Fall 2022C 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 1:45-3:15PM.

Prerequisites: BIOL221 (required); BIOL251 and BIOL421 (recommended).
If you have not taken Biol 221 you must talk to Dr. Bonini!!!

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.

Tentative Course Syllabus

Date **Topic**

Introduction to the course & medical genetics: Overview of approaches to the genetic basis of neurological disease, including refresher on terminology, techniques and anatomy
Alzheimer's disease 1: What it is & cloning of the first mutation
AD2: Cloning of the second AD gene & insight from model organisms
AD3: What about tau?
AD4: Putting APP & tau together
AD5: A new AD mutation with wholely new insight: Assignment 1
Huntington's disease 1: The disease & cloning the gene
HD2: Finding the gene & the mutation
HD3: Modelling in a mouse & mechanistic insight
HD4: Yet another mouse with profound insight! AD Assignment Due
HD5: A wholely new approach to disease therapy: Assignment 2
Fragile X Syndrome 1: Discovery of the gene
FXS 2: Cloning of the gene & insight into genetic mechanism
FALL BREAK
FXS 3 : 1 gene, multiple diseases—FXTAS
FXS 4: A totally new way to look at developmental disease.
Amyotrophic Lateral Sclerosis 1: SOD1 is mutated & the nature of the mutations HD Assignment Due
ALS 2: Non-autonomy of the disease—glia kill the neurons
ALS 3: Entirely new insight from the accumulations
ALS 4: Discovery of the most common mutation in ALS
ALS5: In class activity & assignment 3: "non-coding" RNAs
Prion 1: What is a prion disease?
Prion 2: Concept of prion strains.
Prion 3: Parkinson's disease ALS Assignment Due
Prion 4: Trans-synaptic spreading
THANKSGIVING
Special topic 1: LOAD & GWAS
Special topic 2: iPS breakthrough, leading to disease in a dish
Final Assignment: Is it the nerves or not?
Special topic 3: Where we are today.

Last day of reading period: Final assignment due