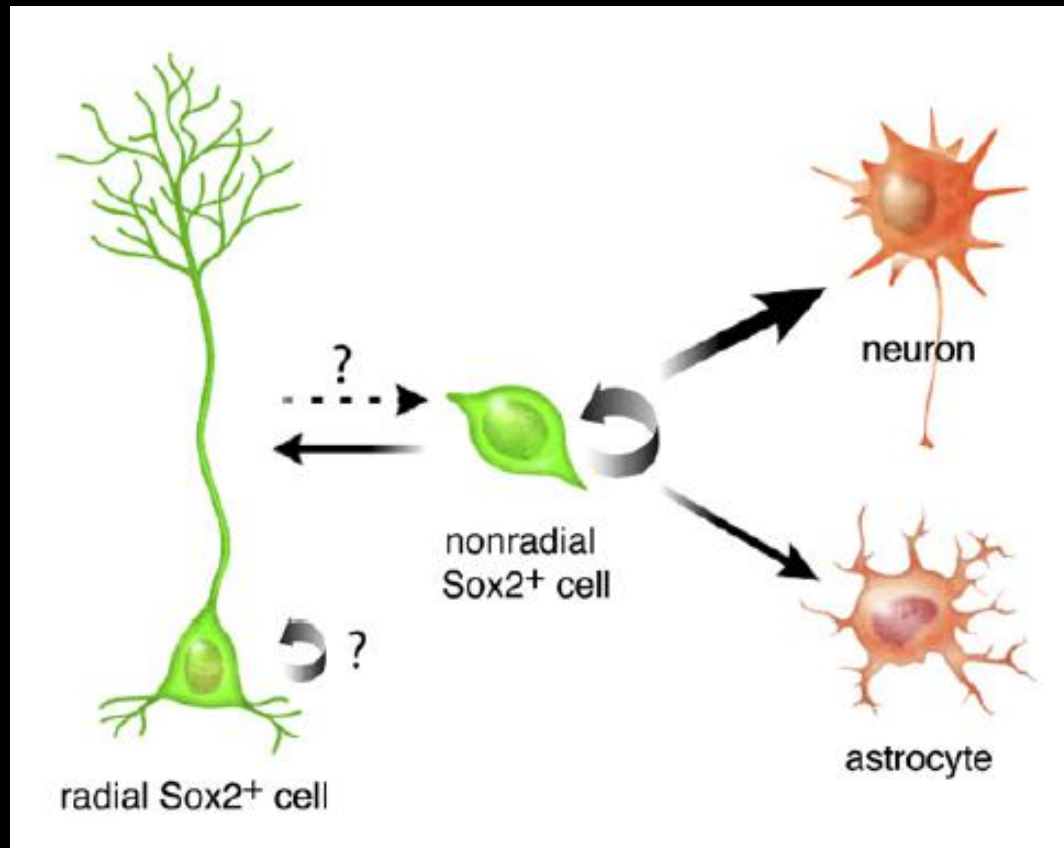
Embryonic Neural Stem Cells
Post-embryonic Neural Stem Cells

Neuroepithelial Stem Cells

Radial Glial Cells (Gli, GFAP, GLAST, Nestin)

Non-radial Glial Cells (Sox2)

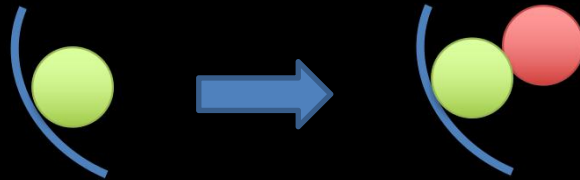
Non-radial Glial Cells

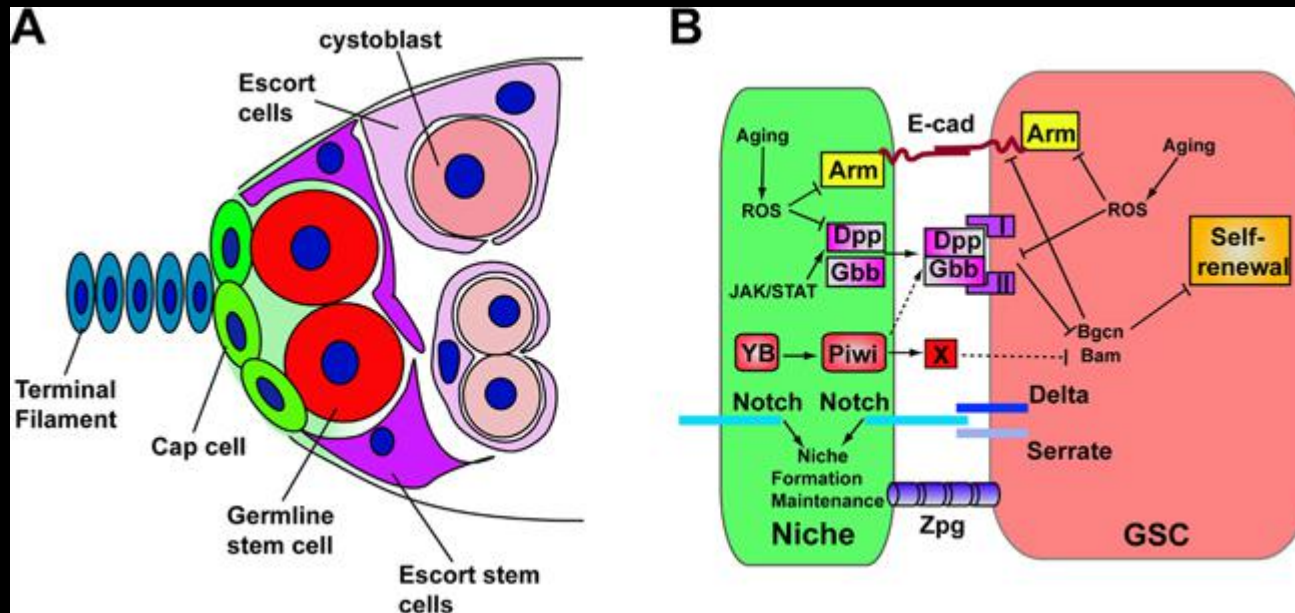


Neural stem cells are self-renewing and multipotent cells that generate the main phenotypes of the nervous system.

Self-renewing and Multipotent?

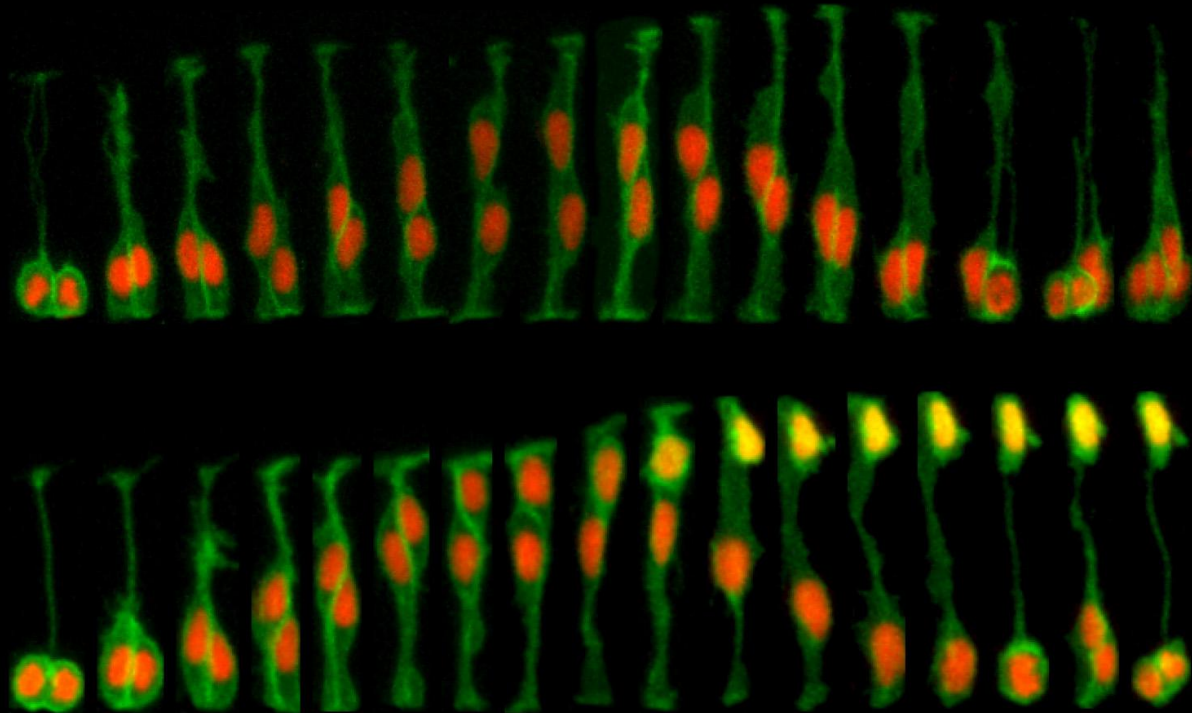
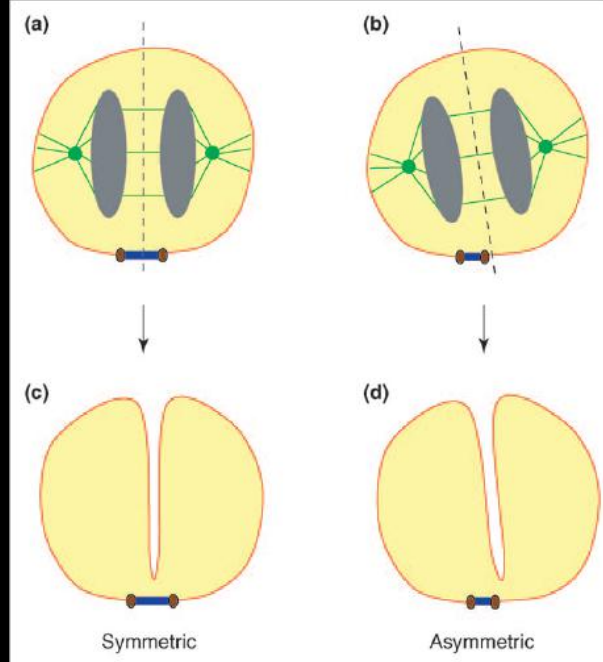
Classic Asymmetrical Cell Division





