THE CELLULAR AND MOLECULAR BASIS OF NEURAL DEVELOPMENT II: REGULATION OF NEURAL CONNECTIVITY

Department of Neuroscience Elective Course (ME:440.705)

Spring, 2018 (March 20→May 17)

Tuesdays and Thursdays, 2:30 pm-4.00 pm, Rm. 1022 PCTB

Course Directors: Alex Kolodkin, Chris Potter and Shan Sockanathan

PARTICIPATING FACULTY: Solange Brown (WBSB 906; 7-0522); **Shu-Ling Chiu**; **Loyal Goff** (MRB449, 7-0251), Rebecca James (PCTB 1000, 4-9497); **Alex Kolodkin** (1001 PCTB; 4-9499); **Chris Potter** (Rangos 434; 7-4151); Ron Schnaar (WBSB 324; 5-8392); **Shan Sockanathan** (1004 PCTB; 2-3084**); Charlotte Sumner** (Rangos 248; 2-6085); **FengQuan Zhou (Ross 215; 7-5649)**

This is a seminar and reading course devoted to the discussion of the cellular and molecular processes underlying neuronal development. Topics and dates covered include Axon guidance; Growth cone motility and steering mechanisms; Target Matching; Guidance at the CNS Midline; Synaptic differentiation in the NMJ; Activity-dependent plasticity in the PNS and CNS; Regulation of process self-avoidance, tiling and mosaic spacing; Pruning; Developmental diseases; Glial influences on connectivity; Sexual dimorphism in neural circuits; Viral tracing and single neuron RNAseq; Neural Regeneration.

This course is designed to complement The Cellular and Molecular Basis of Neural Development I: Neuronal Differentiation, which is offered in alternate years (next offering, Spring 2019). Students must have either completed Introduction to Neuroscience and Cognition I or have received the consent of the course directors prior to registering for this course.

The course will meet on **Tuesdays and Thursdays from 2:30–4:00pm in PCTB 1022**. The **first class** will meet **Tuesday, March 20**, and the **last class** will be held **Thursday, May 10**. A **writing assignment** will be due on **Thursday, May 17.** THE FIRST CLASS (**3/20**) WILL COVER MATERIAL LISTED BELOW—STUDENTS ARE EXPECTED TO HAVE READ THE PAPERS FOR THIS CLASS AND TO BE PREPARED TO DISCUSS THE MATERIAL COVERED IN THESE STUDIES.

READING ASSIGNMENTS: Reading assignments will consist of primary research articles. Students should be prepared to discuss these articles in depth during class. There will be one writing assignment, due at the end of the course, which is a short proposal on a topic related to one covered in the course.

GRADING: Evaluation of performance in this class will be based on the following criteria: class participation, knowledge of reading assignments, and a short written proposal. The proposal should be ~5 double-spaced pages. It should contain a brief Background section that introduces the area of interest, a central Specific Aim and the rationale for this aim, and an Experimental Procedures section that outlines the strategy for addressing the Specific Aim and considers the possible outcomes and implications of your experiment(s). Please consult one faculty member about your proposal before you start. The proposal is due May 21. **Since class participation is an integral portion of this course, we require attendance at ALL sessions—a Mini-review is required covering subjects discussed in your absence.**

SCHEDULE:

MARCH 20 AXON GUIDANCE (AK)

Bastiani, M.J., du Lac, S. and Goodman, C.S. (1986). Guidance of neuronal growth cones in the grasshopper embryo I. Recognition of a specific axonal pathway by the pCC neuron. *J. Neurosci.* 6: 3518-3531.

McConnell, SK, et al. (1989). Subplate neurons pioneer the first axon pathway from the cerebral cortex. *Science* 245: 978-982.

Kitsukawa, T., et al. (1997). Neuropilin-Semaphorin III/D-mediated chemorepulsive signals play a crucial role in peripheral nerve projection in mice. *Neuron* 19: 995-1005.

MARCH 22 GUIDANCE AT THE CNS MIDLINE (AK)

Serafini, T., Kennedy T.E., Galko M.J., Mirzayan, C., Jessell, T.M., and Tessier-Lavigne, M. The netrins define a family of axon outgrowth-promoting proteins homologous to C. elegans UNC-6. *Cell*, 78:409-24.

