

BISC 541: Cell Biology of Neurodegenerative Diseases

A. Logistics

Mode	Section	Day	Time	Room
Lecture	All	M, W, F	9:00-9:50 am	114 Shoemaker

B. Course Instructor

1. Mika Jekabsons, Ph.D.
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Office hours: M 3-5, F 12-1

Office: 110 Shoemaker
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C. Course Reading Materials

1. Required textbook: none
2. Assigned journal articles

D. Course Description

This is a one semester course focusing our current understanding of the cellular basis of neurodegenerative diseases. The course is centered around reading scientific journal articles that span from the 1980s to 2000s. The articles follow a logical progression of investigation and understanding of neurodegenerative diseases. This course is appropriate for graduate students as well as advanced undergraduates with a background in neuroscience, cell biology and/or biochemistry. The course provides a brief overview of Parkinson's disease, Amyotrophic Lateral Sclerosis, Huntington's disease, and Alzheimer's disease. Much of the course will focus on factors that contribute to the development of sporadic and familial forms of Parkinson's Disease. We will focus on some of the biochemical and genetic alterations that have been found to have important consequences on neuronal function. Mitochondrial function and the cellular redox state are two important aspects of neuronal function which will be considered. These topics are the focus of intense biomedical research efforts, and as such, our understanding of the details in these areas is incomplete. Consequently, a significant amount of information to be covered will be presented not as fact, but as current models that may ultimately be revised as future studies bring new insight. Because of the dynamic nature of the information, there is no textbook available that covers all these areas in a comprehensive, current way. A series of journal articles will serve as our textbook, and background information on the articles will be presented through a set of lectures preceding each group of articles.

E. Learning Objectives

Upon completing this course, students should have an understanding of (a) the pathology of different neurodegenerative diseases, (b) reactive oxygen species, (c) antioxidant defenses, (d) mitochondrial function, (f) specific factors contributing to Parkinson's disease, and (e) how to properly read and understand scientific journal articles.

F. Grading

F.1. All students

1. Exam 1	100
2. Exam 2	100
3. Exam 3	100
4. Final Exam (oral or written)	100

All exams will be in-class. Depending on enrollment, the final exam may be a 25 minute oral PowerPoint presentation or a typed paper reviewing a scientific paper whose research encompasses a neurodegenerative disease. Exams will generally be short answer and essay. Oral final exams are for graduate students. Be punctual, as extra time will not be given if you are late. One or more take-home quizzes are possible.

F.2. Graduate students

1. Literature review paper (minimum 10 pages; 1.5 line spacing, 1 inch margins, maximum 11 point font size).

The literature review paper is an opportunity to summarize the work of many (at least 20) scientific articles focused on one neurodegenerative disorder, and to additionally use this knowledge to suggest future avenues of research. Your goal is to gain a deep understanding of a particular disorder by organizing and critiquing the papers, explaining topics where consensus appears to exist, as well as detailing unresolved topics that continue to be debated. The paper is worth 100 points.

Letter grades will be assigned as follows: **A:** 90-100%; **B:** 80-89.9%; **C:** 70-79.9%; **D:** 60-69.9%; **F:** <60%. These are percentages of total possible points accumulated from the in-class exams and the written summaries of journal articles (and review paper for grad students). Graduate students will be graded on a straight scale, with no curve applied. For undergraduates, in the event that 10% of the class does not score 90% or higher, the A cutoff will be lowered until a minimum of 10% of the class receives an A. However this does come with restrictions, as the A cutoff will not be lowered below 85% of total possible points even if less than 10% of the class score greater than or equal to 85%. Therefore, you should expect that the minimum A will fall somewhere between 85-90%. In the event that the A cutoff is lowered below 90%, the range of all other letter grades will be increased from 9.9 to 10.9%. As an example, if the A's are greater than or equal to 87%, then the B range will be 76-86.9%, the C range 65-75.9%, the D range will be 54-64.9%, and scores less than 54% will receive an F. The greatest possible 'curve' applied to the class would be: A: greater than or equal to 85%, B: 74-84.9%, C: 63-73.9%, D: 52-62.9%, F: less than 52%.

Note that I will be implementing the +/- grading system for this course. The additional grades possible are: A-, B+, B-, and C+ (no C-, D+, D-). The +/- grading will be applied to students within two percentage points below a letter grade cutoff. Students falling short of a higher letter grade by 0.1-1.0% will receive the higher letter grade, designated with a minus. Students falling short of a higher letter grade by 1.1-2.0% will receive the lower letter grade designated with a plus. For example, if the A cutoff is 87%, then an A- would be 86.0-86.9%, and a B+ would be 85.0-85.9%. The B range is then 76.0-84.9%.

G. Attendance and Policies

1. Discussion during the lectures is encouraged.
2. The instructor reserves the right to alter the schedule of topics covered depending on circumstances and interest from those enrolled in the course.
3. The instructor reserves the right to change the exam schedule, the exam format, and the points allocated to each as may be required.

G. Tentative outline of topics

I. Introduction to neurodegeneration

- A. Alzheimer's
- B. Parkinson's
- C. ALS
- D. Huntington's
- E. LHON

II. Basic neuroanatomy

III Parkinson's disease details

A. MPTP story

- 1. Langston et al 1983 paper
- 2. Langston et al 1984 paper

B. Consequences of MPTP

- 1. Javitch et al 1985 paper
- 2. Ramsay & Singer 1986 paper
- 3. review of mitochondrial function
- 4. Davey et al 1992 paper

C. Rotenone model

- 1. Betarbet et al 2001 paper
- 2. Greenamyre et al 2001 paper

* **First exam- mid Feb.**

D. Reactive oxygen species

- 1. definition, types
- 2. sources
- 3. relevance to PD
- 4. Sherer et al 2003 paper- complex I, rotenone, and ROS
- 5. Chinta et al 2007 paper

***Second exam- mid March**

E. Familial PD: α -synuclein mutations

- 1. function of wild type α -synuclein: Abeliovich et al 2000 paper
- 2. effects of mutant α -synuclein: Kirik et al 2002 paper or Xu et al 2002 paper
- 3. mitochondria and α -synuclein: Devi et al 2008 paper
- 4. spread of PD via α -synuclein mutation: Desplats et al 2009 paper

***Third exam- final day of class**

IV. Final Exam: Wednesday 8May2013, 8am

A. Graduate students to present 30 min PowerPoint presentation

B. Undergraduates must turn in review paper by this time, and listen to the presentations by the graduate students.