Syllabus: CMB551
Cell and Molecular Biology Core Course
Fall 2017 MWF 10:20-11:40 AM

The Cell and Molecular Biology core course (CMB551) offers 24 topic areas covering a wealth of cell and molecular biology in a flexible modular format. This class is assigned 4 graded credit hours per semester. The module topics emphasize either in-depth critical discussion of the primary literature, an emphasis on developing quantitative/mathematical approaches to the biology, or both. The course consists of a sequence of six consecutive modules – within each module there are four or five topics. Students choose one topic per module. Each module contributes 10% of the final grade (60%) with the remaining 40% of the grade deriving from the final symposium or workshop.

To help you prepare for each module, the instructors have included a listing of summer readings. You should **complete the readings for your six selected module topics in advance of the start of classes**. All of the readings are either from common textbooks (you can substitute similar chapters from related textbooks if necessary) or can be accessed as PDFs from the CMB website:
https://medschool.duke.edu/education/degree-programs-and-admissions/program-cell-and-molecular-biology/curriculum/cmb-551-modules

It is important that first year students select additional module topics as backup choices, as some may be oversubscribed and second year students are given preference in their selections. Please submit your topic choices online at the following link ***no later than July 21, 2017***:
https://duke.qualtrics.com/jfe/form/SV_eG8P7q7KqnvFuZf

There will be a **short** online **entrance tests** on the reading materials for all topics on the first day of class (**Aug 28th**). This is to ensure that everyone wishing to take a given topic has sufficient background to benefit from it. The tests are mostly closed book, pass/fail, and will not require you to go beyond the assigned readings. You only take entrance tests for the module topics you will take during the semester. If you do not pass, you will have to contact the module instructor who will either meet with you for a make-up test (oral), suggest additional reading to better prepare you for the module, or ask you to select a different module topic for that slot, in which case you will have to take another (written) test. **The first module starts Wed., Aug. 30th**.

At the conclusion of Module 6, second- year students and above form two-person teams and devise a research proposal that is honed over a two-week period with an assigned faculty coach. *It is important that participating students think about this requirement as the course progresses – is there a classmate that you feel you can work very effectively with? Topic areas that you find particularly interesting?* Senior students present their proposals orally to the class (students and instructors) in a **one-day symposium on the 8th of Decembe**r.

At the conclusion of Module 6, first-year students participate in a four-class, graded workshop. The workshop is meant to help students prepare and evaluate research proposals in the context of the Symposium. During the course of the workshop, students will be paired and work in pairs on their proposal. There is very little time between the end of the 6th module and the start of the workshop to come up with a pertinent topic that can be developed during the workshop. First-year students should think ahead as far as potential partners (which they can request) and a particular topic. Students are expected to have selected a suitable topic and question(s) before the first session of the workshop. Also keep in mind that there is limited time during the workshop to refine the proposal to the point where it can be given as a presentation during the last session of the workshop. Therefore, students are encouraged to think ahead and be proactive over the course of the semester. Lastly, first-year students are **required** to attend the Symposium. They will be asked to provide feedback on symposium proposals given by the senior students.

A final note to students: Remember the date of the Symposium (**December 8**) when you make plans for traveling in preparation for your holiday break.

Course Director:
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	A	B	C	D
Module 1	**Lew** Controlling the cell cycle	**McClay** Mechanisms of early development	**Di Talia** Quantitative cell and developmental biology	**Alvarez** Animal models of cancer
Module 2	**Bagnat** Cellular mechanisms controlling animal patterning	**Boyce** Glycobiology	**Cameron/Carlson** Microscopy in cell biology	**Lechler** The cytoskeleton – Dynamics and function
Module 3	**Erickson** Understanding & manipulating protein-protein interactions	**Sherwood** Cell migration/invasion in development and cancer	**Capel** Germ cells and sex determination	**Mathey-Prevot** Signaling: how activation leads to specificity
Module 4	**Arshavsky** The eye as a digital camera	**Wood** Intersection of signaling and therapeutics	**Tata** Stem cells in tissue homeostasis and disease	**Goetz** The biology of cilia and flagella
Module 5	**Hogan** Organogenesis	**Hirschey** Regulation of mitochondrial metabolism	**Poss** Regeneration	**Soderling** Cell biology of the synapse
Module 6	**MacAlpine** Bioinformatics and genomics for the biologist	**Yildirim** Nuclear structure/gene regulation	**Fox** Genome instability	**Bennett** Humans as model organisms

