Neurobiology of Developmental Brain Disorders

Department of Human Genetics, HG 480/580

Meeting Time and Location: Winter Semester, Tu/Th, 1-2:30 via ZOOM

Course Director: Stephanie Bielas - sbielas@umich.edu/(734) 647-8890

Participating Faculty: Shigeki Iwase - siwase@umich.edu/(734) 647-8832 and Kenneth Kwan – kykwan@umich.edu/(734) 615-2444

Course Description:

This seminar and discussion course is focused on cellular and molecular aspects of mammalian developmental neurobiology. Genetic and epigenetic principles underlying the emergence and maintenance of the mammalian nervous system will be explored in the context of human disorders that lead to structural brain abnormalities, intellectual disability and autism. The intent of this course is to present current topics in developmental neuroscience in the context of human genetics and mammalian models of brain development.

Undergraduate Prerequisites:

BIO225 and BIO305

Online office hours:

Any organizational/administrative or course content questions can be raised during online office hours. I will be available in the Canvas Chat Room Monday and Wednesday afternoons from 3-5 PM.

Grading:

Your grade will be based on a possible total of 500 points.

In-Class Quizzes (200 points): 40% of your grade will be based on performance on quizzes, which will occur first thing prior to presentations. These quizzes will assess your in-depth understanding of material from the previous days’ lectures, and the reading(s) assigned for that week’s discussion. Quizzes will be open-book (paper) - i.e., you will be able to refer to the previous day’s lecture notes and the assigned paper in framing your response to quiz questions. Your 12 highest quiz scores of 15 quizzes total will count toward the final total of 200 points. If you miss a quiz for any reason (medical, family, personal), there will be no make-up assignment; that quiz grade will be one of three dropped from your total.

\* 15 minutes of class time will be allotted for you to complete the quiz.

Participation (100 points): 20% of your grade will be based on your contribution to in-class discussion of assigned readings and in-class responses to questions posted on Canvas during lectures. Preparing for discussion will improve your grades on in-class quizzes, and active participation will make subsequent discussion more interesting and productive. You should come to discussion sections ready to discuss how experiments in the papers were carried out, how the authors interpreted their data, and how their findings fit with prior hypotheses. You will be expected to raise technical and conceptual questions about the authors’ research strategy, and to propose alternative strategies, critical next experiments, or alternate interpretations of data. During lectures, questions will be posted on Canvas. Your responses to these questions will count towards your participation grade.

Presentations/Student-led discussions (200 points): 40% of your grade will be based on one short 25 minute presentations on an assigned scientific papers. There will be two presentations by teams of two students per class. Successful presentations will address the following criteria:

- Summarize what is currently known about the problem (5 points).

- Explain why addressing the issues presented in the scientific papers are important and of general interest to neuroscience (6 points).

- State the hypothesis when a hypothesis is being tested, or the major goal of the work if the paper is discovery-based (5 points).

- Describe the experiments being used to address the scientific issues (20 points).

- Explain the strengths and weaknesses of experimental strategy being used to address their research question (10 points).

- Describe the potential outcomes of their experiments (predicted and not predicted) and how they interpret the data (10 points).

- Explain any caveats, describe alternative strategies, and subsequent future directions (6 points).

- Adhere to the time limit (5 points).

Class Schedule:

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| Date: | Lecture or discussion topic: | Required reading: |
|  | Instructor: Stephanie Bielas |  |
| Tu 19 Jan | Introduction to the course, roles human genetics and mouse models have played in informing us about mammalian neurodevelopment (Lecture 1). Stephanie Bielas |  |
| Tu 19 Jan | General Principles of CNS development and neurogenesis (Lecture 2) |  |
| Th 21 Jan | Genetics that informed cortical neuron migration (Lecture 3) |  |
| Tu 26 Jan | Quiz 1; Discussion of:  Evolution of mammalian neurogenesis | Hansen et al. 2010 Nature & Qian et al. 2016 Cell |
| Th 28 Jan | Quiz 2; Discussion of:  Modeling human brain size | Li et al. 2017 Cell Stem Cell; Li et al. 2016 AJHG |
| Tu 2 Feb | Quiz 3; Discussion of:  Cortical neuron migration | Poirier et al. 2013 Nature Genetics & Koizumi et al. 2006 Nature Neuroscience |
| Th 4 Feb | Epigenomic regulation of brain development (Lecture 4) |  |
| Tu 9 Feb | Quiz 4; Discussion of: Epigenomic mechanisms of brain development | Yang et al. 2012 Cell & Nitarska et al. 2016 Cell Reports |
| Th 11 Feb | Cilia in brain development (Lecture 5) |  |
| Tu 16 Feb | Quiz 5; Discussion of: Cilia in brain development | Cantegral et al. 2008 AJHG & Higginbotham et al. 2013 Nature Neuroscience |
| Th 18 Feb | Instructor: Shigeki Iwase |  |
|  | Introduction of intellectual disability; cellular and molecular basis (Lecture 6) |  |
| Tu 23 Feb | Quiz 6; Discussion:  Chromatin regulations in neurons | Stroud H, et al. 2017 Cell & Farrelly, et al.  2019 Nature. |
| Th 25 Feb | Introduction of epigenetics and synaptic plasticity (Lecture 7) Shigeki Iwase |  |
| Tu 2 Mar | Quiz 7; Discussion:  Roles of histone methyl transferases in neuronal plasticity, learning and memory. | Benevento M et al. 2016 Neuron & Jakovcevski M et al. 2016  Journal of Neuroscience |
| Th 4 Mar | Quiz 8; Discussion:  Kabuki syndrome: genetics, animal models, and molecular mechanisms. | Laarhoven PM, et al. 2015 Hum. Mol. Gen. & Fasciani,A, et al. 2020 Nature Genetics |
| Tu 9 Mar | IDs associated with defective "writing" or "erasing" of epigenetic marks (Lecture 8) |  |
| Th 11 Mar | Quiz 9; Discussion:  Transcriptional enhancers in neuronal activity-dependent transcription.  - Genomic imprinting disorders. | Joo JY et al. 2016 Nature Neuroscience &  Trezza, RA et al. 2019, Nature Neuroscience |
| Tu 16 Mar | IDs associated with defective "reading" of epigenetic marks. (Lecture 9) |  |
| Th 18 Mar | Quiz 10; Discussion:  Towards amelioration of intellectual disability. | Benjamin JS. 2017 PNAS. & Sinnamon JR et al. 2017. PNAS |
| Tu 23 Mar | Well-Being Break – No class |  |
| Th 25 Mar | Instructor: Kenneth Kwan |  |
|  | An introduction to autism spectrum disorders (Lecture 10) |  |
| Tu 30 Mar | Quiz 11; Discussion of:  Cellular and molecular pathologies of ASD. | Stoner et al. 2014 Nature & Voineagu et al. 2011 Nature |
| Th 1 Apr | The genetics of autism (Lecture 11) |  |
| Tu 6 Apr | Quiz 12; Discussion of:  Insights into ASD etiology through human genetics. | Willsey et al. 2013 Cell; Gompers, et al, 2017 Nature Neurosci |
| Th 8 Apr | Syndromic forms of autism (Lecture 12) |  |
| Tu 13 Apr | Quiz 13; Discussion of:  Animal models of ASD. | Jung et al. 2017 Nature Neurosci; Dong et al. 2019 Neuron |
| Th 15 Apr | Towards targeted treatment in ASD (Lecture 13) |  |
| Tu 20 Apr | Quiz 14; Discussion of:  Insights into ASD etiology through ASD-related syndromes. | Darnell et al. 2011 Cell; Osterweil et al. 2013 Neuron |