GSC niche in the drosophila ovary

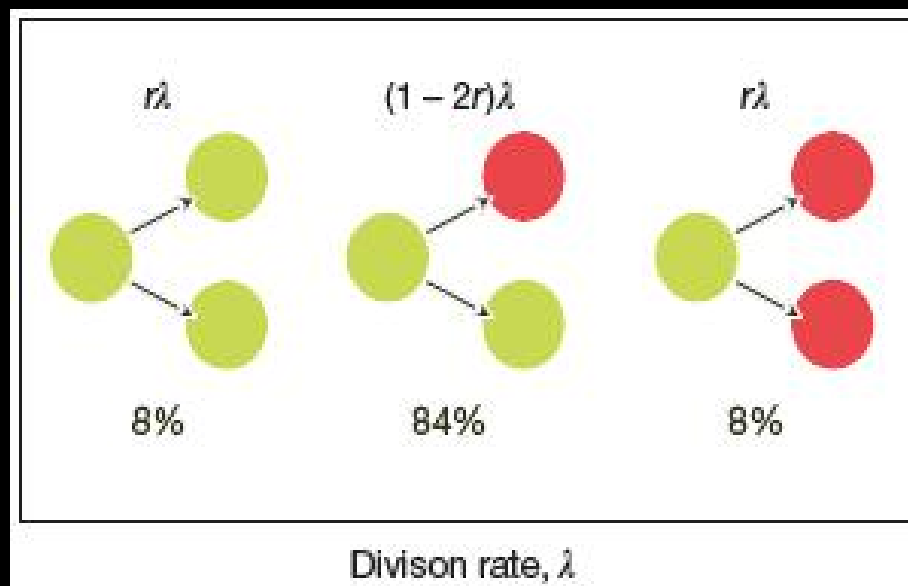
Xie and Spradling, 2000



LETTERS

A single type of progenitor cell maintains normal epidermis

Elizabeth Clayton¹, David P. Doupé¹, Allon M. Klein², Douglas J. Winton³, Benjamin D. Simons² & Philip H. Jones¹



Intestinal Crypt Homeostasis Results from Neutral Competition between Symmetrically Dividing Lgr5 Stem Cells

Hugo J. Snippert,¹ Laurens G. van der Flier,¹ Toshiro Sato,¹ Johan H. van Es,¹ Maaïke van den Born,¹ Carla Kroon-Veenboer,¹ Nick Barker,¹ Allon M. Klein,^{2,3} Jacco van Rheenen,¹ Benjamin D. Simons,³ and Hans Clevers^{1,*}

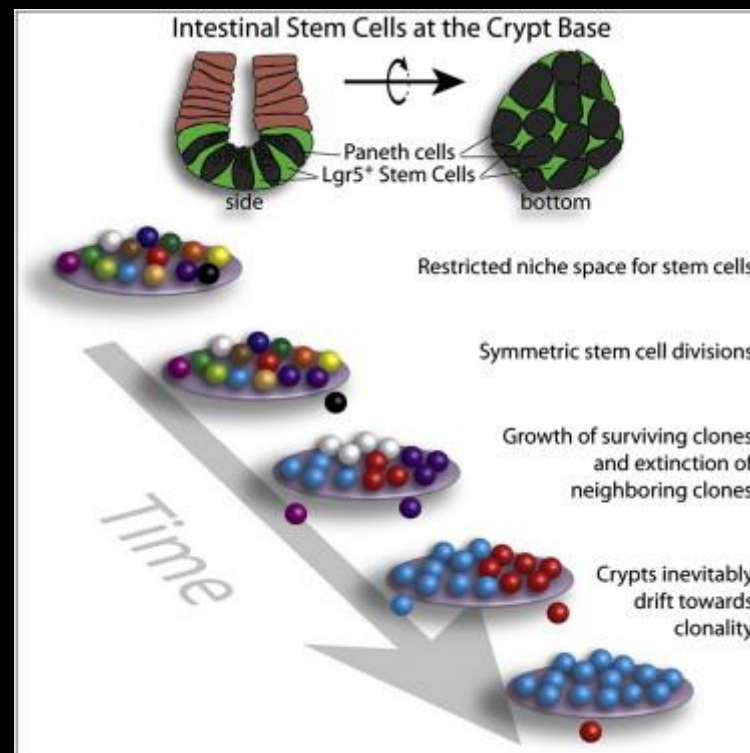
¹Hubrecht Institute, KNAW and University Medical Center Utrecht, Uppsalalaan 8, 3584 CT Utrecht, The Netherlands

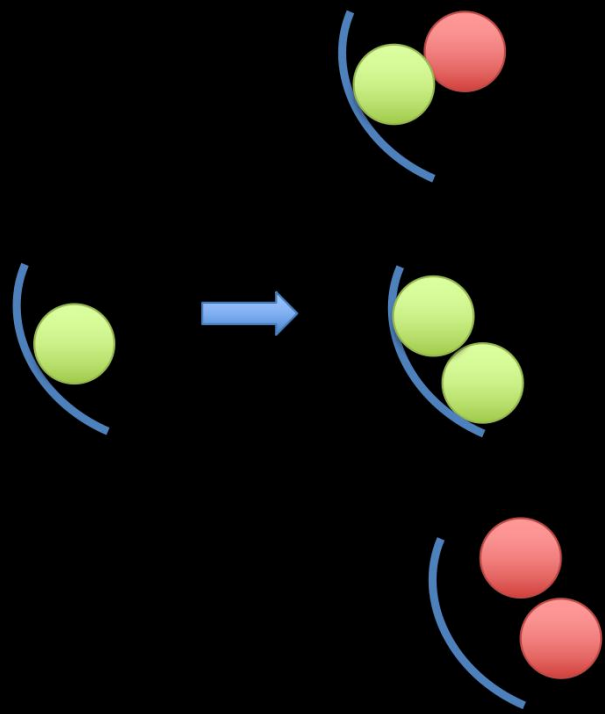
²Department of Systems Biology, Harvard Medical School, 200 Longwood Avenue, Boston, MA 02115, USA

³Department of Physics, Cavendish Laboratory, J.J. Thomson Avenue, Cambridge CB3 0HE, UK