Morphology, molecular machines & cellular processes
Stem cells, development & regeneration
Signaling
Quantitative biology & Genomics
Physiology & disease

COURSE CALENDAR

	Day	Date	Module
	Monday	August 28	***Class Introduction & Entrance Tests***
Module 1	Wednesday	August 30	1
	Friday	September 1	1
	Monday	September 4	***(LABOR DAY)*** 1
	Wednesday	September 6	1
	Friday	September 8	1
	Monday	September 11	1
Module 2	Wednesday	September 13	2
	Friday	September 15	2
	Monday	September 18	2
	Wednesday	September 20	2
	Friday	September 22	2
	Monday	September 25	2
Module 3	Wednesday	September 27	3
	Friday	September 29	3
	Monday	October 2	3
	Wednesday	October 4	3
	Friday	October 6	3
	Monday	***October 9***	***NO CLASSES – FALL BREAK***
	Wednesday	October 11	3
Module 4	Friday	October 13	4
	Monday	October 16	4
	Wednesday	October 18	4
	Friday	October 20	4
	Monday	October 23	4
	Wednesday	October 25	4
Module 5	Friday	October 27	5
	Monday	October 30	5
	Wednesday	November 1	5
	Friday	November 3	5
	Monday	November 6	5
	Wednesday	November 8	5
Module 6	Friday	November 10	6
	Monday	November 13	6
	Wednesday	November 15	6
	Friday	*November 17*	6
	Monday	*November 20*	6
	Thursday	***November 23***	***Thanksgiving Holiday***
	Monday	*November 27*	*6*
	Wednesday	***November 29***	***1st Year Prep #1/2nd Year Contact Coaches***
	Friday	***December 1***	***1st Year Prep #2***
	Monday	***December 4***	***1st Year Prep #3***
	Wednesday	***December 6***	***1st Year Prep #4***
	Friday	***December 8***	***CMB 551 SYMPOSIUM***

Module Descriptions:

Module 1A: Controlling the Cell Cycle

Instructor: Danny Lew
Summary: The accurate copying of a cell's contents and their distribution to produce two daughter cells is a stunning feat requiring exquisite coordination. The set of carefully orchestrated steps by which proliferating cells make copies of themselves constitutes the cell cycle. In this module, we will discuss landmark papers that established the conserved mechanisms underlying cell cycle control, as well as recent papers dissecting the control circuitry.

In addition to learning about a fundamental process, this module will explicitly deal with strategies for reading primary Journal articles to critically assess the validity of their conclusions. We will also discuss how to turn cartoon diagrams of regulatory pathways into equations and graphs producing quantitative predictions of pathway behavior, and address the importance of feedback pathways and bistable systems in generating sharp transitions in cell behavior.

Readings:
Molecular Biology of the Cell, Alberts, et al., - Chapter 17 (First part: The Cell Cycle)

Module 1B: Mechanisms of Early Development

Instructor: David McClay
Summary: This module will cover the maternal to zygotic transition, initial asymmetries that launch cellular diversity, onset of signaling, mechanisms of specification, and control mechanisms necessary for morphogenesis. It will emphasize the means by which genomic information is used to drive development. Each class period will be a combination of primary literature review, lecture and discussion. Animal examples will be drawn from across the animal kingdom.

Readings:
Molecular Biology of the Cell, Alberts, et al., 6th edition - Chapter 21
Developmental Biology, Gilbert, 10th edition - Chapters 1-3

Module 1C: Quantitative Cell and Developmental Biology

Instructor: Stefano Di Talia
Summary: It is a common belief that biology is the least quantitative and theoretical of the natural sciences. However, many fundamental discoveries in biology (e.g. membrane excitability, spikes, proofreading) have come from the use of modeling and theoretical ideas. The goal of this module is to show how theoretical and mathematical ideas can contribute to develop deeper

insights on biological problems. Focusing on primary literature, we will discuss how recent advancements in imaging technologies are improving our understanding of cell and developmental biology. Ideally by the end of this module, students will be able to distinguish good informative mathematical models from less informative models.

