

Fall 2023C 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. 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, and how such diseases can be modeled in simpler systems for mechanistic insight. Biol221 is a required pre-requisite; Seniors have priority for enrollment.

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

Prerequisites: BIOL221/BIOL2210 (absolutely required!); BIOL251 and BIOL421 (recommended).

Because the class is over-subscribed, the class is typically 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.

2023C: BIOL 4266 Tentative Course Syllabus

| Date | Topic |
|-------------|---|
| Tue | Introduction to the course & medical genetics: Overview of approaches to the genetic basis of neurological disease, including refresher on terminology, techniques and anatomy |
| Th | Alzheimer's disease 1: What it is & cloning of the first mutation |
| Tue | AD2: Cloning of the second AD gene & insight from model organisms |
| Th | AD3: What about tau? |
| Tue | AD4: Putting APP & tau together |
| Th | AD5: A new AD mutation with wholly new insight: Assignment 1 |
| Tue | Huntington's disease 1: The disease & cloning the gene |
| Th | HD2: Finding the gene & the mutation |
| Tue | HD3: Modelling in a mouse & mechanistic insight |
| Th | HD4: Yet another mouse with profound insight! AD Assignment Due |
| Tue | HD5: A wholly new approach to disease therapy: Assignment 2 |
| Th | FALL BREAK |
| Tue | Fragile X Syndrome 1: Discovery of the gene |
| Th | FXS 2: Cloning of the gene & insight into genetic mechanism |
| Tue | FXS 3 : 1 gene, multiple diseases—FXTAS |
| Th | FXS 4: A totally new way to look at developmental disease. |
| Tue | Amyotrophic Lateral Sclerosis 1: SOD1 is mutated & the nature of the mutations HD Assignment Due |
| Th | ALS 2: Non-autonomy of the disease—glia kill the neurons |
| Tue | ALS 3: Entirely new insight from the accumulations |
| Th | ALS 4: Discovery of the most common mutation in ALS |
| Tue | ALS5: In class activity & assignment 3: "non-coding" RNAs |
| [Th] | No class |
| Tue | Prion 1: What is a prion disease? |
| Th | Prion 2: Concept of prion strains. ALS Assignment Due |
| Tue | Prion 3: Parkinson's disease |
| Thu | THANKSGIVING |
| Tue | Prion 4: Trans-synaptic spreading |
| Th | Special topic 1: LOAD & GWAS |
| Tue | Final Assignment: Is it the nerves or not? |
| Th | Special topic 2: iPS breakthrough, leading to disease in a dish |