*Correspondence: h.clevers@hubrecht.eu

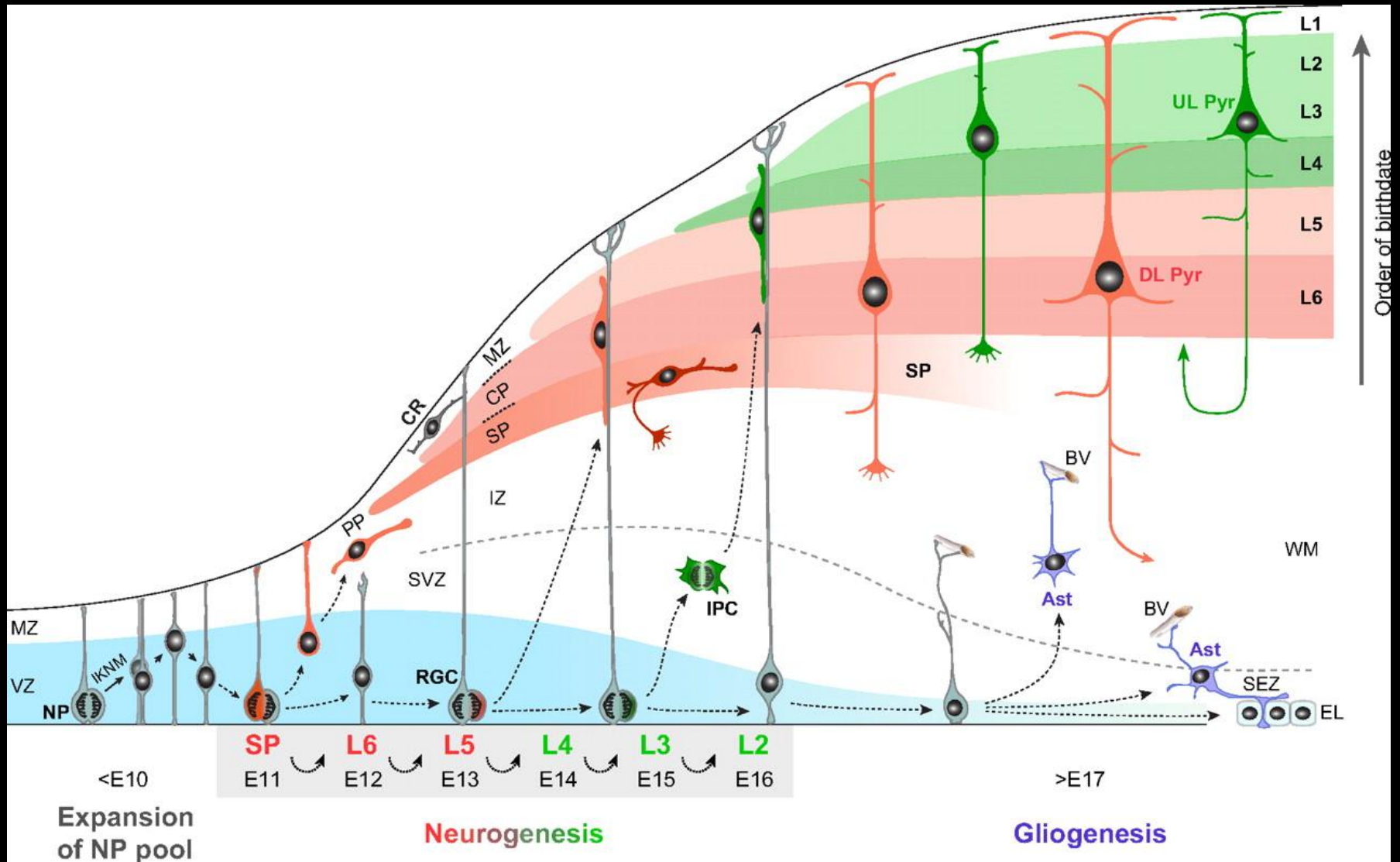
DOI 10.1016/j.cell.2010.09.016



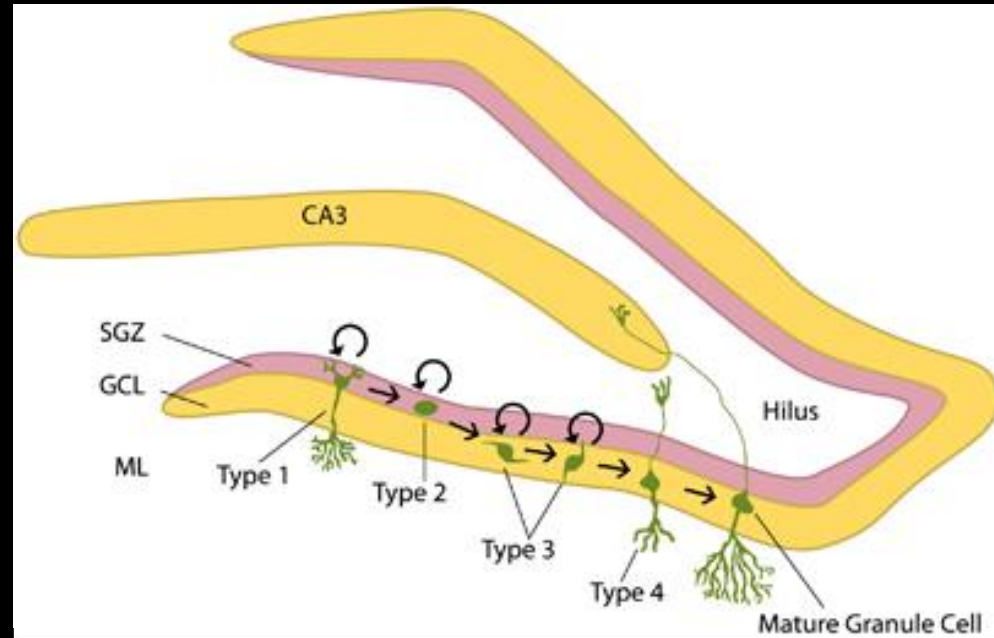
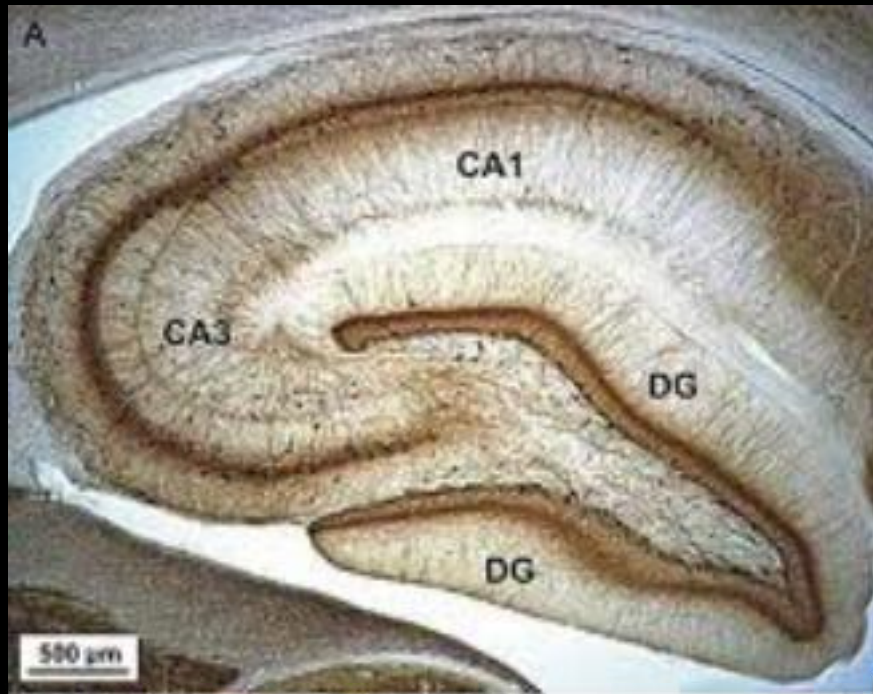


Neurogenic niches

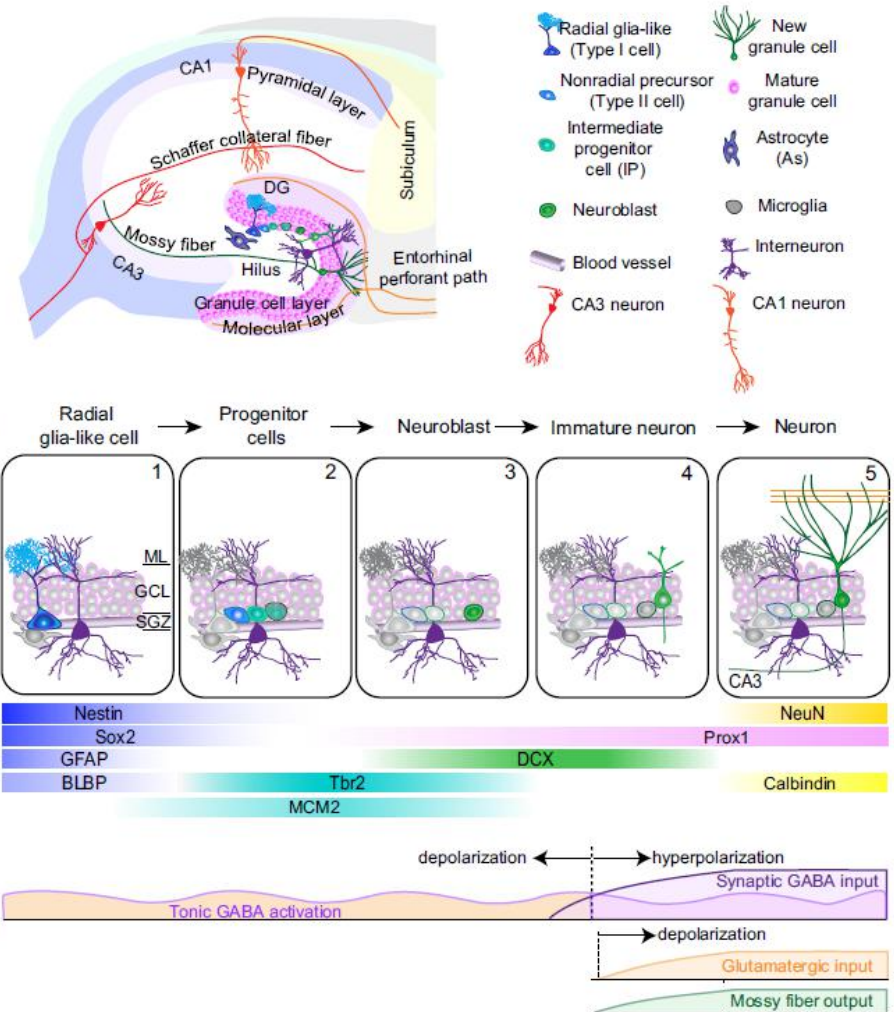
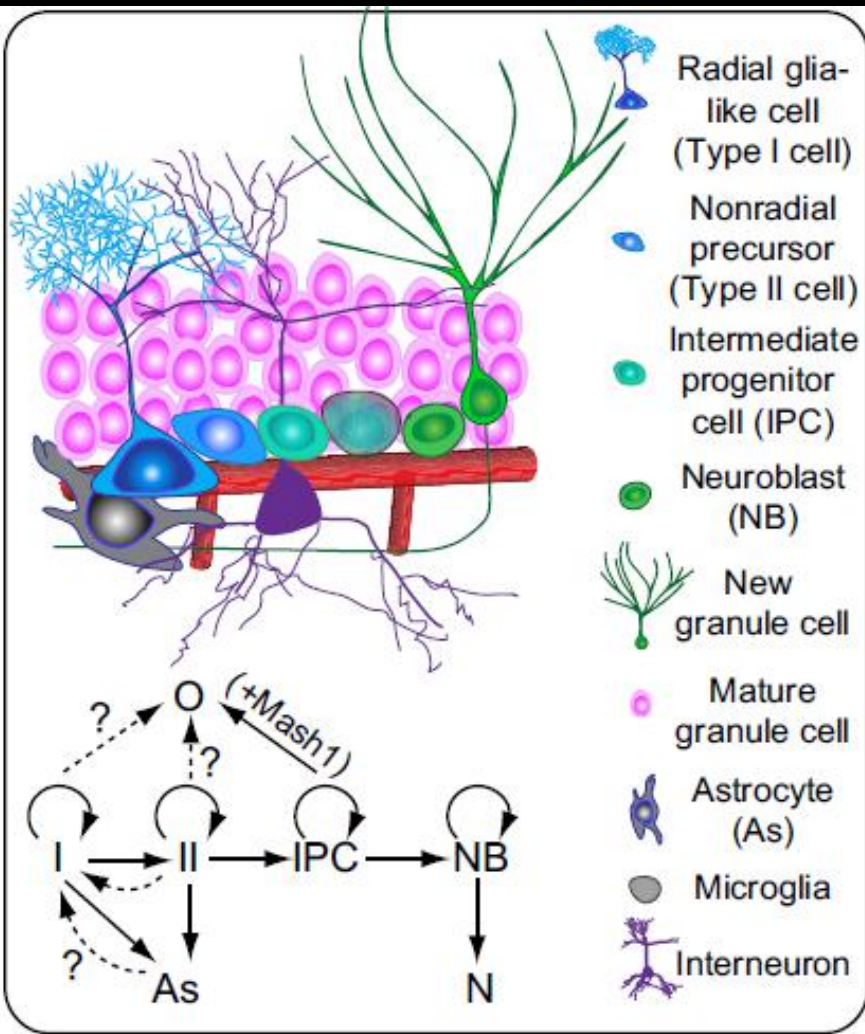
Embryonic Ventricular Zone