Suggested Readings:

1) Nurse, P and Hayles, J (2011) *The Cell in an Era of Systems Biology.* Cell, **144** (6), 850-854
2) Oates, AC, Gorfinkiel, N, Gonzalez-Gaitan, M, Heisenberg, CP (2009) *Quantitative approaches in developmental Biology.* Nature Reviews Genetics, **10**, 517-530.

Module 1D: Animal Models of Cancer

Instructor: James Alvarez

Summary: Animal models have provided important insights into the development, progression, and treatment of cancer. This module will cover the fundamentals of animal models of cancer, with a particular focus on mice. We will describe methodological approaches to generating mouse models of cancer, and discuss the advantages and limitations of different approaches. We will then focus on specific areas across tumor types in which mouse models have provided critical mechanistic insights into tumor biology. Each class will involve a discussion of primary research articles from the literature.

Readings:

1) Hanahan D, Weinberg RA: *Hallmarks of cancer: the next generation*. Cell 2011, 144(5):646-674.
2) Kersten K, de Visser KE, van Miltenburg MH, Jonkers J: *Genetically engineered mouse models in oncology research and cancer medicine*. EMBO Molecular Medicine 2017, 9(2):137-153.

Module 2A: Cellular Mechanisms Controlling Animal Patterning

Instructor: Michel Bagnat

Summary: In this module, we will examine basic cellular processes that underlie patterning events in metazoans including the formation of boundaries, body segments and specific cell arrangements within tissues. We will discuss how specific programs such as segmentation are executed in different taxa and how key genetic pathways are deployed in various contexts to produce diverse patterning outcomes. To do this we will go over the common themes in patterning illustrated by classic experiments and discuss how these apply to specific examples from recent literature. Students will then take one process of their interest and identify conserved or re-purposed cellular mechanisms and how they relate to its ancestral origin.

Readings:

Chapters 2, 4, 9 and 17 of *Developmental Biology*, 11th edition, Gilbert and Barresi.
http://11e.devbio.com/index.html

Module 2B: Glycobiology

Instructor: Mike Boyce
Summary: Glycosylation is found in all kingdoms of life and underlies every aspect of cell biology. In addition, glycobiology has major implications for an enormous range of fields, from human health to renewable energy to materials science. Recently, new technologies and experimental approaches have triggered explosive progress in the modern glycosciences. This module will sample some very recent papers – all published in 2017 – on a range of glycobiology topics, with an emphasis on protein glycosylation in mammalian health and disease. Our goals will be to get an overview perspective on current research in glycobiology, and to hone our critical reading skills.

Reading: Chapter 1 of Varki *et al., Essentials of Glycobiology*, available at http://www.ncbi.nlm.nih.gov/books/NBK1931/

Module 2C: Microscopy in Cell Biology

Instructor: Lisa Cameron and Benjamin Carlson
Summary: Microscopy has been revolutionized by fluorescence and now provides a vast array of tools with which to investigate biology. This module will cover the principles and possibilities of microscopy – how microscopes and photon-based imaging systems work and what you can do with them. How do you visualize the morphology of microscopic objects using light and fluorescence? Which imaging modality is best for a particular sample? How do you gain information on the dynamics of systems such as the spatial and temporal patterns of signaling events? How do you extract quantitative information from images? We will discuss a range of techniques with a heavy emphasis on imaging living samples from microbes to vertebrate animals - widefield imaging, optical sectioning by confocals, multi-photon excitation and TIRF, protein dynamics, choosing and exploiting fluorescent proteins/probes and super-resolution microscopy. The theory and physical principles of the imaging systems will be explained in the first half of the module to a level giving understanding of how they work and guidance for optimal use. The second part of the module will be a mixture of theory and exercises in FIJI/ImageJ covering the processing, visualization and quantification of microscopy data.

See: http://microscopy.duke.edu/learn/CMB551.html

Readings:
Molecular Biology of the Cell, Alberts, et al., - Chapter 9 (focus on the sections discussing light/fluorescence microscopy)

Module 2D: The Cytoskeleton – Dynamics and Function

Instructor: Terry Lechler

Summary: This is a primary literature reading intensive course that will cover aspects of cytoskeletal dynamics and functions in reconstituted systems, cultured cells and intact organisms. Diverse topics will be discussed, which may include: the role of cytoskeleton in mitosis/cytokinesis, cell migration, cell adhesion, cell signaling, cell shape control and mechanotransduction. Preparation and active participation required.

