MMG 1301H (0.25 FCE): Developmental Neurobiology August 2023

Course Instructors:

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Course Time and Dates: Fall, Mondays 3-5pm

1 Organizational meeting on Monday 3-4pm; September 18th.
6 Classes: Monday Oct 9th to Monday Nov 20th
No class week of Nov. 13th [due to Society for Neuroscience meeting].

Course Location: In-person – Multimedia Room – 3rd floor; PGCRL, SickKids Research Institute (no visitor badges are required for the 3rd floor).

Total Student Contact Hours (0.25 FCE): 13 hrs

Prerequisite: Student must be in YR 2 or higher of their graduate study.

Course Description and Format:

- This course will focus on selected topics in Developmental Neurobiology and Mechanisms of Nervous System Disorders. Through discussion of research articles, we will explore molecular and cellular mechanisms that guide nervous system development. We will also read about exciting new concepts that link disruptions to neural wiring to the etiology of neurodevelopmental and psychiatric diseases, and that harness neurodevelopmental processes for new therapeutic strategies.
- The first class will be an organizational meeting (virtual), and then followed by 6 classes (in-person). Each discussion class will comprise a short introduction followed by presentation of selected research papers by two students. Other students in the class will be responsible for reading the papers and for participating in the discussion.
- Each student will present a short introduction on the topic, 1 or 2 research papers, and a final assignment.

Course Objectives and Learning Outcomes:

- Through group discussions of research articles, we will evaluate current topics in developmental neurobiology. We will also examine the importance of developmental mechanisms in brain disorders, such as autism spectrum disorder, anxiety and bipolar disorder. We will probe how developmental mechanisms advances our understanding of brain disease and inform future therapeutic strategies.

- Learn about fundamental principles of nervous system development, spanning steps such as neurogenesis and generation of diverse cell types; neuronal wiring and synapse formations; synaptic pruning by microglia; and circuit formation.
- Explore the following emerging concepts in the neurodevelopmental origins of brain disorders and therapeutic strategies. For example:
    - We will examine Autism Spectrum Disorder (ASD) within the context of neurodevelopmental molecular hubs and also explore possible contributions from unpredicted neuronal circuitry and maternal inflammation.
    - We will discuss the developmental windows critical for anxiety disorder susceptibility and the harnessing of neuronal plasticity to provide resilience to and treatment for depression.
    - We will consider the unique cell biological features of neurons implicated in bipolar disorder.
- Gain exposure to diverse model systems (animal and human cellular models) and state-of-the-art experimental techniques that are being used to profile and interrogate CNS development and disorders.
- Develop skills to interpret and critically evaluate experimental data.

Delivery of the course: Weekly group discussions, in-person.

Method of Evaluation:
Students will be assessed on their paper presentation as well as on their participation in the discussion of the other papers. In addition, students will identify an important/timely topic in Developmental Neuroscience for a final written assignment.

- 30% paper presentation
- 15% Background presentation
- 30% class participation, including questions and comments on paper, suggestions for next experiments.
- 25% Written assignment: **TBD**, depending on class size. [Examples from previous years: 'Letter of Intent' for a 'New Idea' research grant proposal to a Disease Foundation; or 'News and Views' on a recent research paper that weighs in on current controversies in neurobiology (ie. neurogenesis in the adult human brain; glia-to-neuron reprogramming)].

Background presentation: Each student will give a short presentation on background information, key concepts and outstanding questions related to the topic. The instructors will give guidance and examples of classic papers and reviews that provide foundational knowledge.

Research paper presentation and chairing the discussion: Each student will select a research paper and lead the discussion. The student will prepare powerpoint slides for the introduction and data figures. Using the 'chairing' format used for the previous MMG1002/1003H Colloquium, the student will engage the group to interpret and critically evaluate the article.
Examples of questions to stimulate discussion?

1) What does this figure show? How does this technique work? What are caveats and limitations? Do the data support the conclusions presented?

2) Are there sufficient data to support the generalized statements made by the authors?
3) What experiment produces the authors' most convincing data? What experiment is the least convincing or weakest? Why?
4) What hypothesis derived from this paper would you set out to test next, and how?

Policies for attendance and withdrawing from the course

Class attendance is mandatory. Since a large part of the final mark is based upon class participation, missing classes will lead to grade deductions. Students must notify the instructor(s) with a valid reason for absence before class and provide medical documentation, if appropriate. Students who miss 16.6% of contact hours (e.g., more than 1 of 6 module sessions for an 0.25 FCE) will not got credit for course (e.g. assigned a failing grade - FZ). We will accommodate students presenting with COVID or other symptoms to join virtually.

The Topics and Readings for the Fall 2023 will be finalized shortly. *Students will select a topic and research article at the organizational meeting. The topics for Fall 2023 will address key neurodevelopmental processes and the importance of neurodevelopment in the disorders of mood and mind* ***outlined above.***

This is an example from Fall 2021 (but topics and research papers will change for 2023).

Class organizational meeting (1 hr): Discuss syllabus, expectations, and assign readings.
Week 1: Neuronal fate specification and neuronal diversification
Week 2: Patterning connections: Axon guidance and dendrite patterning
Week 3: Synaptogenesis and synapse refinement by neural activity.
Week 4: The role of glia in synapse development and circuit formation.
Week 5: Visual circuit formation; and emergence of network activity in the zebrafish and mouse visual systems.
Week 6: Studying Human neural development and developmental origins of brain disorders.

Week 1: Neuronal diversification: temporal fate specification and generation of neural cell types in the cortex.

Paper #1: Neuronal fate specification: When & Where are neurons born?

Temporal plasticity of apical progenitors in the developing mouse neocortex. Oberst, Fièvre S, Baumann N, Concetti C, Bartolini G, Jabaudon D. Nature. 2019 Sep;573(7774):370-374. PMID 31462778.

Paper #2: Neuronal Diversification. What can we learn from scRNA-Seq and scATAC-Seq?

Genetic and epigenetic coordination of cortical interneuron development

Allaway KC, Gabitto MI, Wapinski O, Saldi G, Wang C-Y, Bandler RC, Wu SJ, Bonneau R, & Fishell G. Nature volume 597, pages 693–697 (2021). PMID: 34552240

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