The Cell and Molecular Biology core course (CMB551) offers 27 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: [http://cmb.duke.edu//program/cmb-core-courses](http://cmb.duke.edu//program/cmb-core-courses)

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 24, 2015:**
[https://duke.qualtrics.com/jfe/form/SV_6R0iBYoILvJwUbr](https://duke.qualtrics.com/jfe/form/SV_6R0iBYoILvJwUbr)

There will be a **short** online **entrance tests** on the reading materials for all topics on the first day of class (Aug 24th). 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. 26th.**

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 **11th of December.**

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 11) when you make plans for traveling in preparation for your holiday break.

Course Director:
Bernard Mathey-Prevot: bernard.mathey-prevot@dm.duke.edu, 684-8043, C104A LSRC
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<th>Module</th>
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<td>Module 1</td>
<td>Aug 26</td>
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<td>Johnson Microscopy in Cell Biology</td>
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<td>Lew Controlling the Cell Cycle</td>
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<td>Module 2</td>
<td>Sept 9</td>
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<td>Bagnat Cellular Processes Driving Morphogenesis</td>
<td>Buchler Genetic switches and oscillators</td>
<td>Nicchitta Sensing and Signaling Cell Stress</td>
<td>Eroglu Cell-Cell Interactions</td>
<td>Mathey-Prevot Signaling: How Activation Leads to Specificity</td>
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<td>Sept 23</td>
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<td>Poss Regeneration</td>
<td>Sherwood Cell migration/invasion in Development and Cancer</td>
<td>Boyce Glycobiology</td>
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<td>Oct 7</td>
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<td>Arshavsky The Eye As A Digital Camera</td>
<td>Yildirim Nuclear Structure/Gene Regulation</td>
<td>Lechler The Cytoskeleton – Dynamics and Functions</td>
<td>Hirschey Regulation of Mitochondrial Metabolism</td>
<td>Capel Germ Cells and Sex Determination</td>
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<td>Oct 23</td>
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<td>Wood Intersection of Signaling and Therapeutics</td>
<td>Bennett Humans as model organisms</td>
<td>Fox Genome Instability</td>
<td>Di Talia Quantitative Cell and Developmental Biology</td>
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<td>Module 6</td>
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<td>Soderling Cell Biology of the Synapse</td>
<td>Muoio Metabolism: Cell Biology to Systems Physiology</td>
<td>Hogan Organogenesis</td>
<td>MacAlpine Bioinformatics and Genomics for the Biologist</td>
<td>Kuehn Cell Biology from a Bacterial Perspective</td>
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Module Descriptions:
Module 1A: Microscopy in Cell Biology

Instructor: Sam Johnson
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 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: Stem Cells and their Molecular Regulation

Instructor: Chuan-Yuan Li
Summary: In this module, we will read original papers describing the discovery of mouse and human embryonic stem cells, the invention of methods to reprogram differentiated cells into induced
pluripotent stem cells, and the identification of human cancer stem cells. We will also discuss several studies that describe the molecular mechanisms regulating normal and cancer stem cells. We hope to understand some of the basic concepts, important questions, and unresolved controversies in stem cell biology research.

Readings:
2) Induced Pluripotent Stem Cells: Past, Present, and Future. Cell Stem Cell 10, 678-684 (2012);

Module 1D: 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 2A: Cellular processes driving morphogenesis

Instructor: Michel Bagnat
Summary: We will cover some of the basic cellular processes controlling several key morphogenetic events in metazoans. We will discuss genetic and cell biological approaches for studying morphogenesis and how these are being changed by new biophysical, modeling and physiological models. We will discuss from a cell biological perspective: Meeting 1: symmetry breaking events and early embryonic patterning (AP and DV axis, embryonic layer separation LR asymmetry, etc.); Meeting 2: morphogenetic movements and axis elongation (migration, intercalation, etc.); Meeting 3: morphogenetic movements and organogenesis (epithelial folding, invagination, budding, etc.); and Meeting 4: tubulogenesis; Meetings 5,6: Two sessions of “chalk-talk” presentations of key papers by students.