Dominici, C. et al….Chédotal (2017). Floor-plate netrin-1 is dispensable for commissural axon guidance. *Nature*, 545: 350-354

Lyuksyutova, A.I., et al….Zou (2003). Anterior-posterior guidance of commissural axons by Wnt-frizzled signaling. Science 302: 1984-1988.

MARCH 27 GROWTH CONE MOTILITY AND STEERING MECHANISMS (FQ)

Schaefer AW, Schoonderwoert VT, Ji L, Mederios N, Danuser G, Forscher P. Coordination of actin filament and microtubule dynamics during neurite outgrowth. Dev Cell. 2008 Jul;15(1):146-62.

Preitner N, Quan J, Nowakowski DW, Hancock ML, Shi J, Tcherkezian J, Young-Pearse TL, Flanagan JG. APC is an RNA-binding protein, and its interactome provides a link to neural development and microtubule assembly. Cell. 2014 Jul 17;158(2):368-82.

MARCH 29 TARGET MATCHING-OLFACTORY SYSTEM (CP)

Hong, W., Mosca, T.J., and Luo, L. (2012). Teneurins instruct synaptic partner matching in an olfactory map. Nature *484*, 201–207.

Ward A, Hong W, Favaloro V, Luo L. (2015) Toll receptors instruct axon and dendrite targeting and participate in synaptic partner matching in a Drosophila olfactory circuit. *Neuron* 85(5):1013-28.

APRIL 3 TOPOGRAPHIC MAPPING CP

Takeuchi, H, Inokuchi, K, Aoki, M, Suto, F, Tsuboi, A Matsuda, I, Suzuki, M, Aiba, A, Serizawa, S, Yoshihara, Y, Fujisawa, H, and Sakano, H (2010). Sequential Arrival and Graded Secretion of Sema3F by Olfactory Neuron Axons Specify Map Topography at the Bulb. *Cell* 141(6): 1056–67.

Assens, A, Dal Col JA, Njoku, N, Dietschi, Q, Kan, C, Feinstein, P, Carleton, A, and Rodriguez, I. (2016) Alteration of Nrp1 signaling at different stages of olfactory neuron maturation promotes glomerular shifts along distinct axes in the olfactory bulb. Development *143*, 3817-3825.

APRIL 5 SYNAPTOGENESIS I: SYNAPTIC DIFFERENTIATION IN THE NMJ (SS)
Lin W, Burgess RW, Dominguez B, Pfaff SL, Sanes JR, Lee KF. Distinct roles of nerve and muscle in postsynaptic differentiation of the neuromuscular synapse. Nature. 2001 Apr 26;410(6832):1057-64.

Korkut C, Ataman B, Ramachandran P, Ashley J, Barria R, Gherbesi N, Budnik V. Trans-synaptic transmission of vesicular Wnt signals through Evi/Wntless. Cell.2009 Oct 16;139(2):393-404.

APRIL 10 SYNAPTOGENESIS II: CNS SYNAPTIC DIFFERENTIATION (SC)
Grutzendler, J., Kasthuri, N., and Gan, W.B. (2002). Long-term dendritic spine stability in the adult cortex. *Nature* 420**,** 812-816. doi: 10.1038/nature01276.

Traunmüller, L., Gomez, A.M., Nguyen, T.M., and Scheiffele, P. (2016). Control of neuronal synapse specification by a highly dedicated alternative splicing program. Science 352(6288): 982-6

APRIL 12 ACTIVITY-DEPENDENT PLASTICITY IN SENSORY SYSTEMS (CP)
Nakashima, A., Takeuchi, H., Imai, T., Saito, H., Kiyonari, H., Abe, T., Chen, M., Weinstein, L.S., Yu, C.R., Storm, D.R, Nishizumi, H. and Sakano, H. (2013). Agonist-Independent GPCR Activity Regulates Anterior-Posterior Targeting of Olfactory Sensory Neurons. Cell *154*, 1314–1325.

Sachse, S., Rueckert, E., Keller, A., Okada, R., Tanaka, N.K., Ito, K., and Vosshall, L.B. (2007). Activity-dependent plasticity in an olfactory circuit. Neuron *56*, 838–850.

