

BIOL 74.02: Diseases of the Nervous System

INSTRUCTOR

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Office Hours LSC 322: Thursdays 2:30-3:30 pm, or by appointment

COURSE DESCRIPTION

This course will investigate the cellular basis of several common neurodegenerative diseases. For each condition we will take a holistic approach to understand: 1) the cell types and pathways that are dysfunctional, 2) the mechanisms of disease presentation, heterogeneity and patient prognosis and 3) the current state of the scientific literature. Diseases covered will include Alzheimer's, demyelinating disorders and ALS, among others. Commonalities will be studied to bring about a broader understanding of how dysfunction in multicellular interactions results in a degenerative cascade of mind and body.

LEARNING OBJECTIVES

1. Gain a working knowledge of the cellular taxonomy and organization of the nervous system focusing on cell-cell interactions and the functional output of these interactions.
2. Become familiar with major neurodegenerative diseases of the nervous system and understand the underlying cellular mechanisms that are disrupted in these diseases.
3. Develop an appreciation for the connection between cellular processes and human disease.
4. Understand how to read, interpret, and critique primary literature on neurobiology of disease.
5. Develop presentation and scientific communication skills through group presentations and scientific writing.

COURSE ASSESSMENT

Written summaries of journal articles (40%) - Students will submit <500 word written summaries for each primary literature article that is presented by their peers. Written summaries are not required when presenting. These summaries should include the background, purpose, main findings and conclusions in addition to any potential critiques or issues with the study.

Student presentations (25%) - Students will present 1-2 primary papers from the literature during the course. Presentations will be ~60 minutes and will involve leading the class through an interactive journal article discussion and critique.

Final project (30%) - Students will design and write a short proposal based on a hypothetical experiment and treatment for a specific disease condition. Any neurodegenerative disease can be selected in any model system. The proposal will culminate in a <1500-word proposal and 5 min presentation to describe how they would test their treatment and hypothesis.

Engagement (5%) - Engagement during class discussions which includes asking questions, listening to others, and participating in the furthered education of all members of the course.

HONOR PRINCIPLE

During this course, it is expected that students will abide by the Honor Principle. The Academic Honor Principle can be found [here](#) and the Arts and Sciences Academic Honor Policy for Undergraduates can be found [here](#). If you have any questions or concerns regarding this during the course, please contact Dr. Hill.

STUDENT ACCOMMODATIONS

Students requesting disability-related accommodations and services for this course are required to register with Student Accessibility Services (SAS; [Apply for Services webpage](#); student.accessibility.services@dartmouth.edu; 1-603-646-9900) and to request that an accommodation email be sent to me in advance of the need for an accommodation. Then, students should schedule a follow-up meeting with me to determine relevant details such as what role SAS or its [Testing Center](#) may play in accommodation implementation. This process works best for everyone when completed as early in the quarter as possible. If students have questions about whether they are eligible for accommodations or have concerns about the implementation of their accommodations, they should contact the SAS office. All inquiries and discussions will remain confidential.

STUDENT WELLNESS

The academic environment at Dartmouth can be challenging, the terms can be intensive, and classes are sometimes not the only demanding part of your life. There are a number of resources available on campus to support your wellness, and you are encouraged to use these resources and take care of yourself throughout the term. These resources include: Undergraduate Deans: <http://www.dartmouth.edu/~upperde/>
Counseling and Human Development: <http://www.dartmouth.edu/~chd/>
Student Wellness Center: <http://www.dartmouth.edu/~healthed/>

At Dartmouth, we value integrity, responsibility, and respect for the rights and interests of others, all central to our Principles of Community. We are dedicated to establishing and maintaining a safe and inclusive campus where all have equal access to the educational and employment opportunities Dartmouth offers. We strive to promote an environment of sexual respect, safety, and well-being. In its policies and standards, Dartmouth demonstrates unequivocally that sexual assault, gender-based harassment, domestic violence, dating violence, and stalking are not tolerated in our community.

The Sexual Respect Website (<https://sexual-respect.dartmouth.edu/>) provides a wealth of information on your rights and obligations with regard to sexual respect and resources that are available to all in our community. As a faculty member, we are obligated to share disclosures regarding conduct under Title IX with Dartmouth's Title IX Coordinator. Should you have any questions, please feel free to contact Dartmouth's Title IX Coordinator Kristi Clemens (Kristi.Clemens@Dartmouth.edu).

STUDENTS' RELIGIOUS OBSERVANCES

Dartmouth has a deep commitment to support students' religious observances and diverse faith practices. Some students may wish to take part in religious observances that occur during this academic term. If you have a religious observance that conflicts with your participation in the course, please meet with me as soon as possible—before the end of the second week of the term at the latest—to discuss appropriate course adjustments.

COURSE SCHEDULE

September 17 - Intro for the course and how to read the primary literature

<https://www.sciencemag.org/careers/2016/03/how-seriously-read-scientific-paper>

<http://www.owl.net.rice.edu/~cainproj/courses/HowToReadSciArticle.pdf>

September 19 - Brain cellular architecture

Kasthuri N, et al. Saturated Reconstruction of a Volume of Neocortex. *Cell*. 2015 Jul 30;162(3):648-61. doi: 10.1016/j.cell.2015.06.054. PMID: 26232230

September 24 - Paper #1 Amyloid beta and antibody treatment in AD?