Readings:
1) Molecular Biology of the Cell, Alberts, et al., Fifth Edition - Chapter 22 (Development of Multicellular Organisms)


Papers will be assigned for each class.

Module 2B: Genetic switches and oscillators

Instructor: Nicolas Buchler

Summary: Genetic switches and oscillators are essential for proper patterning, cell proliferation, and cellular differentiation in biological systems. This "systems biology" module will cover the underlying principles behind epigenetic switches (bistability) and clocks (oscillators) in gene networks. I will also discuss the origins and consequences of molecular noise in biological networks. My goal is to make you literate enough to read a "systems biology" paper, understand how the authors transform a biochemical model into equations, and use basic computer simulations to run and critically evaluate the modeling conclusions. This module will require an understanding of calculus (derivatives, integrals).

Readings: Molecular Biology of the Cell, Alberts et al., - Chapter 7 (Control of Gene Expression, all sections up to Post-transcriptional Controls)

Module 2C: Sensing and Signaling Cell Stress

Instructor: Christopher Nicchitta

Summary: The biological consequences of protein misfolding are often lethal and “proteinopathies” (diseases of protein folding), including Alzheimer’s, Parkinson’s, Type II diabetes, cystic fibrosis, and prion diseases, now number in the hundreds. Given the potentially lethal outcome of protein misfolding, the question of how cells respond to the accumulation of unfolded proteins has proven to be both critically important and fascinating.

Many forms of cell stress, including glucose deprivation and oxidative stress, disrupt protein folding through effects on post-translational modifications of secretory and integral membrane proteins. These experimental findings provided a useful entry point for investigations into the cellular response to the accumulation of unfolded proteins. In this module we will discuss, in depth, landmark papers that report the discovery of the Unfolded Protein Response (UPR), an endoplasmic reticulum-based regulatory response to the accumulation of unfolded proteins. We will trace the field from its inception - how was a cellular response to the accumulation of unfolded proteins discovered? - to current research, which has identified critical roles for the UPR in development and human disease.

Readings:
Module 2D: Cell-Cell Interactions

Instructor: Cagla Eroglu

Summary: Coordinated communication between individual cells is crucial for their organization into tissues, organs and systems that comprise the body plan of multicellular organisms. To orchestrate this complex organization each cell should be capable 1) of exchanging chemical signals between each other 2) of sensing chemical, physical or mechanical cues from its immediate environment 3) of integrating these external cues to alter cellular functions.

Membrane proteins are central players in cell-cell interactions. For instance, they form tight junctions that serve to attach neighboring cells together and prevent passage of substances between the two cells. Other surface proteins are involved in cell-cell recognition (e.g. immunological synapse). Other membrane proteins serve functions in communication between the inside of the cell and the cell’s immediate environment (e.g. focal adhesions).

The module will encompass cellular and molecular approaches to understand the components and properties of cell-cell interactions. Examples from the literature will integrate diverse experimental approaches ranging from genetic screens to biophysics. In this way we hope to examine intercellular signaling mechanisms from multiple experimental angles.

Readings:
Molecular Biology of the Cell, Alberts et al.
Chapter 15 - Cell Communication
Chapter 19 - Cell Junctions, Cell Adhesion, and the Extracellular Matrix

Module 2E: 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:

Module 3A: 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:

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:

Module 3C: 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 2015 – 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.


Module 3D: 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 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:

Module 4B: 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.
Module 4C: 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 4D: 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:
2) Molecular Biology of the Cell, Alberts et al., - Chapter 14 (pages 813-840)

Module 4E: 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 5A: 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:

Module 5B: Humans as Model Organisms

Instructor: Vann Bennett

Summary: This section will develop the theme that study of human disease has led to fundamental insights into biology, and with emerging tools is likely to be a very productive area for future research. We will focus on how studies of anemia, heart disease, Alzheimer’s disease, and Bardet Biedel syndrome have resulted in major contributions of broad scientific significance. We also will discuss papers utilizing new methodologies to explore disease mechanisms including whole genome/exome sequencing of kindreds, caspr/cas9 gene editing, and patient-derived iPS cells. Students will benefit from basic knowledge in cell biology, biochemistry, and physiology.
Readings: This course will focus on lessons from human mutations resulting in monogenic disease. To place these examples in context, it would be helpful to read the following articles reviewing current knowledge of the genetic basis for complex diseases.


