MMG 1301H (0.25 FCE): Developmental Neurobiology July 2025

Course Instructors:

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

1 Organizational meeting: Oct 21st 2025;
6 classes:

Oct 14	Orientation
Oct 21	Week 1 paper discussions
Oct 28	**no class**
Nov 4	Week 2 paper discussions
Nov 11	Week 3 paper discussions
Nov 18	**no class [due to SfN].**
Nov 25	Week 4 paper discussions
Dec 2	Week 5 paper discussions
Dec 9	Week 6 paper or final assignment presentation [tentative]
Dec 16	final assignment due [tentative]

Course Location: In-person: LTRI room 1062
Lunenfeld-Tanenbaum Research Institute, 600 University Ave, Toronto, ON M5G 1X5, or 66 Murray St.

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, 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, including fundamental and disorder-related concepts*. We will also examine the importance of developmental mechanisms in brain disorders. We will probe how developmental mechanisms advances our understanding of brain disorders, such as rare diseases and autism spectrum disorders, 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 formation; 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.
- *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: Peer review assignment. Students will select a preprint from Biorxiv, and write a peer review, including summary of the advance made in this paper and its potential significance to the field, major weaknesses and suggestions to the authors, and minor comments.

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 MMG1003H 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?

Final assignment: Peer review assignment. Students will select a preprint from Biorxiv, and write a peer review. We will provide guidelines and a framework for the review: ie. summary of the advance made in this paper and its potential significance to the field, major weaknesses and suggestions to the authors, and minor comments.

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 2025 will be finalized shortly after class size is determined.
Students will select a topic and research article at the organizational meeting.

This is an example from Fall 2023 (but topics and research papers will change for 2025).

Class organizational meeting (1 hr): Discuss syllabus, expectations, and assign readings.
Week 1: Neurogenesis and neuronal diversification
Week 2: Patterning connections: Axon guidance and dendrite patterning
Week 3: The cell biology of bipolar disorder: Ankyrin G (Ank3).
Week 4: Activity-dependent synapse refinement, and the involvement of glia.
Week 5: Maternal immune activation and autism spectrum disorders.
Week 6: Studying Human neural development and developmental origins of brain disorders.

Week 1: Neurogenesis

Background: Cortical neurogenesis and neural diversification; adult neurogenesis.
Paper #1: Vitali et al. *Progenitor Hyperpolarization Regulates the Sequential Generation of Neuronal Subtypes in the Developing Neocortex*. Cell. 2018 Aug 23;174(5):1264-1276.e15. doi: 10.1016/j.cell.2018.06.036. PMID: 30057116..
Paper #2: Adult neurogenesis and brain disorders
The paper that started it all: Santarelli et al., Requirement of Hippocampal Neurogenesis for the behavioral effects of Antidepressants. Science. 2003, Vol.301 (5634), p.805-809.

DOI: 10.1126/science.10833284

Week 2: Patterning connections and hard-wiring neural circuits
Background: Molecular and cellular mechanisms that guide neuronal migration, axon and dendrite patterning, and synaptic specificity (ie. attraction, repulsion, adhesion.
Paper #1. Duan X, et al. *Type II cadherins guide assembly of a direction-selective retinal circuit.* Cell. 2014 Aug 14;158(4):793-807. PMID:25126785. DOI: 10.1016/j.cell.2014.06.047

Week 3: The cell biology of bipolar disorder: Ankyrin G (Ank3)
Background: Synapse diversity and their subcellular, molecular and functional features; mechanisms of synaptic transmission, maintenance; Ank3; links between genes encoding synaptic genes and brain disorders; neurobiology of bipolar disorder.
Paper: AD Nelson et al. *Ankyrin-G regulates forebrain connectivity and network synchronization via interaction with GABARAP.* Molecular Psychiatry. 2020 Nov;25(11):2800-2817. PMID: 30504823 PMCID: PMC6542726 DOI: 10.1038/s41380-018-0308

Week 4: Activity-dependent plasticity and synapse refinement, and the involvement of glia.
Background: Sensory mediated refinement of the visual and somatosensory systems; 'critical periods' in brain development; synaptic pruning; microglia and glial interactions controlling synapse formation and elimination.
Paper: Sensory lesioning induces microglial synapse elimination via ADAM10 and fractalkine signaling. Gunner G et al. Nat Neurosci. 2019 Jul;22(7):1075-1088. PMID 31209379.

Week 5: Maternal immune activation and autism spectrum disorders.
Paper: Yeong Shin Yim et al. *Reversing behavioural abnormalities in mice exposed to maternal inflammation.* Nature. 2017 Sep 28;549(7673):482-487. doi:10.1038/nature23909. (PMID: 28902835)

Week 6: Human neural development and cell models to study rare disorders.