Readings:
Molecular Biology of the Cell, Alberts et al. Chapter 16 (Cytoskeleton)

Module 3A: Understanding and Manipulating Protein-Protein Interactions

Instructor: Harold P. Erickson
Summary: Proteins are the machines of the cells. A few enzymes operate alone, but most proteins interact with others to form more complex machines. In this unit we will learn the basic principles of protein-protein interaction and bonding, and address the following questions.

How big is a protein molecule; how do you determine if it is a monomer or tetramer; how do you determine its shape? What is the structure of a protein-protein bond? How many amino acids are in contact? How does the dissociation constant relate to the strength of the bond? How fast do two proteins form a bond, and once formed how long does the complex last before it dissociates? If you want to eliminate or reduce a protein-protein bond by mutagenesis, how many amino acids to you need to change? How do you decide which ones?

Readings:
Molecular Biology of the Cell", Alberts et al.
Chapter 3 - Proteins.
Chapter 2 (to review basic biochemistry. Most important is to know the amino acids, which ones are hydrophobic, hydrophilic, charged)

Module 3B: Cell Migration / Invasion in Development and Cancer

Instructor: David Sherwood
Summary: Cell migration/invasion through extracellular matrix and tissues play crucial roles in the development, maintenance and regeneration of multicellular organisms. Inappropriate and defective cell migration also underlies numerous diseases, including inflammatory diseases (i.e. asthma, rheumatoid arthritis, multiple sclerosis, psoriasis and Crohn's disease), developmental disorders, and tumor spread. Understanding cell migration is also important for regenerative therapies, including stem-cell grafting, where defective migration/invasion is a major limitation. Cell migration takes on a variety of forms, and this course covers how cells migrate and invade as individuals, in groups as well as the plasticity of migration modes in development and cancer.

Readings: *Plasticity of cell migration: a multiscale tuning model.* Friedl P1, Wolf K. J., Cell Biol. 2010 Jan 11;188(1):11-9. doi: 10.1083/jcb.200909003. Epub 2009 Dec 1.

Module 3C: Germ Cells and Sex Determination

Instructor: Blanche Capel
Summary: This module will cover the formation, pluripotent characteristics, and male vs. female development of primordial germ cells in multiple species including Drosophila, C. elegans, fish and mammals. It will also cover sex determination and cell fate commitment in somatic cells of the gonad, including genetic and temperature/hormone-dependent mechanisms. We will likely also consider how sex chromosomes evolve and how species transition between sex determining mechanisms.

Readings:
Developmental Biology, Gilbert:
Chapter 15 - Sex Determination
Chapter 17 - The Saga of the Germ Line

Module 3D: Signaling: How Activation Leads to Specificity

Instructor: Bernard Mathey-Prevot
Summary: Detection of external cues at the cell membrane sets in motion a cascade of events that culminates in the deployment of a nuclear program, ensuring the appropriate response of that cell to an external ligand. Signal propagation is carried by a series of effector proteins that have been identified through genetic and biochemical approaches and shown to belong to distinct signal transduction pathways. The dominant view until recently had been to consider each of these pathway as a separate cassette consisting of tens of core proteins, being highly compartmentalized, hierarchical, and independent from the rest of the proteome. Recent high-throughput genetic and biochemical data suggest two major revisions to this traditional, canonical view: (1) a massive increase in the number of components linked to a particular pathway and (2) extensive crosstalk between these pathways. This new understanding, however, raises the important question of how specificity can be achieved in such a highly interconnected network.

This module will concentrate on general principles of signaling pathways. It will not dwell on an enumeration of the various components for each pathway. Rather, through students' presentations of primary research articles, we will focus on how experimental strategies and technical innovations have changed our ability to measure and follow pathway activation. We will discuss various strategies used by the cell to insure specificity, and look into the increasing role that systems biology and quantitative approaches have had on current views of signaling networks under normal and disease conditions.

