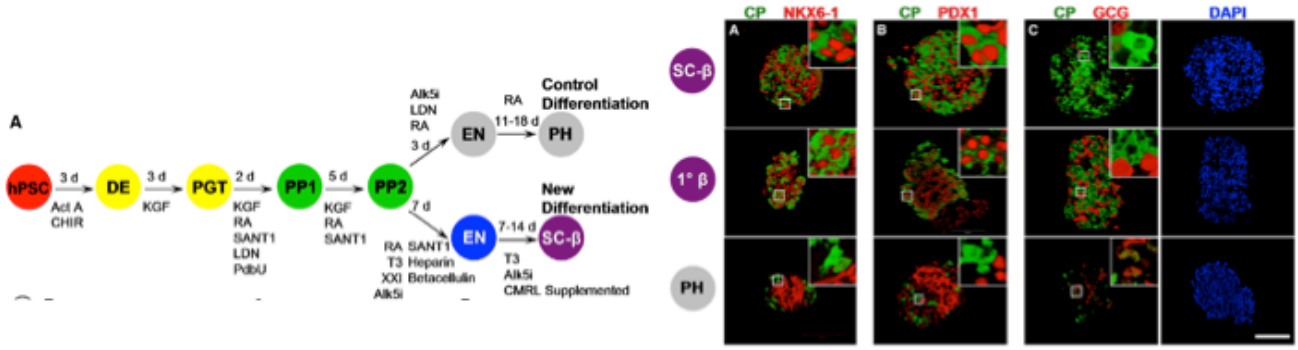

Cellular Mechanisms – BIOL 4260 – SPRING 2016 (10/27/15)

Course Description

"Common sense tells us that if scientists find ways to greatly improve human capabilities, there will be no stopping the public from happily seizing them."
James D. Watson (1928–) Co-recipient with Francis Crick and Maurice Wilkins of the 1962 Nobel Prize in Physiology or Medicine for determining the double helical structure of DNA.

This course will use a case study approach to examine diverse genetic diseases including, but not necessarily limited to, Amyotrophic Lateral Sclerosis, Cystic Fibrosis, Duchenne Muscular Dystrophy, Type I Diabetes, and different cancers. Additional or different, diseases may be considered based on student interests and recent research advances. The overall goal is to examine specific regulatory or mechanistic events that underlie the diseased state and their associated molecular components that may serve as new therapeutic targets. This underlies the transition from "basic" to "translational" research. We will explore novel treatment options under development and consider their relative strengths and weaknesses. These approaches range from small molecules that function variously as chaperones, nonsense suppressors or RNA splicing modulators to induced pluripotent stem cells and gene repair. We will also discuss new findings that elucidate the basis for diseases for which there are currently no treatments, and consider how novel therapeutic options could be developed. Assigned reading will come from the primary scientific literature. As such, a major objective of this course will be to provide an opportunity, to learn how to critically read, interpret, and evaluate primary research papers. Although no textbook will be used, relevant background material can be found in the Lodish et al Molecular Cell Biology text used in BIOL 3000 which is the sole course prerequisite for BIOL 4260.

Course Objectives

The overall goal of BIOL 4260 is for you to gain experience in critically reading and assessing the primary scientific literature and to learn to think like an experimental molecular cell biologist addressing "translational research". By the end of this course you will be able to:

1. Critically read and assess, interpret, and present the data and conclusions posed in primary research articles.
2. Describe and explain the pertinent molecular and cellular processes that underlie the specific diseases under discussion.
3. Describe and explain how specific genes and/or their mRNA or protein products can be validated as therapeutic targets to develop new treatment options and approaches.

4. Identify the strengths and weaknesses of different drug discovery approaches utilized to develop new therapeutic options for genetic diseases.
5. Develop the ability to work collaborative in a "team setting".

Meeting Times and Location 9:30 – 10:45 AM Tues., Thurs., GIL 141

Instructor Information

Mike Wormington, Associate Professor of Biology. My hometown is Overland Park, Kansas, and I attended the University of Kansas (Go Jayhawks!) where I earned my BA with Honors in Biology and my PhD in Biochemistry. I was an NIH Postdoctoral fellow at the Carnegie Institution for Science, Dept. of Embryology, in Baltimore, MD. I joined the UVa Biology faculty in 1989. My longstanding research interest is the regulation of gene expression during oogenesis and embryogenesis and the interplay between genetic and metabolic reprogramming. When I'm not in the lab or teaching, I spend my time with my wife Susan, who's the Art Director at UVa's Darden School of Business. Our two daughters and sons-in-law and our 3 year old granddaughter Sophie keep us busy. I'm also a search and rescue, disaster relief mission pilot and director of operations for the Virginia wing of the US Civil Air Patrol which is the civilian auxiliary of the United States Air Force.

Office: PLSB 206 Phone: 982-5803 email: ww2t@virginia.edu
Office Hours: By appointment

Collab Website

The BIOL 4260 Collab Course site is an important resource that you will use to access assigned readings. The Resources section will contain pdf files of assigned readings and any pertinent powerpoint slides for each case study. Each reading assignment will have an associated list of questions that will serve as the basis for class discussions. Since this will be a discussion-based course, you will be expected to complete the assigned reading and go over the pertinent questions *before* the class in which they will be covered.

Evaluation and Grading

This is a discussion-intensive class. Therefore, class attendance and active participation are essential. You will be working in small groups to discuss the assigned papers using a set of specific questions provided beforehand as guidelines. Each group will then be tasked with summarizing their discussions of various questions with the entire class. 60% of your course grade will be based on class participation. 20% of your course grade will be based on short take-home "open book" exercises associated with each topic. 20% of your course grade will be based on a final project in which you will have the opportunity to identify and validate a molecular target, and develop a therapeutic approach for a disease of your choice. Details on presentation length & format will be provided once the course is under way.

Important College Dates

- Add Deadline: Weds. Feb. 3
- Drop Deadline: Thurs. Feb. 4
- Spring Break: Mon. Mar. 7, Weds. Mar. 9 and Fri. Mar. 11 (No class)
- Withdrawal Deadline: Weds. Mar. 16

Case Studies from Spring, 2015

Case Study #1 Dystrophin rescue of Duchenne Muscular Dystrophy by nonsense suppression.

Case Study #2 Dystrophin rescue of Duchenne Muscular Dystrophy by exon skipping.

Case Study #3 Dystrophin repair of Duchenne Muscular Dystrophy by CRISPR/Cas9 Genome editing.

Case Study #4 Corrector and potentiator therapies for Cystic Fibrosis.

Case Study #5 Targeting a rogue transcription factor in Acute Myeloid Leukemia.

Case Study #6 Drug repurposing to target resistant BCR-ABL1 in Chronic Myeloid Leukemia.

Case Study #7 C9orf72: Toxic RNA & toxic protein in Amyotrophic Lateral Sclerosis.

Case Study #8 Induced pluripotent stem cells: Game changer for medicine.

Case Study #9 iPSC to Pancreatic β cells: Type I Diabetes

Case Study #10 Stem cell rogues & frauds.