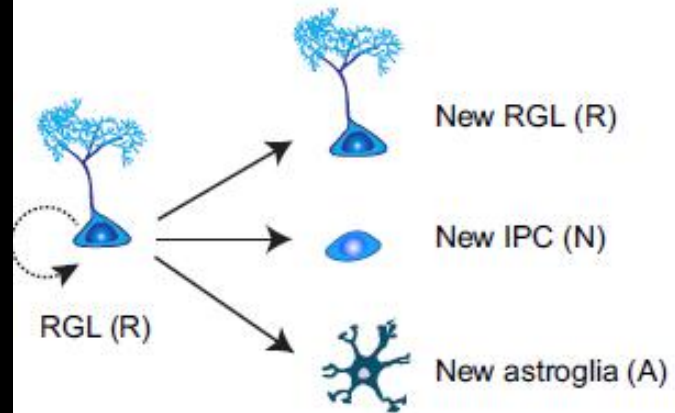
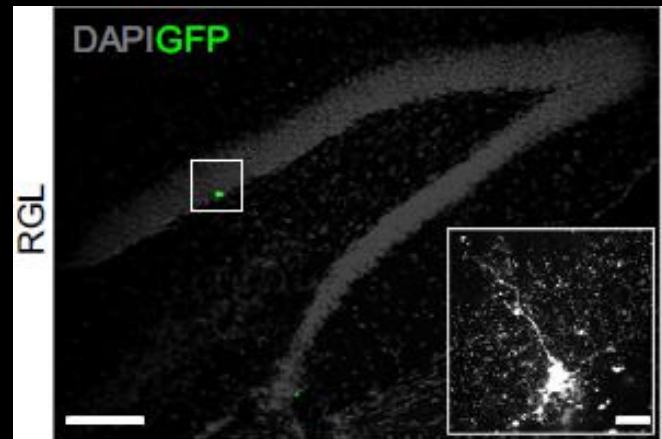
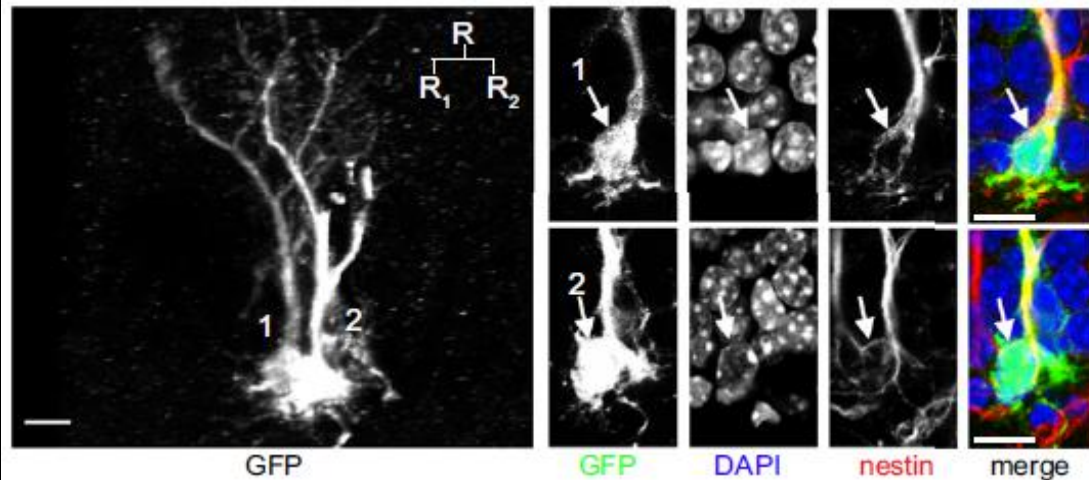
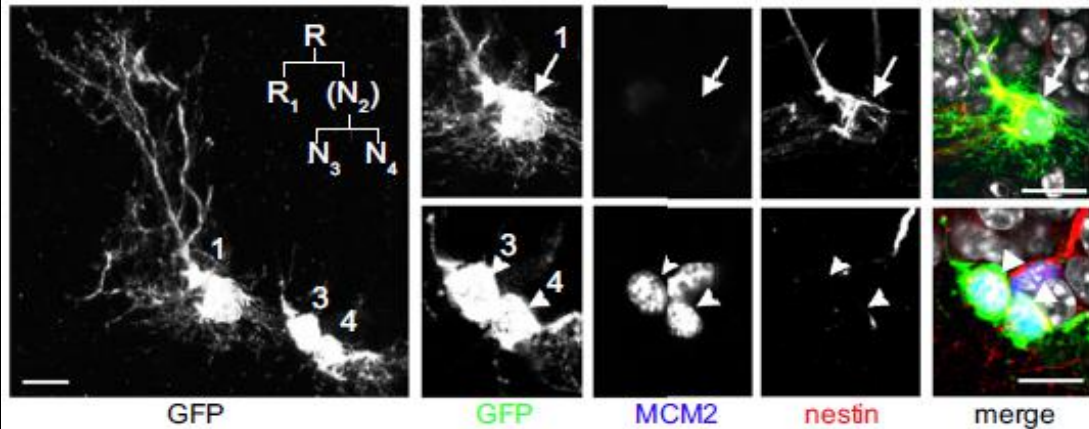
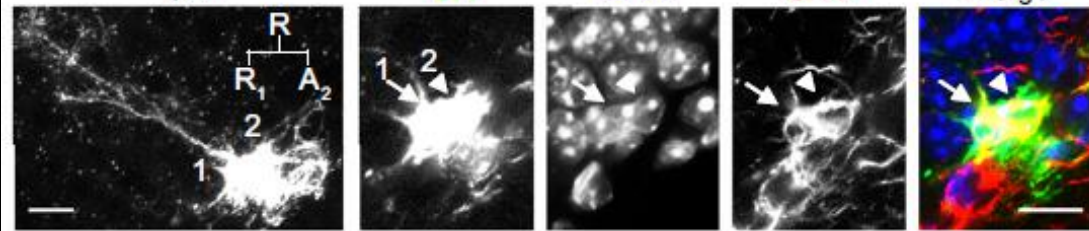
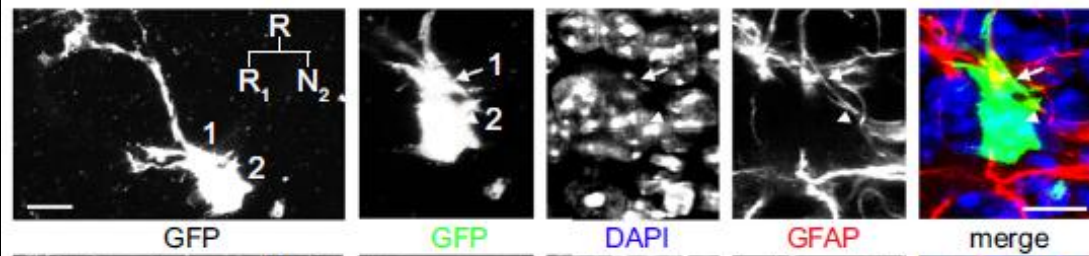