Readings:

1) *Domains, Motifs, and Scaffolds: The Role of Modular Interactions in the Evolution and Wiring of Cell Signaling Circuits.* Roby P. Bhattacharyya et al., Annu. Rev. Biochem. 75:655–80 (2006)
2) *Assembly of Cell Regulatory Systems Through Protein Interaction Domains.* Pawson and Nash, Science 300:445-452 (2003)
3) *Scaffold Proteins: Hubs for Controlling the Flow of Cellular Information.* Matt C. Good et al., Science 332:680-686 (2011)

Module 4A: The Eye as a Digital Camera

Instructor: Vadim Arshavsky

Summary: We are well familiar with the metaphor comparing the eye with a photographic camera. Indeed, both rely on refraction and lenses to form images. What is perhaps less appreciated is that the eye functions as a digital camera. Information about the surrounding world reaches the back of the eye in the form of photons of variable wavelength, which are absorbed by rod and cone photoreceptor cells of the retina. The light-evoked electrical signals produced by photoreceptors are next processed by a network of retinal neurons, so that information about each point in visual space becomes digitized and reaches the brain through multiple channels, each reporting a different feature of the visual world (brightness, contrast, color, motion, etc.).

In this module, we will follow each step of this analog-to-digital transition by discussing critical experimental papers in three areas: phototransduction (the transformation of a light signal into an electrical signal); the functioning of the first synapse in the retina; and the split of visual information into multiple channels each carried by a highly-specialized type of the retinal ganglion cells. Our goal would be to integrate the findings of molecular, cellular and electrophysiological studies into a single big picture of how the retina works.

Readings:

1) Burns, M.E., Arshavsky, V.Y. *Beyond counting photons: trials and trends in vertebrate visual transduction.* Neuron (2005) 48, 387–401.
2) Masland, R.H. *Cell populations of the retina: The Proctor Lecture.* Inverst. Ophthalmol. Vis. Sci. (2011) 52, 4581-4591.

Module 4B: Intersection of Signaling and Therapeutics

Instructor: Kris Wood

Summary: It is now possible to comprehensively map the numerous genomic alterations present in individual human tumors. As a result of this stunning technological advance, we can now begin to design therapeutic strategies that function by "targeting" these alterations. However, identifying the optimal therapeutic targets for a given tumor is challenging, and this challenge is further exacerbated by the problem of drug resistance, which commonly emerges as

tumors evolve under pharmacological selection pressures. In this module, we will construct a framework for understanding the related topics of pharmacogenomics and drug resistance in cancer, discussing landmark papers that established the guiding principles in each field.

Readings:

1) McLeod, *Cancer pharmacogenomics: Early promise, but concerted effort needed.* Science **339**, 1563 (2013).
2) Glickman and Sawyers, *Converting cancer therapies into cures: Lessons from infectious diseases.* Cell **148**, 1089 (2012).

Module 4C: Stem Cells in Tissue Homeostasis and Disease

Instructor: Purushothama Rao Tata

Summary: Most tissues rely on specialized cells called stem/progenitor cells for their day-to-day turn over. Stem cells in some tissues directly differentiate into mature cells, whereas in other cases they undergo replication and generate intermediate cells which then differentiate into mature cell types. Both systemic and micro-environmental factors dynamically control the behavior of stem cells in a context dependent manner. In this module, we will be discussing how different factors such as microenvironment, cell-cell communication and cell plasticity influence stem cell behavior to control tissue homeostasis, regeneration and tumorigenesis. We will also discuss some of the new tools developed to unravel emerging concepts that are put forward in the recent years in stem cell biology.

Readings:

Developmental Biology by Scott F. Gilbert; 9th or 10th or 11th edition; Chapters- 2, 4 and 5.

Module 4D: The Biology of Cilia and Flagella

Instructor: Sarah Goetz

Summary: Cilia and flagella are microtubule-based cellular projections that perform a variety of important functions in eukaryotes including motility, generating fluid flow, and sensory perception. Non-motile primary cilia also play a critical role in modulating key developmental signaling pathways. Through critical reading of the primary literature, this module will examine the structure, function, and evolution of these important organelles. We will focus in particular on the relationship between cilia and cellular functions linked to human diseases including genetic syndromes, neurological disorders, and cancer.

