CELLULAR AND MOLECULAR BASIS OF NEURAL DEVELOPMENT I:
NEURONAL DIFFERENTIATION
2019
Revised April 2019

COURSE DESCRIPTION

A seminar and reading course devoted to the discussion of the cellular and molecular processes underlying neuronal development. Topics include cell proliferation and migration, nervous system patterning, differentiation of neurons and glia, morphogen and growth factor signaling mechanisms, neuronal polarity, neural stem cell biology, and neurovascular biology. Examples from vertebrate and invertebrate model systems will be covered. This course is designed to complement The Cellular and Molecular Basis of Neural Development II: Axon Guidance and Synaptogenesis, offered alternate years. Students must have completed Introduction to Neuroscience and Cognition I or receive the consent of course directors prior to registering for this course.

The course will meet on **Tuesdays from 9:30-11am** and **Thursdays from 2:30 pm to 4:00pm** in PCTB 1022. The first class will meet Tuesday, March 26, and the last class will be held Tuesday, May 14. A writing assignment will be due on Tuesday, May 21. The first class (3/26) will be a short (~15 mins) introduction devoted to course organizational issues and a short general introduction to the material that will follow—there is no assigned reading for the first class, and reading assignments for all remaining classes will be distributed at this time (but can also be obtained earlier by contacting any one of the course Directors.

Course Directors: Alex Kolodkin (4-9499), Uli Mueller (7-4762), and Chris Potter (7-4151).

Participating Faculty: Seth Blackshaw, Dwight Bergles, Angelika Doetzlhofer, Alex Kolodkin, Uli Mueller, Jeremey Nathans, Chris Potter, and FengQuan Zhou

3/26 (Tues) INTRODUCTION-COURSE ORGANIZATION (KOLODKIN, MUELLER, POTTER)

15 min. Course organizational meeting.

3/28 (Thurs) NEURAL INDUCTION (MUELLER)

Smith WC, Harland RM. Expression cloning of noggin, a new dorsalizing factor localized to the Spemann organizer in Xenopus embryos. Cell. 1992 Sep 4;70(5):829-40. PubMed PMID: 1339313.

Cho A, Tang Y, Davila J, Deng S, Chen L, Miller E, Wernig M, Graef IA. Calcineurin signaling regulates neural induction through antagonizing the BMP pathway. Neuron. 2014 Apr 2;82(1):109-24. doi: 10.1016/j.neuron.2014.02.015. PubMed PMID: 24698271; PubMed Central PMCID: PMC4011666.

4/2 (Tues) NEURONAL POLARITY (ZHOU)

Witte H, Neukirchen D, Bradke F.
Microtubule stabilization specifies initial neuronal polarization. J Cell Biol. 2008 Feb 11;180(3):619-32. doi: 10.1083/jcb.200707042.

Ambrozkiewicz MC, Schwark M, Kishimoto-Suga M, Borisova E, Hori K, Salazar-Lázaro A, Rusanova A, Altas B, Piepkorn L, Bessa P, Schaub T, Zhang X, Rabe T, Ripamonti S, Rosário M, Akiyama H, Jahn O, Kobayashi T, Hoshino M, Tarabykin V, Kawabe H.
Polarity Acquisition in Cortical Neurons Is Driven by Synergistic Action of Sox9-Regulated Wwp1 and Wwp2 E3 Ubiquitin Ligases and Intronic miR-140. Neuron. 2018 Dec 5;100(5):1097-1115.e15. doi: 10.1016/j.neuron.2018.10.008. Epub 2018 Nov 1.

4/4 (Thurs) NEURAL CELL DEATH AND LIFE (POTTER)

Nikoletopoulou, V., Lickert, H., Frade, J. M., Rencurel, C., Giallonardo, P., Zhang, L., Bibel, M, Barde Y-A.. (2010). "Neurotrophin receptors TrkA and TrkC cause neuronal death whereas TrkB does not." *Nature*, *467*(7311), 59–63.

