NRSC 4413
Cellular Structure and Neurological Disorders

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Office Hours: Thursdays 10am-12pm and by appointment
Class Location: Cohen 337
Class Meeting Time: Tuesdays/Thursday 8:30am – 10:00am

Course Description:

Microtubules are dynamic cytoskeletal filaments that are crucial to the structure and function of neurons. From providing the scaffolding for the unique architecture of neurons, to guiding intracellular trafficking, to supporting neuronal migration and connectivity, microtubules are important for a variety of neuronal roles. Consequentially, the dysfunction of microtubules and microtubule-associated-proteins is associated with a number of nervous system disorders. This seminar will explore the role of microtubules in a number of neurobiological diseases and disorders including Neurodevelopmental disorders (ex. Fragile X, Lissencephaly), Neurodegenerative Disorders (ex. Alzheimer's and the Tauopathies, Hereditary Spastic Paraplegia), Psychiatric Disorders (Ex. Schizophrenia and Mood disorders), and also in Traumatic Brain Injury. We will use readings from the primary literature as a basis for lectures, student presentations, and papers.

Learning Objectives:

By the end of this course, students will:

- Understand how microtubules contribute to the overall function of the brain as well as to disorders of the nervous system
- Build their skills in reading, evaluating, critiquing, and discussing primary research articles from leading academic journals
- Hone their ability to present scholarly scientific research
- Learn how to independently identify notable scientific papers in the field and write about them in a real-world genre

Canvas: canvas.upenn.edu

Lecture slides, course materials, and announcements will be posted on this site.

Grading:

Your final grade in this class will be determined as follows:

Attendance and Participation: 25%
Student Presentations: 30%
Reading Pre-Questions: 20%
News and Views Article: 25%

Attendance and Participation Policy:

25% of your grade will come from Attendance and Participation. Attendance is required for this course. It is a small-discussion based class, so it is important to be present to participate in these discussions. Additionally, you are expected to be on time for the course. Repeated lateness will count as an absence for the course. Additionally, you will be expected to be an engaged participant in the class discussions. I will be looking for questions and comments that show that you have read the papers with a critical eye.

Class Structure:

There will be readings assigned for each class period. These readings will come from the scholarly literature and should be read before the class starts so that you are able to participate in discussions about the articles during class. During the first two weeks of class, class will consist of a lecture component along with discussions about the assigned readings for that class period. An instructor lecture and discussion will also occur periodically throughout the semester at the start of each new topic unit. Starting on the third week of class, most classes will consist of student presentations and discussion. For each of these classes, two students will give a presentation on the journal article that was assigned for that day. One student will present on the first half of the paper, and another student will present on the second half of the paper (see more details below). There will be a discussion portion following each presentation (see additional details below).

Student Presentations:

Beginning on the third week of the semester, students will give presentations on an assigned journal article related to the class topic. On each day, two different students will present. One student will present the first half of the paper (Background and Introduction, First half of Figures) and the other student will present the second half of the paper (Second half of Figures, Discussion and Future Directions). These students will be graded independently of one another for their presentations. Each student will give a total of two presentations throughout the course of the semester (one on the first half of a paper, one on the second half of a different paper).

Presentations should include: background information to contextualize the paper, results of the paper – including a discussion of specific figures from the paper – and a discussion about the implications of the paper. Following the presentations, students in the audience will be encouraged to ask questions about the paper, and the presenters should be prepared to field these questions lead a discussion about the paper that they just presented.

Each student's presentation should last 20-25 minutes, for a total of 40-50 minutes across both students. It should in a "Powerpoint presentation" style and uploaded to Canvas.

Students will be asked to meet with a CWIC advisor at least 48 hours before their presentations in order to get feedback on their presentations.

