BIOL 74.02: Diseases of the Nervous System

INSTRUCTOR

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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 Dartmouth College Student Handbook (page iii) states "Fundamental to the principle of independent learning are the requirements of honesty and integrity in the performance of academic assignments, both in the classroom and outside. Dartmouth operates on the principle of academic honor, without proctoring of examinations. Students who submit work which is not their own or who commit other acts of academic dishonesty forfeit the opportunity to continue at Dartmouth." If you have any questions or concerns regarding this during the course, please contact Dr. Hill. Honor Principle: http://student-affairs.dartmouth.edu/policy/academic-honor-principle.

STUDENT ACCOMMODATIONS

Students requesting disability-related accommodations and services 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) (and deputies if appropriate).

STUDENTS' RELIGIOUS OBSERVANCES

Some students may wish to take part in religious observances that occur during the academic term. If you have a religious observance that conflicts with your participation in the course, please contact Dr. Hill as soon as possible to discuss appropriate accommodations.

COURSE SCHEDULE

September 13 - 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.owlnet.rice.edu/~cainproj/courses/HowToReadSciArticle.pdf

September 15 - 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 20 - Paper #1 Amyloid beta and antibody treatment in AD?
Sevigny J, et al. The antibody aducanumab reduces Aβ plaques in Alzheimer's disease. Nature. 2016 Sep 1;537(7618):50-6. doi: 10.1038/nature19323. PMID: 27582220

September 22 - Paper #2 Disrupted perivascular clearance in AD?
Iliff 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

September 27 - 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

September 29 - Paper #4 A role for microglia in AD?
Yuan P, et al TREM2 Haplodeficiency in Mice and Humans Impairs the Microglia Barrier Function Leading to Decreased Amyloid Compaction and Severe Axonal Dystrophy. Neuron. 2016 May 18;90(4):724-39. doi: 10.1016/j.neuron.2016.05.003. PMID: 27196974

October 4 - Paper #5 Faulty lysosome function in AD?
Lee JH, et al. Faulty autolysosome acidification in Alzheimer's disease mouse models induces autophagic buildup of Aβ 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 6 - Paper #6 Myelin disruption in AD?
Chen JF et al. Enhancing myelin renewal reverses cognitive dysfunction in a murine model of Alzheimer's disease. Neuron. 2021 Jul 21;109(14):2292-2307.e5. doi: 10.1016/j.neuron.2021.05.012. Epub 2021 Jun 7. PMID: 34102111

October 11 - 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 13 - 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 18 - 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 20 - Paper #10 Myelin disruption with COVID?
Fernández-Castañeda A, et al. Mild respiratory COVID can cause multi-lineage neural cell and myelin dysregulation. Cell. 2022 Jul 7;185(14):2452-2468.e16. doi: 10.1016/j.cell.2022.06.008. Epub 2022 Jun 13. PMID: 35768006

October 25 - 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 27 - Paper #12 Microglia replacement in ALS?
Spiller KJ, et al. Microglia-mediated recovery from ALS-relevant motor neuron degeneration in a mouse model of TDP-43 proteinopathy. Nat Neurosci. 2018 Mar;21(3):329-340. doi: 10.1038/s41593-018-0083-7. PMID: 29463850

November 1 - 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 3 - 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 8 - Paper #15 Glial dysfunction in Huntington's?
Osipovitch M, et al. Human ESC-Derived Chimeric Mouse Models of Huntington's Disease Reveal Cell-Intrinsic Defects in Glial Progenitor Cell Differentiation. Cell Stem Cell. 2019 Jan 3;24(1):107-122.e7. doi: 10.1016/j.stem.2018.11.010. PMID: 30554964

November 10 - Proposal presentations