Southwell, Paredes, Galvao, Jones, Froemke, Sebe, Alfaro-Cervello, Tang, Garcia-Verdugo, Rubenstein, Baraban. Alvarez-Buylla. (2012) "Intrinsically determined cell death of developing cortical interneurons." Nature 491, 109–113 (01 November 2012) doi:10.1038/nature11523

4/9 (Tues) DORSAL-VENTRAL PATTERNING OF THE SPINAL CORD (KOLODKIN)

Yamada T, Placzek M, Tanaka H, Dodd J, Jessell TM. Control of cell pattern in the developing nervous system: polarizing activity of the floor plate and notochord. Cell. 1991 Feb 8;64(3):635-47. PubMed PMID: 1991324.

Briscoe J, Pierani A, Jessell TM, Ericson J. (2000). A homeodomain protein code specifies progenitor cell identity and neuronal fate in the ventral neural tube. Cell, 101, 435-45.

Tozer S, Le Dreau G, Marti E, Briscoe J (2013) Temporal control of BMP signalling determines neuronal subtype identity in the dorsal neural tube. Development 140: 1467–1474.

4/11 (Thurs) ROSTRAL CAUDAL PATTERNING (KOLODKIN)

Dasen JS, Liu JP, Jessell TM. Motor neuron columnar fate imposed by sequential phases of Hox-c Activity. 2003. Nature, *425,* 926-33. PMID: 14586461

Jung, H. et al….Dasen, J.S. The ancient origins of neural substrates for land walking. 2018. Cell, *172,* 667-682. PMID: 29425489

4/16 (Tues) NEURAL CELL FATE SPECIFICATION-NOTCH AND PRONEURAL GENES (DOETZLHOFER)

Imayoshi I, Isomura A, Harima Y, Kawaguchi K, Kori H, Miyachi H, Fujiwara T, Ishidate F, Kageyama R. Oscillatory control of factors determining multipotency and fate in mouse neural progenitors. Science. 2013 Dec 6;342(6163):1203-8. doi: 10.1126/science.1242366. PubMed PMID: 24179156.

Wang VY, Hassan BA, Bellen HJ, Zoghbi HY. Drosophila atonal fully rescues the phenotype of Math1 null mice: new functions evolve in new cellular contexts. Curr Biol. 2002 Sep 17;12(18):1611-6. PubMed PMID: 12372255.

4/18 (Thurs) RETINAL NEURON SPECIFCIATION (BLACKSHAW)

Simon, M.A., Bowtell, D.D.L., Dodson, G.S., Laverty, T.R., and Rubin, G.M. (1991). Ras1 and a putative guanine nucleotide exchange factor perform crucial steps in signaling by the sevenless protein tyrosine kinase. Cell, 67, 701-716.

Wang, S., Sengal,C., Emerson, M.M., and Cepko, C.L. (2014). A gene regulatory network controls the binary fate decision of rod and bipolar cells in the vertebrate retina. *Dev. Cell*, *30: 513-527.*

4/23 (Tues) CELL FATE DETERMINANTS, TIMING AND COMPETENCE FOR NEURAL DIFFERENTIATION (KOLODKIN)

Isshiki T, Pearson B, Holbrook S, Doe CQ. (2001). Drosophila neuroblasts sequentially express transcription factors which specify the temporal identity of their neuronal progeny. *Cell*, 106: *511-521*.

Erclik T., Li. ., Courgeon M., et al….Desplan, C. (2017) Integration of temporal and spatial patterning generates neural diversity. *Nature*, 541*:365-370.*

4/30 (Tue) GLIOGENESIS (BERGLES)

Ginhoux F, Greter M, Leboeuf M, Nandi S, See P, Gokhan S, Mehler MF, Conway SJ, Ng LG, Stanley ER, Samokhvalov IM, Merad M. Fate Mapping analysis reveals that adult microglia derive from primitive macrophages. Science. 2010 Nov 5;330(6005):841-5. doi: 10.1126/science.1194637. PMID: 20966214.M.

Kessaris N, Fogarty M, Iannarelli P, Grist M, Wegner M, Richardson WD. Competing waves of oligodendrocytes in the forebrain and postnatal elimination of an embryonic lineage. Nat Neurosci. 2006 Feb;9(2):173-9. doi: 10.1038/nn1620. PMID: 16388308.

5/1 (Wed) 3pm (Special Day/Time) CORTICAL NEURONAL SUBTYPE SPECIFICATION AND MIGRATION (MUELLER)

Arlotta P, Molyneaux BJ, Chen J, Inoue J, Kominami R, Macklis JD. Neuronal subtype-specific genes that control corticospinal motor neuron development in vivo. Neuron 45, 207-221 (2005).