Readings and Pre-Questions

Each class, readings of the scholarly literature will be assigned that correspond to the upcoming class's topic. These readings should be read before you come to class. As a way of promoting discussion and scientific inquiry (and making sure that you do the reading!), you will be required to write down one discussion question, curiosity question, or "I'm confused about ____" question about the paper that you were assigned to read. This question must be submitted in advance of the start of class on the day that it is due. I am looking for specificity

and critical thought in these questions. These pre-questions will be submitted on Canvas. If you are presenting that day, you do NOT need to submit a discussion question about the paper that you are presenting.

News and Views Article

For the "News and Views" assignment, you will write a short article in the format of the journal *Nature's* "News and Views" section. These articles inform non-specialist readers about new scientific advances that have been reported in a recently published paper. For this exercise, the paper that you chose does *not* have to be JUST newly published, but *should* be relatively recent (within the past 10 years). The paper that you choose to write about should NOT be one of the papers that you have otherwise been assigned to read for this class. Instead, you should pick a paper of your own that interests you but relates to microtubules and neurobiological disorders.

The goal of a "News and Views" article is to introduce a significant new finding/paper to scientific community. As a result, these papers must convey the relevance and novelty of the paper, and its impact on the field. Additionally, these papers are written in a more casual journalistic tone that is appropriate for a non-specialist audience. Therefore, you should avoid specialized technical jargon. the News and Views articles are short – aim for 800-1,000 words. You will be provided with examples of News and Views articles on the Canvas site. Further details about the assignment will be posted to the Canvas site.

Academic Integrity:

Penn has strict rules on academic integrity (see www.upenn.edu/academicintegrity). Any violation of the rules will be reported to the Office of Student Conduct and will likely result in automatic failure of the course.

Course Absence Notice:

The Course Absence Notice (CAN) has been designed to provide a consistent way for students to notify course instructors of short-term absences for one or more courses. It also provides a method for advising offices to track absences and coordinate support for students who miss classes. The submission of a CAN does not excuse you from your course obligations; students are still responsible for following up with each instructor directly and adhering to course policies and procedures as outlined in the course syllabus. All students enrolled in a class can submit a CAN during the current term using Path@Penn.

Schedule

See following page

Note: Readings highlighted in Blue are Review articles that are not part of student presentations. To select articles for your presentations, pick articles in Gray or White boxes.