Subgranule zone of dentate gyrus



NSCs in hippocampus

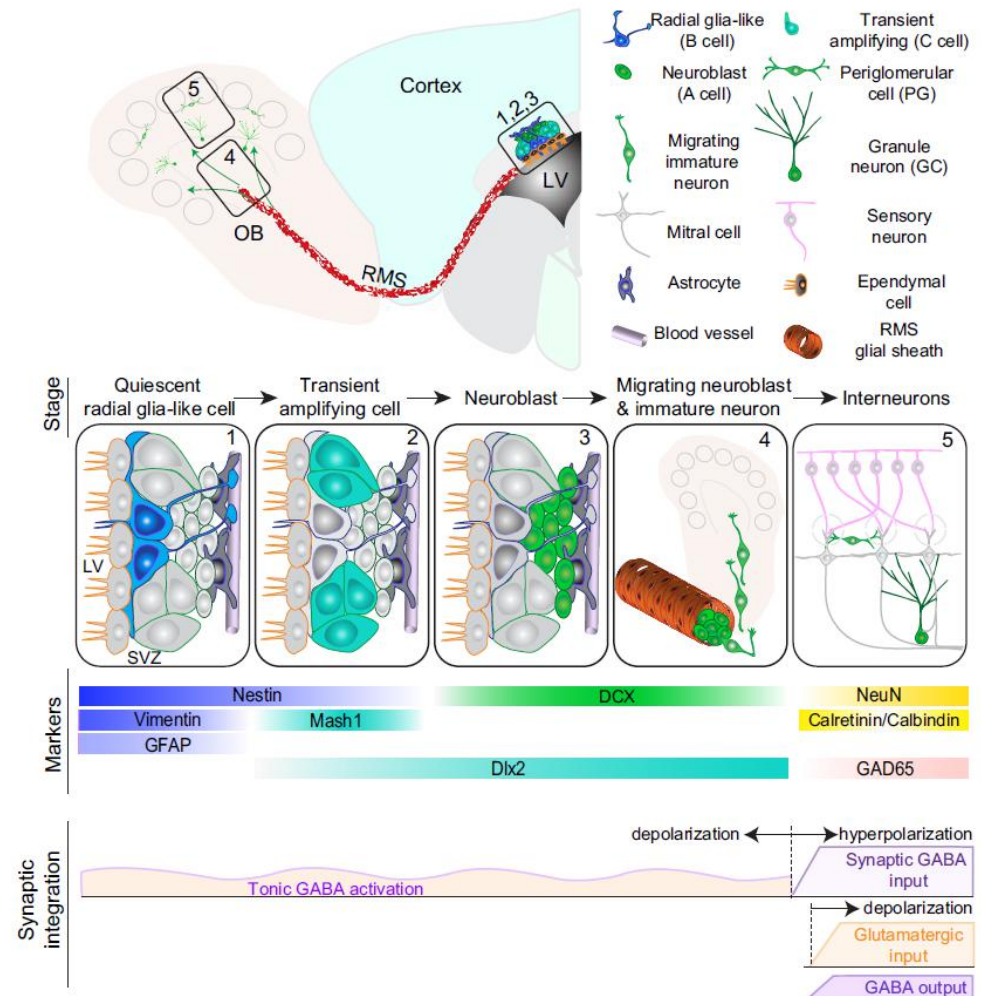
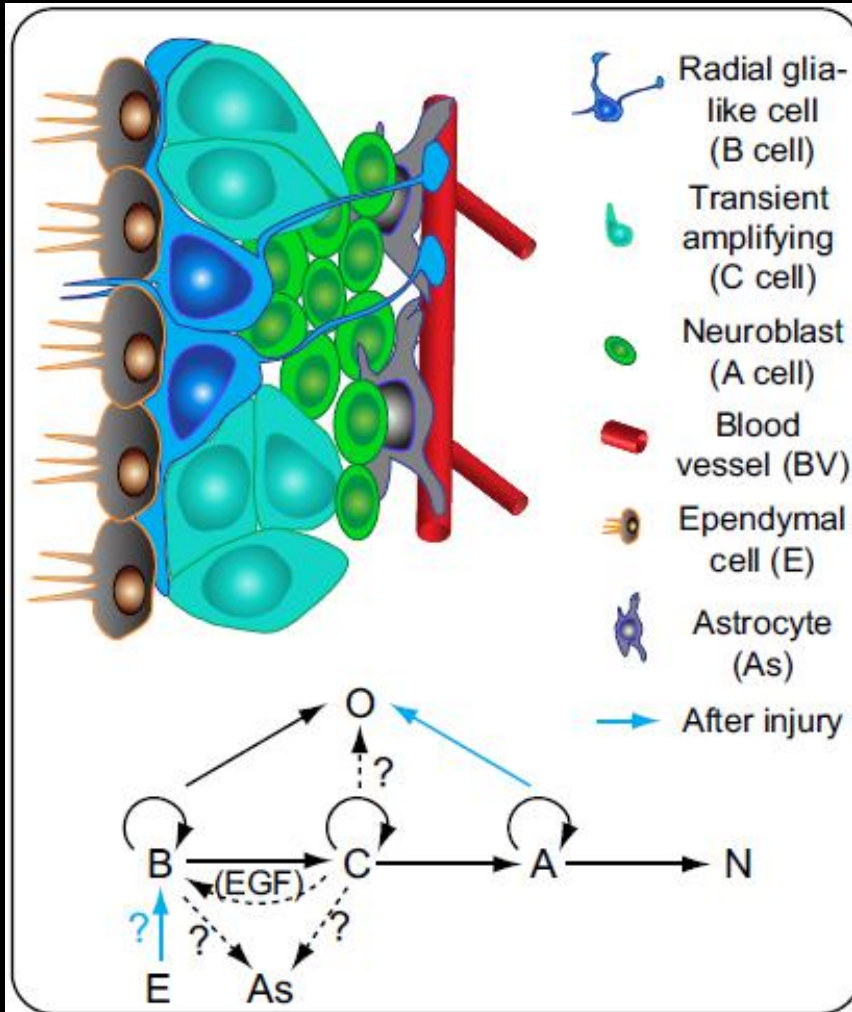




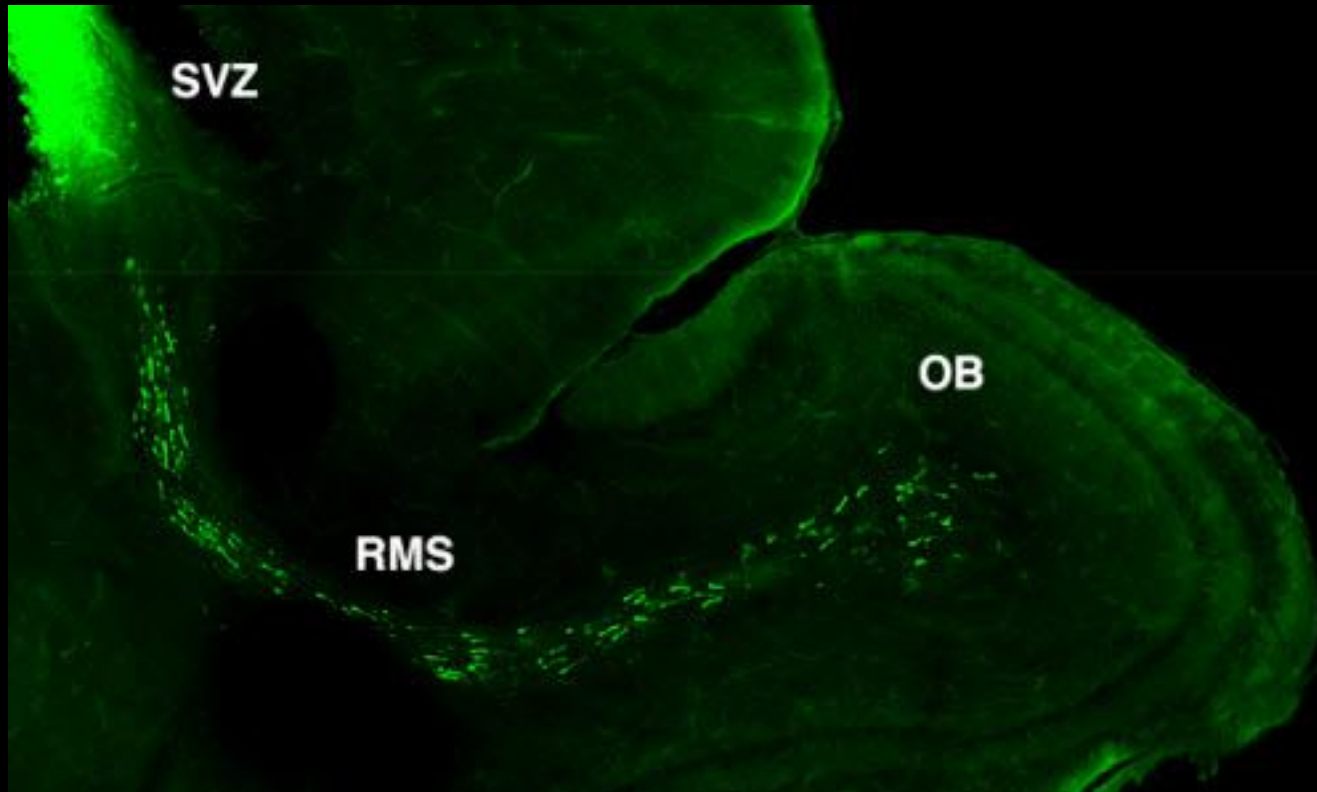
Nestin-CreER
Z/EG

Bonaguidi et al., 2011, Cell

NSCs in the Subventricular Zone



Neurogenesis in Olfactory Bulb



Neurogenesis in Human Brain

Cell

Neurogenesis in the Striatum of the Adult Human Brain

Aurélie Ernst,¹ Kanar Alkass,^{1,2} Samuel Bernard,³ Mehran Salehpour,⁴ Shira Perl,⁵ John Tisdale,⁵ Göran Possnert,⁴ Henrik Druid,² and Jonas Frisén^{1,*}

¹Department of Cell and Molecular Biology

²Department of Oncology-Pathology
Karolinska Institute, 171 77 Stockholm, Sweden

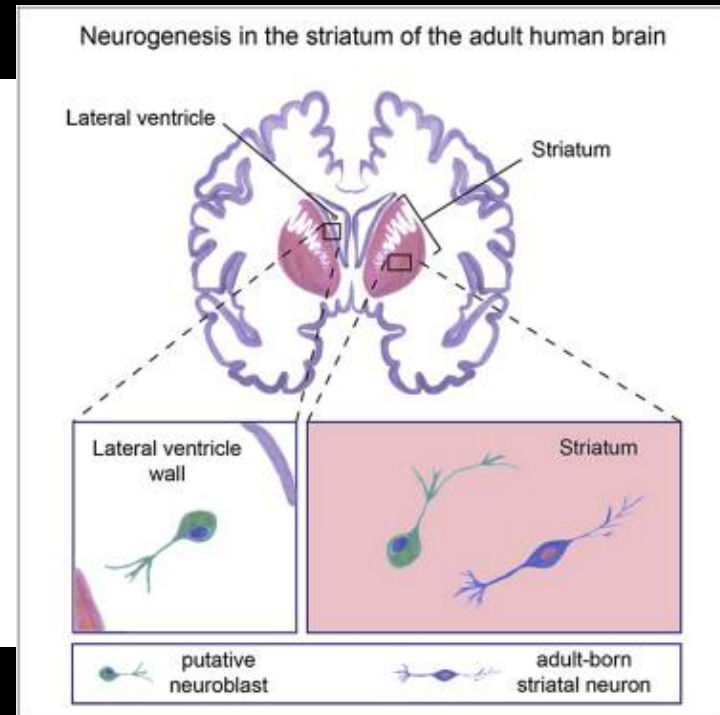
³Institut Camille Jordan, CNRS UMR 5208, University of Lyon, 69622 Villeurbanne, France