Hansen DV, Lui JH, Parker PR, Kriegstein AR. Neurogenic radial glia in the outer subventricular zone of human neocortex. Nature 464, 554-561 (2010).

Franco, S. J. et al. Fate-restricted neural progenitors in the mammalian cerebral cortex. Science 337, 746–749 (2012).

5/2 (Thurs) NEURAL STEM CELL APPROACHES (POTTER)

Espuny-Camacho, Ira, Kimmo A Michelsen, David Gall, Daniele Linaro, Anja Hasche, Jérôme Bonnefont, Camilia Bali, et al. “Pyramidal Neurons Derived From Human Pluripotent Stem Cells Integrate Efficiently Into Mouse Brain Circuits in Vivo.” Neuron 77, no. 3 (February 6, 2013): 440–456. doi:10.1016/j.neuron.2012.12.011.

Transplanted embryonic neurons integrate into adult neocortical circuits.
Falkner S, Grade S, Dimou L, Conzelmann KK, Bonhoeffer T, Götz M, Hübener M.
Nature. 2016 Nov 10;539(7628):248-253. doi: 10.1038/nature20113. Epub 2016 Oct 26.

5/7 (Tues) NEURAL CREST DIFFERENTIATION (MUELLER)

Garcia-Castro, M., Marcelle, C., and Bronner-Fraser, M. (2002). Ectodermal Wnt function as a neural crest inducer. Science, 297, 848-851.

Hong, C., Park, B., and Saint-Jeannet, J. (2008). Fgf8a induces neural crest indirectly through the activation of Wnt8 in the paraxial mesoderm. Development, 135, 3903-3910.

Steventon, B., Araya, C., Linker, C., Kuriyama, S., and Mayor, R. (2009). Differential requirements of BMP and Wnt signalling during gastrulation and neurulation define two steps in neural crest induction. Development, 136, 771-779.

5/9 (Thur) SENSORY NEURAL DIFFERENTIATION- MECHANISMS OF OLFACTORY RECEPTOR CHOICE (POTTER).

Negative feedback regulation ensures the one receptor-one olfactory neuron rule in mouse.
Serizawa S1, Miyamichi K, Nakatani H, Suzuki M, Saito M, Yoshihara Y, Sakano H.
Science. 2003 Dec 19;302(5653):2088-94. Epub 2003 Oct 30.

An epigenetic trap stabilizes singular olfactory receptor expression.
Lyons DB, Allen WE, Goh T, Tsai L, Barnea G, Lomvardas S.
Cell. 2013 Jul 18;154(2):325-36. doi: 10.1016/j.cell.2013.06.039.

Co-Opting the Unfolded Protein Response to Elicit Olfactory Receptor Feedback
Ryan P. Dalton, David B. Lyons, and Stavros Lomvardas
Cell. 2013 Oct 10;155(2):321-32. http://dx.doi.org/10.1016/j.cell.2013.09.033

5/14 (Tues) NEUROVASCULAR DEVELOPMENT AND THE BBB (NATHANS)

Stewart PA, Wiley MJ.
Developing nervous tissue induces formation of blood-brain barrier characteristics in invading endothelial cells: a study using quail--chick transplantation chimeras. Dev Biol. 1981 May;84(1):183-92.

Risau W, Hallmann R, Albrecht U, Henke-Fahle S.
Brain induces the expression of an early cell surface marker for blood-brain barrier-specific endothelium. EMBO J. 1986 Dec 1;5(12):3179-83.

Stenman JM, Rajagopal J, Carroll TJ, Ishibashi M, McMahon J, McMahon AP.
Canonical Wnt signaling regulates organ-specific assembly and differentiation of CNS vasculature. Science. 2008 Nov 21;322(5905):1247-50. doi: 10.1126/science.1164594.

Zhou Y, Nathans J.
Gpr124 controls CNS angiogenesis and blood-brain barrier integrity by promoting ligand-specific

canonical wnt signaling. Dev Cell. 2014 Oct 27;31(2):248-56. doi: 10.1016/j.devcel.2014.08.018. Epub 2014 Oct 16.

5/21 (Thurs) WRITING ASSIGNMENT DUE