Module 5C: 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:
2) Optional reading (if further background is needed): Alberts et al, Chapter 17 (The cell cycle).

Module 5D: 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

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**Module 6A: 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.

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**Module 6B: Metabolism: Cell Biology to Systems Physiology**

**Instructor:** Deborah Muoio  
**Summary:** Control of energy metabolism is accomplished via an intricate network of interdependent biochemical pathways that encompass various subcellular compartments in multiple organ sites. Diseases of metabolic dysregulation (e.g. obesity, diabetes, heart disease) have become increasingly prevalent and now pose an escalating threat to global health. Development of novel pharmacotherapies to successfully combat this epidemic requires comprehensive understanding of the metabolic and signaling circuitry controlling energy homeostasis. This module will cover basic strategies of integrative metabolism; with emphasis on bridging molecular nutrition to whole body physiology.

Discussions will center on tissue-specific metabolic responsibilities, the resident machinery that enables these functions, key biochemical junctions and principal regulatory sites. Examples of specific topic areas to be addressed include; nutrient sensing and mechanisms of nutrient-induced gene regulation, substrate partitioning between catabolic and anabolic fates, and inter-organ trafficking of fuels. We will review several landmark discoveries of the genomics era that have provided a deeper,
molecular view of metabolic control. Additionally, we will critically evaluate recent papers describing gene knockout or transgenic mouse models that have produced unanticipated metabolic phenotypes.

Readings: from Biochemistry, Sixth Edition 2007 (Stryer)  
Available at: (http://www.ncbi.nlm.nih.gov/books/NBK21154/)  
Chapter 15 Metabolism: Basic Concepts and Design  
Chapter 27 Integration of Metabolism

Module 6C: 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:

Optional:

Module 6D: 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/


Module 6E: Cell Biology from a Bacterial Perspective

Instructor: Meta Kuehn
Summary: Bacteria have learned much cell biology during their evolution alongside eukaryotes. They have established relationships with eukaryotes that range from symbiotic and amicable to downright lethal. We will explore eukaryotic features and processes taken advantage of and taken control of by bacteria. We will discuss bacterial-cell membrane interactions and how these lead to endocytic events by co-opting the signaling and cytoskeletal dynamics of the cell. We will also observe how intracellular bacteria can propel through the cytoplasm via comet tails of actin. We will discuss how bacteria can traffic to a safe haven inside cells. We will further discover how some bacterial products have been exploited for cell-biological manipulations that help us in the laboratory today.

Readings:
*Molecular Biology of the Cell*, Alberts et al.
Chapter 13 - Lysosomes, Endocytosis
Chapter 16 - Cytoskeleton (esp. Actin).
Research Proposal Workshop

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

Assignment for first class: submit a potential research question. Max 100 words.

The goal of this workshop is to familiarize you with the process of designing and evaluating research proposals in basic science. It is important that you try to come up with a good research topic before the first class: this needs to indicate what question you would address (not just a general area). Feel free to discuss this with colleagues, mentors, or instructors. In class, we will discuss your ideas, and you will need to come up with more polished ideas for each class. On the last day we will have a NIH-style study section in which proposals will be evaluated by your colleagues. Final grades are based on a combination of the final revised proposal, the written reviews of other proposals, and class participation.

Class 1:  How do I come up with an interesting proposal topic?
Class 2:  How do I come up with a viable proposal topic?
Class 3:  How do I evaluate a proposal?
Class 4:  Study section

\(^1\)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.