Readings:

1) *Molecular Biology of the Cell*, Alberts, et al., 6th edition, Chapter 16 (Section on microtubules, pages 925-944).
2) Bangs, F. and Anderson, KV. (2017) *Primary Cilia and Mammalian Hedgehog Signaling*. Cold Spring Harb Perspect Biol. 9(5). doi: 10.1101/cshperspect.a028175.
3) Spassky, N. and Meunier, A. (2017) *The Development and Function of Multiciliated Epithelia*.

Module 5A: Organogenesis

Instructor: Brigid Hogan

Summary: Many organs of the body – for example the kidney, pancreas, lungs, ear and limbs – are composed of epithelial and mesenchymal cell populations organized into complex three-dimensional tissues with a dedicated blood and nerve supply. How are these adult organs built during development? They originate in the embryo from small collections of cells known as "primordia" that contain progenitors that will give rise to all the different mature epithelial and mesenchymal cell types. In order to understand how the process of organ development - or organogenesis - is controlled we must address many important questions. For example, we need to know how the epithelial and mesenchymal populations communicate with each other so that their proliferation and differentiation are co-ordinated, how they acquire specific 3D shapes specific to each organ and its physiological function, how blood vessels, nerves and lymphatics develop alongside the epithelial and mesenchymal components, and how adult stem cells are sequestered within the adult organ and maintain it throughout life. Answering these questions is important for many reasons: defects in organogenesis underlie many congenital abnormalities; understanding how organs develop in vivo can help us to bioengineer replacement tissues from embryonic stem cells in the lab; deciphering how different cell types cross talk during development can provide clues to processes such as tumor-stromal interactions, wound repair and aging.

In this module we will read and discuss primary research papers relevant to core processes common to the development of many organ systems: (1) Branching morphogenesis – the process by which a simple bud of epithelial and mesenchymal cells gives rise to a branched, tree-like structure with region-specific differentiation of cell types; (2) Self organization of tissues in 3D organoid cultures; (3) Tissue vascularization and innervation during development; and (4) making stem cell niches.

Readings:

1) Guillot, C., and Lecuit, T. (2013) *Mechanics of epithelial tissue homeostasis and morphogenesis.* Science 340: 1185-1189
2) Lancaster, M.A. and Knoblich, J.A. (2014) *Organogenesis in a dish: Modeling development and disease using organoid technologies.* Science 345: DOI: 10.1126/science.1247125
3) Hatch, J and Mukouyama Y.S. (2015) *Spatiotemporal mapping of vascularization and innervation in the fetal murine intestine.* Dev Dyn 244: 56-68
4) Udan, R.S., Culver, J.C. and Dickinson, M.E. (2012) *Understanding vascular development.* Wiley Interdiscip. Rev. Dev Biol. 2
5) Etzrodt, M., Endele, M. and Schroeder, T. (2014) *Quantitative single-cell approaches to stem cell research.* Cell Stem cell 15: 546-58

Optional:

1) Keller, P.J. (2013) *Imaging morphogenesis: technological advances and biological insights.* Science 340, 1234168 DOI: 10.1126/science.1234168
2) Costantini, F. (2012) *Genetic controls and cellular behavior in branching morphogenesis of the renal collecting system.* Wiley Interdiscip. Rev. Dev. Biol. 5: 693-713
3) Heisenberg, C-P., and Bellaiche, Y. (2013) *Forces in tissue morphogenesis and Patterning* (2013) Cell 153: 948-962

Module 5B: Regulation of Mitochondrial Metabolism

Instructor: Matthew Hirschey
Summary: This workshop-style module will examine how post-translational modifications can modulate the structure and function of proteins. Protein phosphorylation, ubiquitination, and acylation will be covered. As a working example, we will focus on protein acetylation, which has been shown to modify the majority of metabolic enzymes in the mitochondria. Students will be exposed to basic mitochondrial biology, including functions and dynamics, and then choose an enzyme to perform a detailed analysis of acetylation sites. Methods for identifying putative acetylation sites and performing basic structural analyses will be discussed. Students will then generate novel predictions as to how acetylation might affect their enzyme of choice. Strategies for assessing these hypotheses will also be covered. Although the focus will be on acetylation of mitochondrial proteins, the skills acquired in this module will be broadly applicable.