Sevigny J, et al. The antibody aducanumab reduces A β plaques in Alzheimer's disease. *Nature*. 2016 Sep 1;537(7618):50-6. doi: 10.1038/nature19323. PMID: 27582220

September 26 - Paper #2 Disrupted perivascular clearance in AD?

Iiff JJ, et al. A paravascular pathway facilitates CSF flow through the brain parenchyma and the clearance of interstitial solutes, including amyloid β . *Sci Transl Med*. 2012 Aug 15;4(147):147ra111. doi: 10.1126/scitranslmed.3003748. PMID: 22896675

October 1 - Paper #3 Blood flow disruption in AD?

Cruz Hernández JC, et al. Neutrophil adhesion in brain capillaries reduces cortical blood flow and impairs memory function in Alzheimer's disease mouse models. *Nat Neurosci*. 2019 Mar;22(3):413-420. doi: 10.1038/s41593-018-0329-4. PMID: 30742116

October 3 - Paper #4 Faulty lysosome function in AD?

Lee JH, et al. Faulty autolysosome acidification in Alzheimer's disease mouse models induces autophagic buildup of A β in neurons, yielding senile plaques. *Nat Neurosci*. 2022 Jun;25(6):688-701. doi: 10.1038/s41593022-01084-8. Epub 2022 Jun 2. PMID: 35654956

October 8 - Paper #5 Axonal spheroids in AD?

Yuan P, et al. PLD3 affects axonal spheroids and network defects in Alzheimer's disease. *Nature*. 2022 Dec;612(7939):328-337. doi: 10.1038/s41586-022-05491-6. Epub 2022 Nov 30. PMID: 36450991

October 10 - Paper #6 Myelin disruption in AD?

Depp C, et al. Myelin dysfunction drives amyloid- β deposition in models of Alzheimer's disease. *Nature*. 2023 Jun;618(7964):349-357. doi: 10.1038/s41586-023-06120-6. Epub 2023 May 31. PMID: 37258678

October 15 - Paper #7 Myelin replacement by stem cells?

Windrem MS, et al. Human Glial Progenitor Cells Effectively Remyelinate the Demyelinated Adult Brain. *Cell Rep*. 2020 May 19;31(7):107658. doi: 10.1016/j.celrep.2020.107658. PMID: 32433967

October 17 - Paper #8 Remyelination by mature oligodendrocytes?

Bacmeister CM, et al. Motor learning promotes remyelination via new and surviving oligodendrocytes. *Nat Neurosci*. 2020 Jul;23(7):819-831. doi: 10.1038/s41593-020-0637-3. PMID: 32424285

October 22 - Paper #9 A role for aging in remyelination?

Iram T, et al. Young CSF restores oligodendrogenesis and memory in aged mice via Fgf17. *Nature*. 2022 May;605(7910):509-515. doi: 10.1038/s41586-022-04722-0. PMID: 35545674

October 24 - Paper #10 Microglia and protection from age related degeneration?

Munro DAD, et al. Microglia protect against age-associated brain pathologies. *Neuron*. 2024 Aug 21;112(16):2732-2748.e8. doi: 10.1016/j.neuron.2024.05.018. Epub 2024 Jun 18. PMID: 38897208.

October 29 - Paper #11 Neurotoxic astrocytes in neurodegeneration?

Guttenplan KA, et al. Neurotoxic reactive astrocytes induce cell death via saturated lipids. *Nature*. 2021 Nov;599(7883):102-107. doi: 10.1038/s41586-021-03960-y. Epub 2021 Oct 6. PMID: 34616039

October 31 - Paper #12 Microglial response to TDP-43?

Xie M, et al. TREM2 interacts with TDP-43 and mediates microglial neuroprotection against TDP-43-related neurodegeneration. *Nat Neurosci*. 2022 Jan;25(1):26-38. doi: 10.1038/s41593-021-00975-6. Epub 2021 Dec 16. PMID: 34916658;

November 5 - Paper #13 Oligodendrocyte dysfunction in ALS?

Kang SH, et al. Degeneration and impaired regeneration of gray matter oligodendrocytes in amyotrophic lateral sclerosis. *Nat Neurosci*. 2013 May;16(5):571-9. doi: 10.1038/nn.3357. Epub 2013 Mar 31. PMID: 23542689

November 7 - Paper #14 Astrocyte release of toxic molecules in ALS?

Arredondo C et al. Excessive release of inorganic polyphosphate by ALS/FTD astrocytes causes non-cell-autonomous toxicity to motoneurons. *Neuron*. 2022 May 18;110(10):1656-1670.e12. doi: 10.1016/j.neuron.2022.02.010. Epub 2022 Mar 10. PMID: 35276083

November 12 - Paper #15 Rod microglia in ALS?

Xie M, et al. Rod-shaped microglia interact with neuronal dendrites to regulate cortical excitability in TDP-43 related neurodegeneration. *bioRxiv* [Preprint]. 2024 Jul 2:2024.06.30.601396. doi: 10.1101/2024.06.30.601396. PMID: 39005475;

November 19 - Proposal presentations