⁴Department of Physics and Astronomy, Ion Physics, Uppsala University, 751 20 Uppsala, Sweden

⁵NHLBI, NIH, Bethesda, Maryland 20892, USA

*Correspondence: jonas.frisen@ki.se

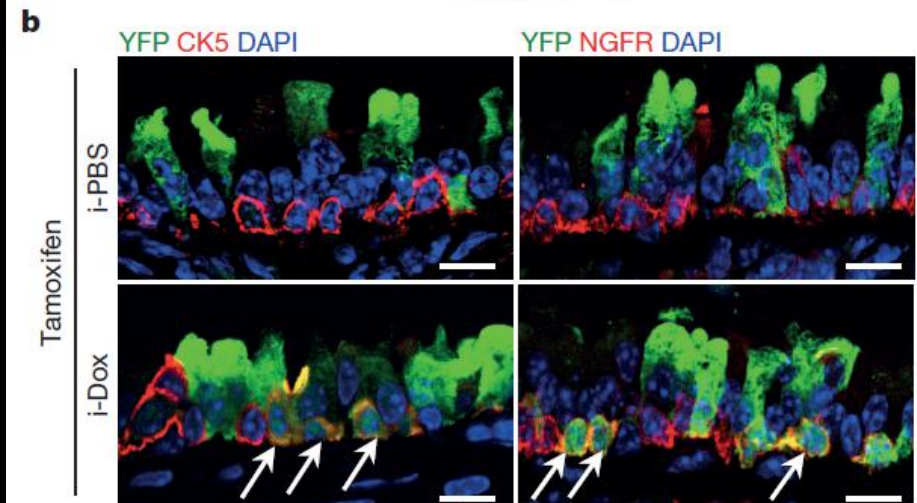
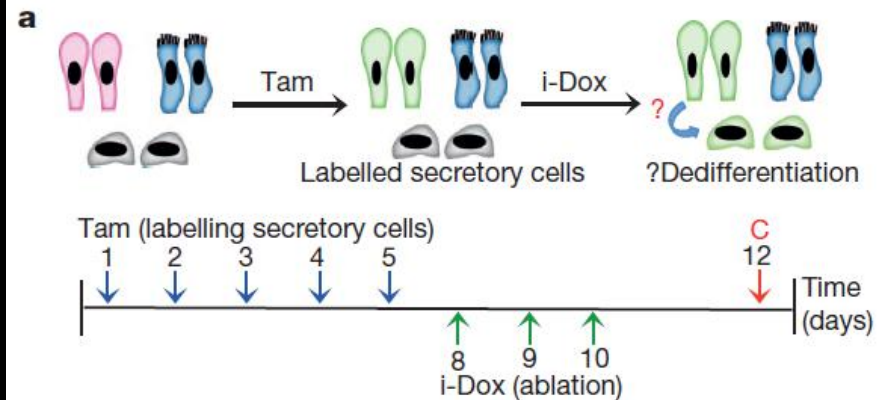
<http://dx.doi.org/10.1016/j.cell.2014.01.044>



Neural stem cell is a cellular function?

Dedifferentiation of committed epithelial cells into stem cells *in vivo*

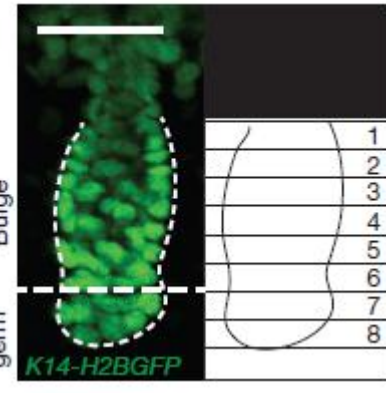
Purushothama Rao Tata^{1,2,3,4}, Hongmei Mou^{1,2,3,4}, Ana Pardo-Saganta^{1,2,3,4}, Rui Zhao^{1,2,3,4}, Mythili Prabhu^{1,2,3,4}, Brandon M. Law^{1,2,3,4}, Vladimir Vinarsky^{1,2,3,4}, Josalyn L. Cho^{3,5}, Sylvie Breton⁶, Amar Sahay^{1,4,7}, Benjamin D. Medoff^{3,5} & Jayaraj Rajagopal^{1,2,3,4}



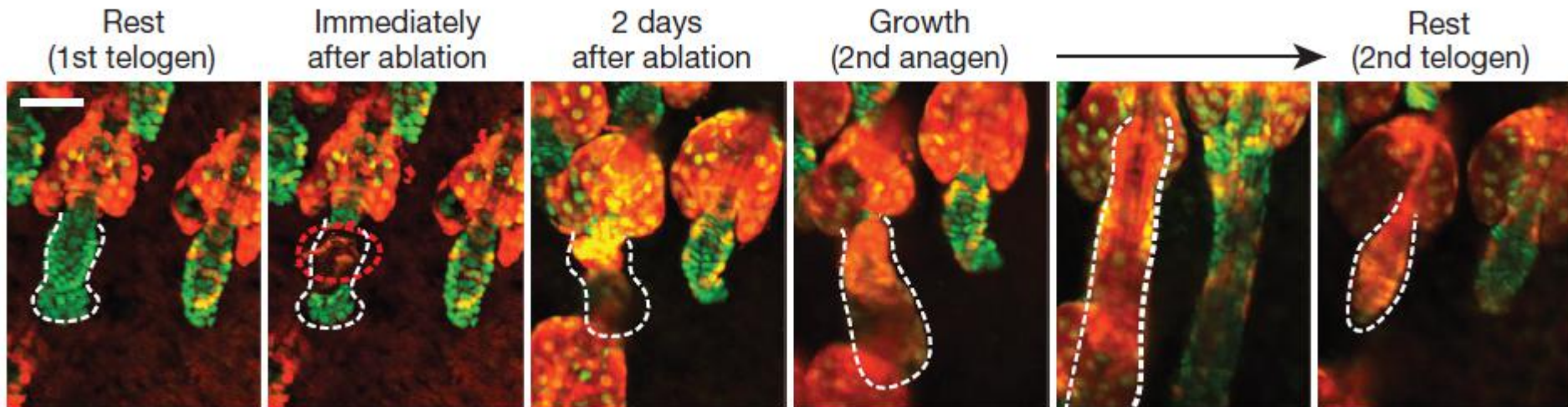
Scgb1a1-creER/LSL-YFP::CK5-rtTA-tet(O)-DTA