Date	Topics / Presentations	Readings Due	News and Views Assignment
8/29	Course Policies ; Introduction to Microtubules I	X	
8/31	Intro to Microtubules II : MT Dynamics & Post-translational Modifications	Kapitein, L. C., & Hoogenraad, C. C. (2015). Building the neuronal microtubule cytoskeleton. Neuron, 87(3), 492-506.	
9/5	Intro to Microtubules III : MT-Associated Proteins	Conde, C., & Cáceres, A. (2009). Microtubule assembly, organization and dynamics in axons and dendrites. Nature Reviews Neuroscience, 10(5), 319-332.	
9/7	Microtubules in Neurodevelopment: Overview	Lasser, M., Tiber, J., & Lowery, L. A. (2018). The role of the microtubule cytoskeleton in neurodevelopmental disorders. Frontiers in cellular neuroscience, 12, 165.	
9/12	Student Presentations : Neurodevelopment - Lissencephapy	Keays, D. A., Tian, G., Poirier, K., Huang, G. J., Siebold, C., Cleak, J., ... & Flint, J. (2007). Mutations in a-tubulin cause abnormal neuronal migration in mice and lissencephaly in humans. Cell, 128(1), 45-57.	
9/14	Student Presentations : Neurodevelopment	Jaglin, X. H., Poirier, K., Saillour, Y., Buhler, E., Tian, G., Bahi-Buisson, N., ... & Chelly, J. (2009). Mutations in the β-tubulin gene TUBB2B result in asymmetrical polymicrogyria. Nature genetics, 41(6), 746-752.	
9/19	Student Presentations : Neurodevelopment	Tischfield, M. A., Baris, H. N., Wu, C., Rudolph, G., Van Maldergem, L., He, W., ... & Engle, E. C. (2010). Human TUBB3 mutations perturb microtubule dynamics, kinesin interactions, and axon guidance. Cell, 140(1), 74-87.	
9/21	Student Presentations : Neurodevelopment - Microcephaly	Poirier, K., Lebrun, N., Broix, L., Tian, G., Saillour, Y., Boscheron, C., ... & Chelly, J. (2013). Mutations in TUBG1, DYNC1H1, KIF5C and KIF2A cause malformations of cortical development and microcephaly. Nature genetics, 45(6), 639-647.	
9/26	Student Presentations : Neurodevelopment -Down Sydrome and Autism	Ori-McKenney, K. M., McKenney, R. J., Huang, H. H., Li, T., Meltzer, S., Jan, L. Y., ... & Jan, Y. N. (2016). Phosphorylation of β-tubulin by the Down syndrome kinase, minibrain/DYRK1a, regulates microtubule dynamics and dendrite morphogenesis. Neuron, 90(3), 551-563.	
9/28	Student Presentations : Neurodevelopment - Fragile X	Zhang, Y. Q., Bailey, A. M., Matthies, H. J., Renden, R. B., Smith, M. A., Speese, S. D., ... & Broadie, K. (2001). Drosophila fragile X-related gene regulates the MAP1B homolog Futsch to control synaptic structure and function. Cell, 107(5), 591-603.	
10/3	Microtubules in Psychiatric Disease: Overview	Marchisella, F., Coffey, E. T., & Hollos, P. (2016). Microtubule and microtubule associated protein anomalies in psychiatric disease. Cytoskeleton, 73(10), 596-611.	
10/5	Student Presentations: Psyhciatric Disease - Schizophrenia	Kamiya, A., Kubo, K. I., Tomoda, T., Takaki, M., Youn, R., Ozeki, Y., ... & Sawa, A. (2005). A schizophrenia-associated mutation of DISC1 perturbs cerebral cortex development. Nature cell biology, 7(12), 1167-1178.	**News and Views Topic Selection Due**
10/10	Student Presentations: Psychiatric Disease - Schizophrenia	Shelton, M. A., Newman, J. T., Gu, H., Sampson, A. R., Fish, K. N., MacDonald, M. L., ... & Sweet, R. A. (2015). Loss of microtubule-associated protein 2 immunoreactivity linked to dendritic spine loss in schizophrenia. Biological psychiatry, 78(6), 374-385.	
10/12	No Class - Fall break	X	
10/17	Student Presentations: Psychiatric Disease - Schizophrenia	Andrieux, A., Salin, P., Schweitzer, A., Bégou, M., Pachoud, B., Brun, P., ... & Job, D. (2006). Microtubule stabilizer ameliorates synaptic function and behavior in a mouse model for schizophrenia. Biological psychiatry, 60(11), 1224-1230.	
10/19	Student Presentations: Psychiatric Disease - Depression	Wei, Y., Wang, G., Chen, J., Xiao, L., Wu, Z., He, J., & Zhang, N. (2021). Maternal deprivation induces cytoskeletal alterations and depressive-like behavior in adult male rats by regulating the AKT/GSK3β/CRMP2 signaling pathway. Physiology & Behavior, 242, 113625.	