Readings:
1) Mitochondrial protein acetylation regulates metabolism. Anderson, K.A., and M.D. Hirschey, 2012, Essays Biochem. 52, 23–35.
2) *Molecular Biology of the Cell,* Alberts et al., - Chapter 14 (pages 813-840)

Module 5C: Regeneration

Instructor: Kenneth Poss
Summary: Questions of how and why tissue regeneration occurs have captured the attention of countless biologists, biomedical engineers, and clinicians. Regenerative capacity differs greatly across organs and organisms, and a range of model systems that use different regenerative strategies and that offer different technical advantages have been studied to understand regeneration. In this module, we will cover key concepts and mechanisms of tissue regeneration, focusing our attention on the cellular and molecular events that drive regeneration of skeletal muscle after trauma.

Readings:
1) Brack, A. and Rando, T. (2012). *Tissue-specific stem cells: lessons from the skeletal muscle satellite cell.* Cell Stem Cell 10, 504-514.
2) Poss, K. D. (2010). *Advances in understanding tissue regenerative capacity and mechanisms in animals.* Nature Reviews Genetics 11, 710-722.

Module 5D: Cell Biology of the Synapse

Instructor: Scott Soderling
Summary: How the brain is wired during development and how these connections are modified by experience are fundamental questions of neural cell biology. In this module we will cover examples of how axons navigate to properly innervate their targets. We will also cover how the synapse is formed and how the strength of the synaptic connection is modified by experience. Finally we will investigate how impairments to these processes are the basis to many neurological disorders.

Readings:
Molecular Biology of the Cell, Alberts et al.
Chapter 11 - Ion Channels and the Electrical Properties of Membranes.
Chapter 21 - Neural Development.

Module 6A: Bioinformatics and Genomics for the Biologist

Instructor: David MacAlpine
Summary: Computational biology and genomics are a mainstay of modern biology. For example, sequence alignments, identification of gene orthologs and paralogs by blast searches, and motif identification are now routine practices in the laboratory. In addition, the explosion of whole genome sequencing in the last decade has led to a variety of genomic approaches (many based on microarray technology and next-generation sequencing) to phenotype the cell at the level of gene expression and identify networks of co-regulated genes. These computational tools and genomic approaches are likely to be integral components of many research projects.

In this module, we will explore the tools and approaches to analyze next-generation sequencing data. We will make extensive use of Unix, bash scripting, and the R environment for statistical computing. The student will not only learn to critically evaluate these complex genomic experiments, but will also gain first hand experience at analyzing primary data.

Readings:
Unix Tutorial
http://www.ee.surrey.ac.uk/Teaching/Unix/

R Tutorial
http://www.cyclismo.org/tutorial/R/

Trapnell C, Roberts A, Goff L, Pertea G, Kim D, Kelley DR, Pimentel H, Salzberg SL, Rinn JL, Pachter L. *Differential gene and transcript expression analysis of RNA-seq experiments with TopHat and Cufflinks.* Nat Protoc. 2012 Mar 1;7(3):562-78. doi: 10.1038/nprot.2012.016. PubMed PMID: 22383036; PubMed Central PMCID: PMC3334321.

Module 6B: Nuclear Structure/Gene Regulation

Instructor: Eda Yildirim
Summary: Understanding how transcriptional status of genes are established, maintained, and regulated is crucial to answer the questions of how diverse cellular functions are orchestrated during development of multicellular organisms. During recent years, it has become evident that gene expression is controlled not only on the basis of DNA sequences at the promoter and enhancer elements, but at the epigenetic level by elements of nuclear structure. These include chromatin modifications of DNA and histones, noncoding RNA-mediated epigenetic regulation, higher-order chromatin arrangements and variable aspects of nuclear architecture. In this module, we will discuss key papers that reveal these levels of gene regulation. We will be learning to approach these exciting papers critically and design experimental ways to test and explore this new area of Cell Biology.