Spatial organization within a niche as a determinant of stem-cell fate

Panteleimon Rombolas¹, Kailin R. Mesa¹ & Valentina Greco¹



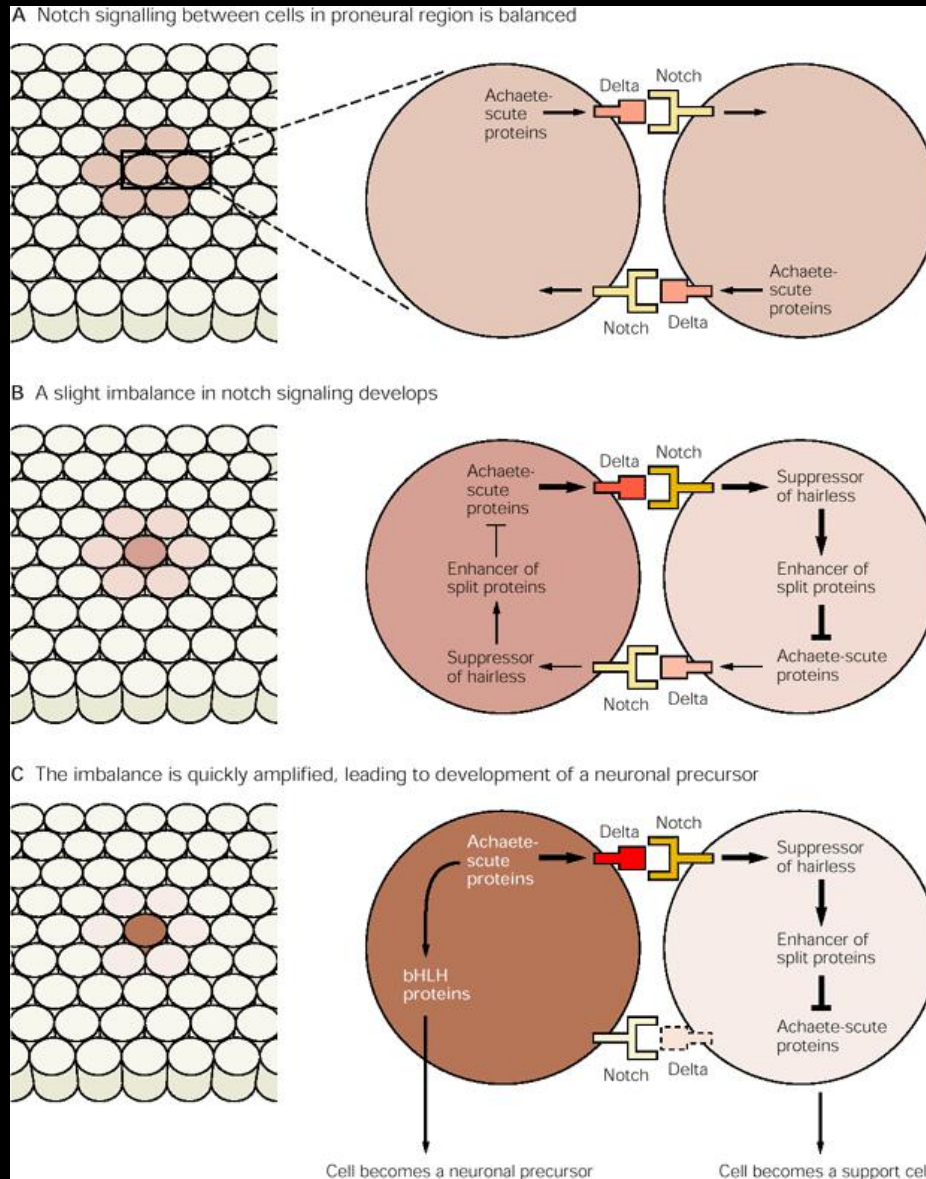
Mouse hair follicle niche



Neuronal differentiation

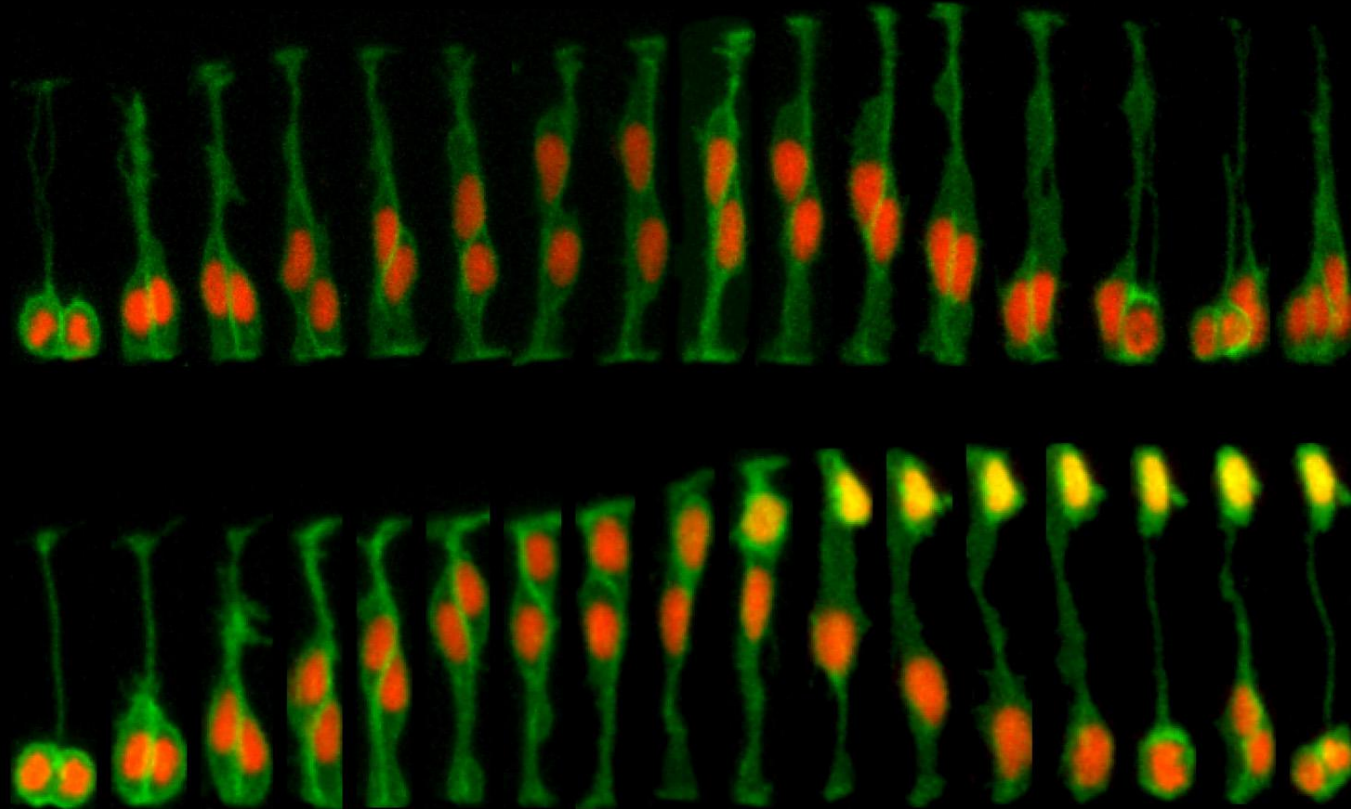
In developmental biology, cellular differentiation is the process by which a less specialized cell becomes a more specialized cell type.

Delta-Notch Signaling



Aguirre et al., 2010, Nature
 Androutsellis-Theotokis., 2006, Nature

Interkinetic Nucleus Migration



Regulation of Neurogenesis by Interkinetic Nuclear Migration through an Apical-Basal Notch Gradient

Filippo Del Bene,¹ Ann M. Wehman,¹ Brian A. Link,^{2,*} and Herwig Baier^{1,*}

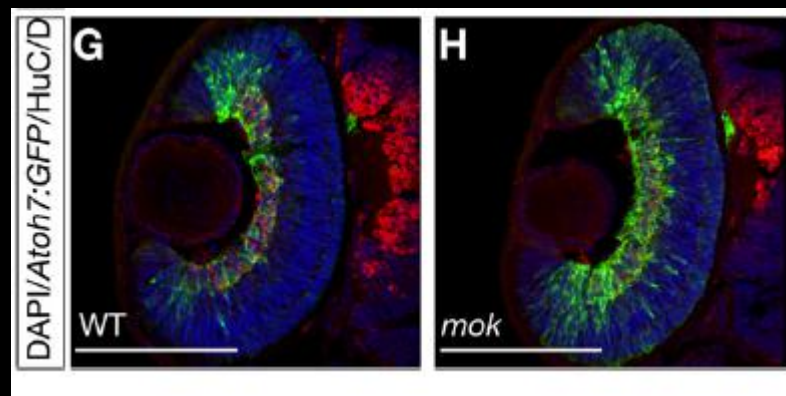
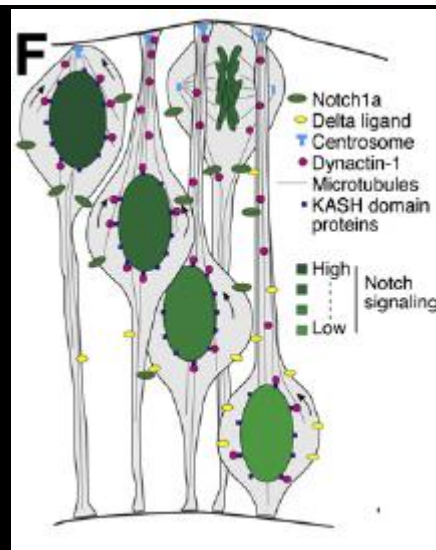
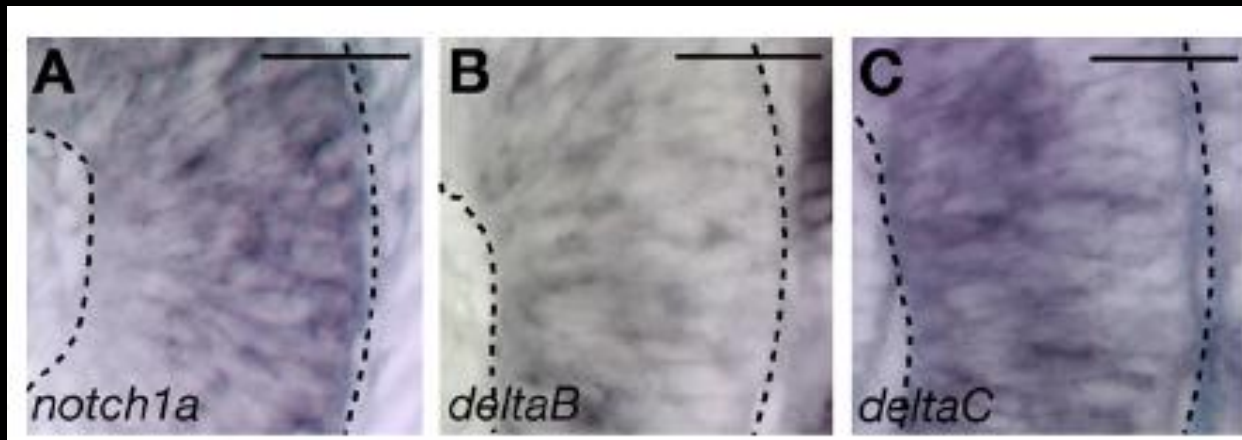
¹Department of Physiology, Programs in Neuroscience, Genetics, and Developmental Biology, University of California, San Francisco, 1550 4th Street, San Francisco, CA 94158-2722, USA

²Department of Cell Biology, Neurobiology, and Anatomy, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, USA

*Correspondence: blink@mcw.edu (B.A.L.), herwig.baier@ucsf.edu (H.B.)

DOI 10.1016/j.cell.2008.07.017

Mok mutant: the motor protein Dynactin-1 is disrupted, INM more rapidly and deeply To the basal side and more slowly to the apical side.