10/24	Student Presentations: Psyhciatric Disease - Depression	Bianchi, M., & Baulieu, E. E. (2012). 3β-Methoxy-pregnenolone (MAP4343) as an innovative therapeutic approach for depressive disorders. Proceedings of the National Academy of Sciences, 109(5), 1713-1718.	
10/26	Microtubules in Neurodegeneration: Overview	Brunden, K. R., Lee, V. M., Smith III, A. B., Trojanowski, J. Q., & Ballatore, C. (2017). Altered microtubule dynamics in neurodegenerative disease: Therapeutic potential of microtubule-stabilizing drugs. Neurobiology of disease, 105, 328-335.	
10/31	Student Presendations: Neurodegeneration - Hereditary Spastic Paraplegia	Nahm, M., Lee, M. J., Parkinson, W., Lee, M., Kim, H., Kim, Y. J., ... & Lee, S. (2013). Spartin regulates synaptic growth and neuronal survival by inhibiting BMP-mediated microtubule stabilization. Neuron, 77(4), 680-695.	
11/2	Student Presentations: Neurodegeneration - KIF2A & Early-Onset Neurodegen	Ruiz-Reig, N., Chehade, G., Hakanen, J., Aittaleb, M., Wierda, K., De Wit, J., ... & Tissir, F. (2022). KIF2A deficiency causes early-onset neurodegeneration. Proceedings of the National Academy of Sciences, 119(46), e2209714119.	**News and Views Outline Due**
11/7	Student Presentations: Neurodegeneration - Alzheimer's	Alonso, A. D. C., Zaidi, T., Grundke-Iqbal, I., & Iqbal, K. (1994). Role of abnormally phosphorylated tau in the breakdown of microtubules in Alzheimer disease. Proceedings of the National Academy of Sciences, 91(12), 5562-5566.	
11/9	Student Presentations: Neurodegeneration - Alzheimer's	Stokin, G. B., Lillo, C., Falzone, T. L., Brusch, R. G., Rockenstein, E., Mount, S. L., ... & Goldstein, L. S. (2005). Axonopathy and transport deficits early in the pathogenesis of Alzheimer's disease. Science, 307(5713), 1282-1288.	
11/14	Student Presentations: Neurodegeneration - Alzheimer's	Barten, D. M., Fanara, P., Andorfer, C., Hoque, N., Wong, P. A., Husted, K. H., ... & Albright, C. F. (2012). Hyperdynamic microtubules, cognitive deficits, and pathology are improved in tau transgenic mice with low doses of the microtubule-stabilizing agent BMS-241027. Journal of Neuroscience, 32(21), 7137-7145.	
11/16	Student Presentations: Neurodegeneration - ALS	Fanara, P., Banerjee, J., Hueck, R. V., Harper, M. R., Awada, M., Turner, H., ... & Hellerstein, M. K. (2007). Stabilization of hyperdynamic microtubules is neuroprotective in amyotrophic lateral sclerosis. Journal of Biological Chemistry, 282(32), 23465-23472.	
11/21	Student Presentations: Neurodegeneration - ALS	San Juan, I. G., Nash, L. A., Smith, K. S., Leyton-Jaimes, M. F., Qian, M., Klim, J. R., ... & Eggan, K. (2022). Loss of mouse Stmn2 function causes motor neuropathy. Neuron, 110(10), 1671-1688.	
11/23	No Class - Thanksgiving break	X	X
11/28	Microtubules in Traumatic Brain Injury: Overview	Blennow, K., Hardy, J., & Zetterberg, H. (2012). The neuropathology and neurobiology of traumatic brain injury. Neuron, 76(5), 886-899.	
11/30	Student Presentations: Traumatic Brain Injury	Tang-Schomer, M. D., Patel, A. R., Baas, P. W., & Smith, D. H. (2010). Mechanical breaking of microtubules in axons during dynamic stretch injury underlies delayed elasticity, microtubule disassembly, and axon degeneration. The FASEB Journal, 24(5), 1401.	
12/5	Student Presentations: Traumatic Brain Injury	Kondo, A., Shahpasand, K., Mannix, R., Qiu, J., Moncaster, J., Chen, C. H., ... & Lu, K. P. (2015). Antibody against early driver of neurodegeneration cis P-tau blocks brain injury and tauopathy. Nature, 523(7561), 431-436.	
12/7	Student Presentations: Traumatic Brain Injury	Cross, D. J., Meabon, J. S., Cline, M. M., Richards, T. L., Stump, A. J., Cross, C. G., ... & Cook, D. G. (2019). Paclitaxel reduces brain injury from repeated head trauma in mice. Journal of Alzheimer's Disease, 67(3), 859-874.	**News and Views Articles Due**