

Fall 2024C BIOL4266: Molecular Genetics of Neurological Disease

Description: This course will focus on the molecular basis of neurological diseases, exploring in detail key papers that cover topics including defining the disease genes, to development of animal models that provide mechanistic insight, and seminal findings that reveal molecular understanding. Diseases covered will include neurological diseases of great research focus today such as Alzheimer's, Fragile-X and autism, dementia, motor neuron degeneration, and microsatellite repeat expansion disorders. The course will provide a perspective from initial molecular determination through to current status. The course will end on more recent studies. Students will gain an understanding of how the molecular basis of a disease is discovered (from classical genetics to modern genomics), a range of techniques that are used to approach mechanistic understanding, how such diseases can be modeled in simpler systems for mechanistic insight, and the current state of mechanistic understanding of the diseases.

*****BIOL2210 is a required pre-requisite**

YOU MAY NOT TAKE THIS COURSE IF YOU HAVE NOT TAKEN BIOL2210.

*****The class is limited to Seniors.***

Time: T Th 10:15-11:45AM.

Prerequisites: **BIOL2210 (absolutely required!);**

BIOL251 and BIOL421 (helpful/recommended).

The class is limited to seniors.

Class Procedure: The hour-and-one-half class periods will consist of lectures, discussions of one or more seminal research papers, with extensive in-class discussion. There will be numerous in-class activity sessions covering the approaches and design of experiments and results to molecularly define, understand and model a disease. Preparation prior to the lectures is essential and includes reading of the material.

Instructor: Dr. Nancy Bonini (204G Lynch Laboratory, appointments by request); email: nbonini@sas.upenn.edu

Textbook: No official textbook. Materials including papers to read prior to class, lecture notes, and papers discussed in class and activities will be distributed on the Canvas courseware site (<https://canvas.upenn.edu>), accessible with your PennKey.

Grading: Grade will be based on in-class participation (25%), and three papers stemming from in-class activities (50%), and the final assignment (25%).

Class attendance: You must sign in for every lecture; you must email Dr. Bonini before class if you are not able to attend. Unexcused absences are taken into account into the final grade.

Background and Lecture Reading: Reading materials will be made available for each lecture for download on the course website. The reading is comprised of research papers and reviews, which must be read PRIOR to the class session. The class sessions will consist of both overview lectures and our working through the research papers figure by figure.

2025C: BIOL 4266 Tentative Course Syllabus

Date	Topic
Tue Aug 26	Introduction to the course & medical genetics: Overview of approaches to the genetic basis of neurological disease, including refresher on terminology, techniques and anatomy
Thu Aug 28	Alzheimer's disease 1: What it is & cloning of the first mutation
Tue Sep 2	AD2: Cloning of the second AD gene & what about tau?
[Thu Sep 4]	[NO CLASS – catch up on reading]
Tue Sep 9	AD3: Putting APP & tau together
Thu Sep 11	AD4: A new AD mutation with wholly new insight: Assignment 1
Tue Sep 16	Huntington's disease 1: The disease & cloning the gene
Thu Sep 18	HD2: Finding the gene & the mutation
Tue Sep 23	HD3: Modelling in a mouse & mechanistic insight
Thu Sep 25	HD4: Yet another mouse with profound insight! AD Assignment Due
Tue Sept 30	HD5: A wholly new approach to disease therapy: Assignment 2
Thu Oct 2	Fragile X Syndrome 1: Discovery of the gene
Tue Oct 7	FXS 2: Cloning of the gene & insight into genetic mechanism
Thu Oct 9	NO CLASS - FALL BREAK
Tue Oct 14	FXS 3 : 1 gene, multiple diseases—FXTAS
Thu Oct 16	FXS 4: A totally new way to look at developmental disease.
Tue Oct 21	Amyotrophic Lateral Sclerosis 1: SOD1 is mutated & the nature of the mutations
Thu Oct 23	ALS 2: Non-autonomy of the disease—glia kill the neurons HD Assignment Due
Tue Oct 28	ALS 3: Entirely new insight from the accumulations
Thu Oct 30	ALS 4: Discovery of the most common mutation in ALS
Tue Nov 4	ALS5: In class activity & assignment 3: "non-coding" RNAs
Thu Nov 6	Prion 1: What is a prion disease?
Tue Nov 11	Prion 2: Concept of prion strains.
Thu Nov 13	Prion 3: Parkinson's disease ALS Assignment Due
Tue Nov 18	Prion 4: Trans-synaptic spreading
Thur Nov 20	Special Topic 1: LOAD & GWAS
Tue Nov 25	Special Topic 2: HD scRNA sequencing for gene expression & repeat length
Thu Nov 27	NO CLASS - THANKSGIVING
Tue Dec 2	Final Assignment: Is it the nerves or not?
Thu Dec 4	Special Topic 3: iPS breakthrough for disease in a dish.