Actomyosin Is the Main Driver of Interkinetic Nuclear Migration in the Retina

Caren Norden,^{1,3} Stephen Young,^{1,3} Brian A. Link,² and William A. Harris^{1,*}

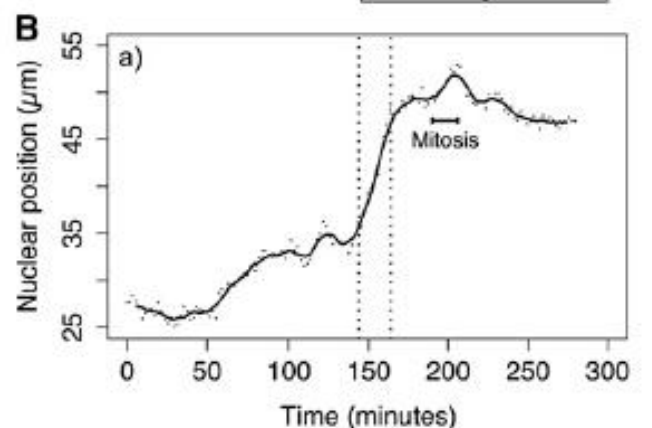
¹Department of Physiology, Development and Neuroscience, Cambridge University, Downing Street, Cambridge CB2 3DY, UK

²Department of Cell Biology, Neurobiology, and Anatomy, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, USA

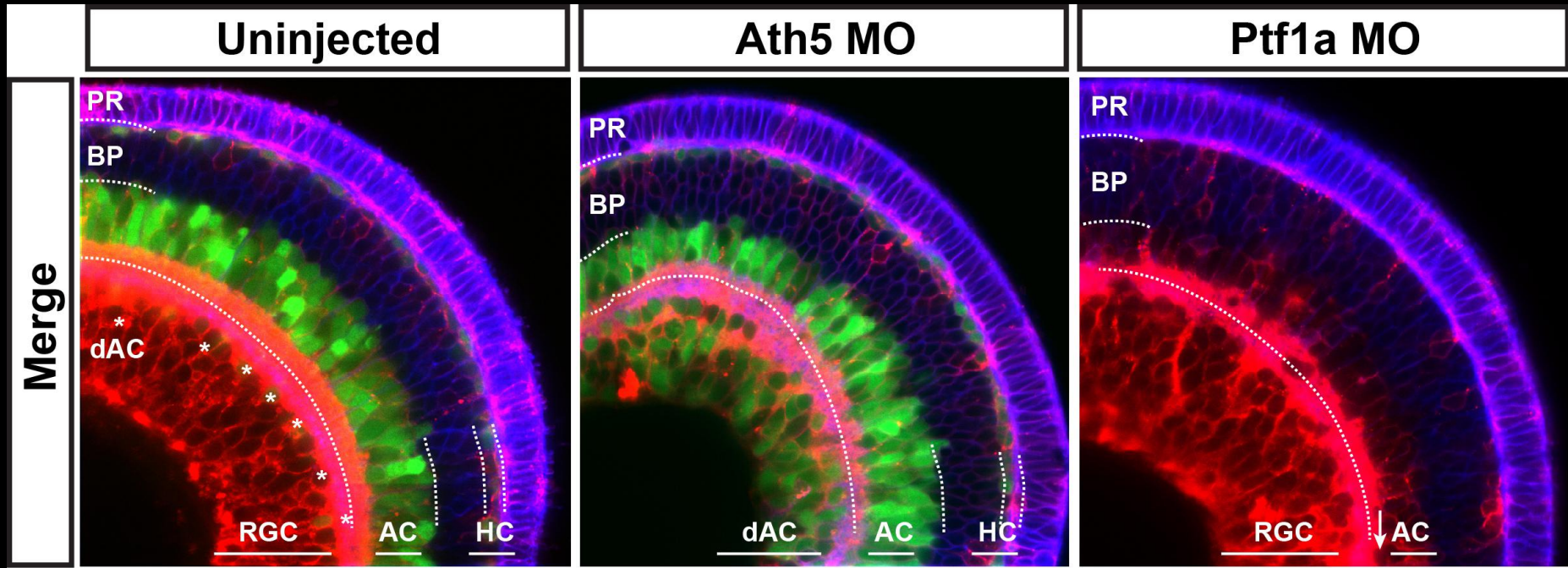
³These authors contributed equally to this work

*Correspondence: harris@mole.bio.cam.ac.uk

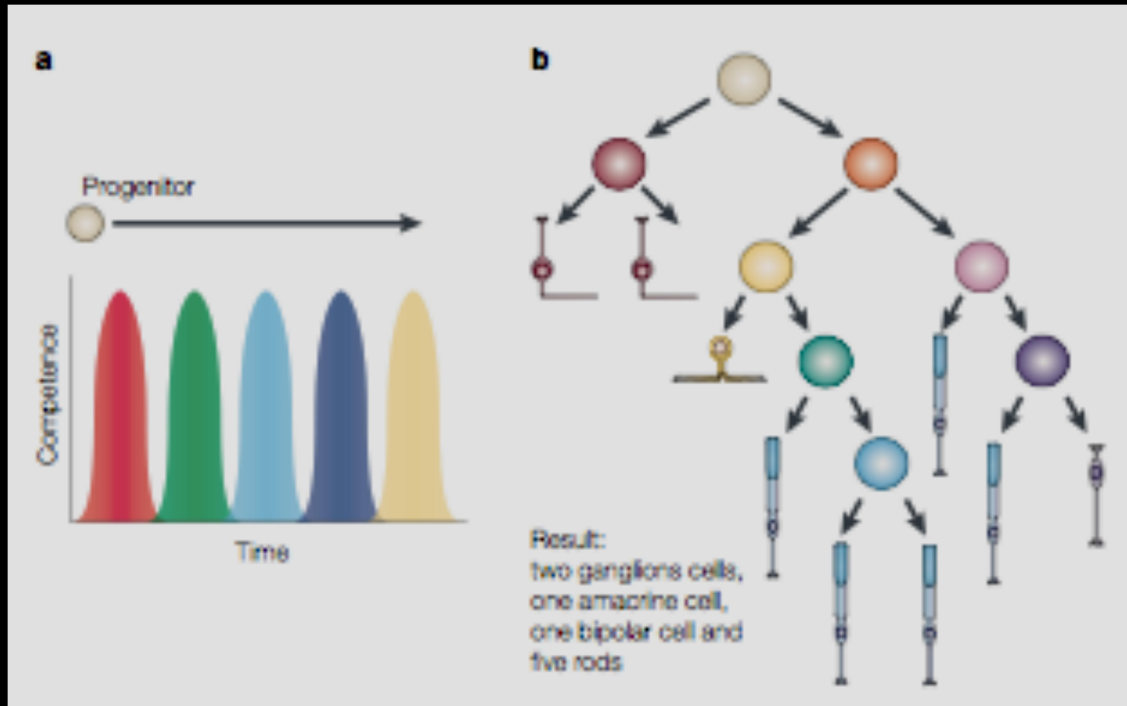
DOI 10.1016/j.cell.2009.06.032



Fate Specification

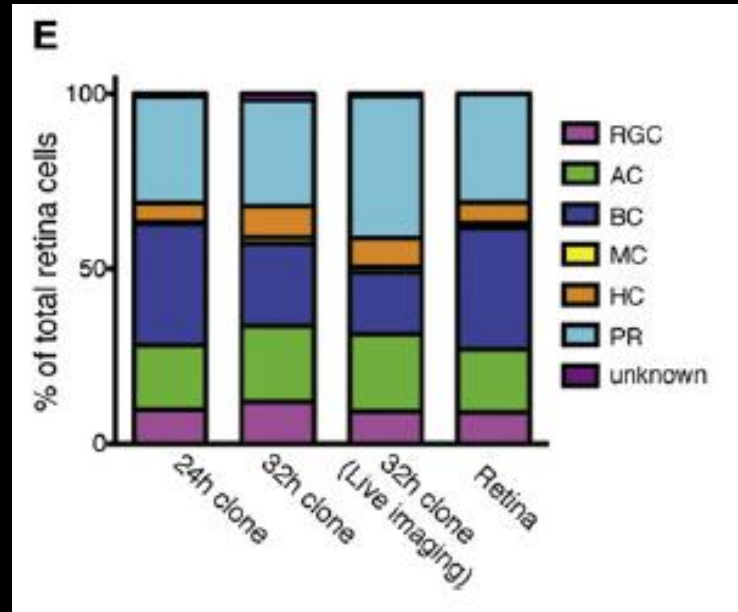
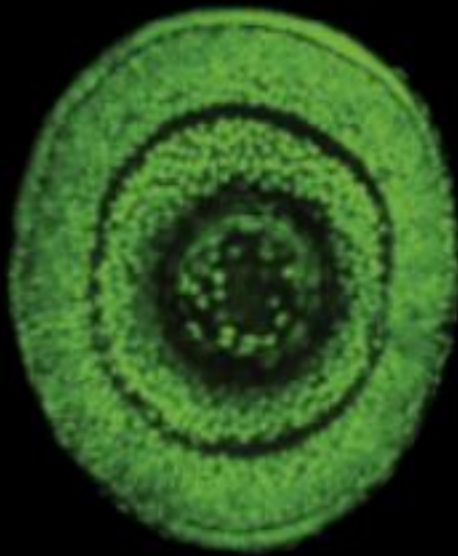


Histogenesis



Competence Model: RPCs pass through a series of competence states, progressively changing their responsiveness to instructive extrinsic cues, which also change over time.

Cell Composition



Outstanding Questions of Adult Neural Stem Cells

- ✓ Whether there exist individual true NSCs or not?
- ✓ What is the heterogeneity of adult NSC properties (Nature vs. Nurture)?
- ✓ What is the lineage relationship of such progenitor heterogeneity?
- ✓ What is the embryonic origin of different neural precursors?
- ✓ What is the multipotency of aNSCs in the physiological condition and upon injury?
- ✓ Why are adult Neural Stem Cells quiescent?

Outstanding Questions of Neural Differentiation

- ✓ What is a neural cell fate?
- ✓ How is a given cell fate specified?
- ✓ How are different cell fates generated sequentially?
- ✓ How are the new-born neurons synapsed together?

谢谢