Readings:
Molecular Biology of the Cell, Alberts et al.
Chapter 4 - Overall Chromatin Structure (limit to pp. 202-245, in 5th edition)
Chapter 7 - Overview of Gene Control (limit to pp. 411-432, in 5th edition)
Chapter 12 - Overview of Nuclear Structure (limit to pp. 704-712, in 5th edition)

Module 6C: Genome Instability

Instructor: Don Fox
Summary: Protection of the genome is key to maintaining normal cellular function. Numerous safeguards exist to detect genome alterations and potential cell division errors, thus maintaining a stable genome. Failure in such regulation leads to genome instability. A variety of human diseases are derived from genome instability, including diseases of aneuploidy such as trisomies. Genome instability is also present in cancer, and a current debate in the literature is whether genome instability is a major cause, rather than a consequence, of cancer.

In this module, we will take a look at recent literature on causes and consequences of genome instability in various model systems and in human disease. In the six papers we will discuss, the wide range of concepts discussed will include cell cycle checkpoints, aneuploidy, and cancer genomics. Methods used in the papers will similarly cover a wide range of genetic, molecular, and cell biological assays. Most importantly, this class is geared towards developing critical literature analysis skills.

Readings:
1) Gordon DJ, Reiso B, and Pellman, D. (2012). *Causes and consequences of aneuploidy in cancer.* Nature Reviews Genetics 13, 189-203
2) Optional reading (if further background is needed): Alberts et al, Chapter 17 (The cell cycle).

Module 6D: Humans as Model Organisms

Instructor: Vann Bennett

Summary: Translational research is frequently viewed as the application of established principles of basic science to promote human health. This section will develop the theme that deciphering the molecular basis for human disease can be far from straightforward, and both require and contribute to elucidation of new fundamental biology. We will focus this year on nervous system-related diseases, beginning with Creutzfeldt-Jacob and related neurodegenerative disorders where molecular breakthroughs have led to the prion concept. We will then consider Alzheimer's disease, where genetic mutations and risk factors are known, but the pathophysiology is still unresolved. We will end with discussion of autism, which since 1980 has transitioned from a rare disorder to one affecting 1% of the population. Autism is heritable and autism susceptibility genes are known. However, autism still lacks a unifying concept and is an attractive target for future research.

Readings:

1) Pruisner's Nobel Lecture (.pdf)

*Research Proposal Workshop

The workshop is for **first year students only**, that is students taking CMB551 for the first time.

The goal of the workshop is to familiarize you with the process of designing and critiquing research proposals in basic science. Before the first class, each pair of students in your group will submit an Abstract summarizing their potential research question. It is important that you try to come up with a significant question and your abstract will need to include specific information on what you wish to address, rather than state a general area of interest. The format on the workshop will be based on class discussions, directed by instructors. Each Abstract will be discussed and critiqued based on the value, significance and feasibility of the question under study. It will be an iterative process of revising and refining the Abstract, with eventually the inclusion of specific Aims, once the research question has been fully fleshed out. Final grades are based on a combination of the final revised proposal and class participation.

Assignment for first class: submit an Abstract.

Class 1: **Submit an Abstract describing your choice of research topic to be developed**

Class 2: **Discussion of the merit and pitfalls of the submitted Abstract**

Class 3: **Refinement of the question or abstract and elaboration of aims**

Class 4: **Final discussion of the proposal**

Suggested reading:

Readings: NIH/NSF criteria[1] and
http://www.asbmb.org/asbmbtoday/201404/PresidentsMessage/

[1]Criteria put out by NIH and NSF:

NIH-Significance: Does the project address an important problem or a critical barrier to progress in the field? If the aims of the project are achieved, how will scientific knowledge and/or technical capability be improved? How will successful completion of the aims change the concepts, methods, or technologies that drive this field? *Choosing a topic is about Significance criterion.*

NIH-Innovation: Does the application challenge and seek to shift current research paradigms by utilizing novel theoretical concepts, approaches or methodologies? Are the concepts, approaches or methodologies novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies proposed? *Not always necessary.*

NIH-Approach: Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of

development, will the strategy establish feasibility and will particularly risky aspects be managed?

NSF-Intellectual Merit: The potential to advance knowledge and understanding within its own field or across different fields. To what extent do the proposed activities suggest and explore creative, original, or potentially transformative concepts? *Choosing a topic is about this.* Is the plan for carrying out the proposed activities well-reasoned, well-organized, and based on a sound rationale? Does the plan incorporate a mechanism to assess success?

NSF-Broader Impacts: The potential to benefit society and contribute to the achievement of specific, desired societal outcomes.