April 17 Activity-dependent plasticity in the developing cortex (SB)
Wiesel and Hubel (1963) Single-cell responses in striate cortex of kittens deprived of vision in one eye. Journal of Neurophysiology 26:1003

Katz and Shatz (1996). Synaptic activity and the construction of cortical circuits. Science. 274: 1133

Ackman, Burbridge and Crair (2012) Retinal waves coordinate patterned activity throughout the developing visual system. Nature. 490: 219

April 19 Formation of retinal circuitry (RJ)
Matthews, B.J., Kim, M.E., Flanagan, J.J., Hattori, D., Clemens, J.C., Zipursky, S.L., and Grueber, W.B. (2007). Dendrite self-avoidance is controlled by Dscam. Cell *129*, 593–604.

Lefebvre, J.L., Kostadinov, D., Chen, W.V., Maniatis, T., and Sanes, J.R. (2012). Protocadherins mediate dendritic self-avoidance in the mammalian nervous system. Nature *488*, 517–521.

Suggested Review (not required reading, but very helpful and may be referred to during class): Li, Z., and Sheng, M. (2003). Some assembly required: the development of neuronal synapses. *Nat Rev Mol Cell Biol* 4, 833-841.

APRIL 24 PRUNING: A MECHANISM TO REFINE CIRCUIT FORMATION (AK)

Watts RJ, Hoopfer ED, Luo L. (2003) Axon pruning during Drosophila metamorphosis: evidence for local degeneration and requirement of the ubiquitin-proteasome system. Neuron. 38: 871-85.

Uesaka et al. …M. Kano (2014). Retrograde simaphorin signaling regulates synapse eleimination in the developing mouse brain. Science 344: 1020-1023.

APRIL 26 GLIAL INFLUENCES ON CONNECTIVITY (SS)
Allen NJ, Bennett ML, Foo LC, Wang GX, Chakraborty C, Smith SJ, Barres BA. Astrocyte glypicans 4 and 6 promote formation of excitatory synapses via GluA1 AMPA receptors. Nature. 2012 May 27;486(7403):410-4.

Chung WS, Clarke LE, Wang GX, Stafford BK, Sher A, Chakraborty C, Joung J, Foo LC, Thompson A, Chen C, Smith SJ, Barres BA. Astrocytes mediate synapse elimination through MEGF10 and MERTK pathways. 2013. Nature, 504: 394-400.

MAY 1 NEURAL DEVELOPMENTAL DISEASES (CS)
Tang G, Gudsnuk K, Kuo SH, et al… Sulzer D. (2014). Loss of mTOR-dependent macroautophagy causes autistic-like synaptic pruning deficits. *Cell*, 83:1131-1143.

Fletcher, EV, Simon CM, Pagiazitis, JG et al….Mentis, G.Z. (2017). Reduced sensory synaptic excitation impairs motor neuron function via Kv2.1 in spinal muscular atrophy. *Nature Neurosci*., 20:905-916.

MAY 3 SEXUAL DIMORPHISM IN NEURAL CIRCUITS (SS)
Liu Y, Rutlin M, Huang S, Barrick CA, Wang F, Jones KR, Tessarollo L, Ginty DD. Sexually dimorphic BDNF signaling directs sensory innervation of the mammary gland. Science. 2012 Dec 7;338(6112):1357-60.

Scott N, Prigge M, Yizhar O, Kimchi T.
A sexually dimorphic hypothalamic circuit controls maternal care and oxytocin secretion. Nature. 2015 Sep 24;525(7570):519-22.

MAY 8 NEW APPROACHES TO ADDRESS CONNECTIVITY IN DEVELOPMENT AND DISEASE: VIRAL TRACING AND SINGLE NEURON RNASEQ (LG)
Chevée, M., Robertson, J. D. J., Cannon, G. H., Brown, S. P. & Goff, L. A. Variation in Activity State, Axonal Projection, and Position Define the Transcriptional Identity of Individual Neocortical Projection Neurons. *Cell Rep.* **22,** 441–455 (2018).

Kebschull, J. M. *et al.* High-Throughput Mapping of Single-Neuron Projections by Sequencing of Barcoded RNA. *Neuron* **91,**975–987 (2016).

May 10 Neural Regeneration (RS)
Modulation of the proteoglycan receptor PTPσ promotes recovery after spinal cord injury. (2015) Lang BT, Cregg JM, DePaul MA, Tran AP, Xu K, Dyck SM, Madalena KM, Brown BP, Weng YL, Li S, Karimi-Abdolrezaee S, Busch SA, Shen Y, Silver J. *Nature.* 518:404-8.

May 17 Proposal Due