2023 MOLECULAR BIOSCIENCES MINICOURSE DESCRIPTIONS

HUAYE ZHANG: *PEEKING INTO THE BRAIN (16:695:621:13061)*

Description: This minicourse will highlight recent in vivo imaging studies of cellular dynamics i n the brain during physiological and pathological processes, as well as novel mechanisms underlying these processes. The latest advances in cutting edge imaging methods will also be discussed. After successful completion of this course, students will have a good understanding of the in vivo imaging approaches used to understand brain functioning. In addition, students will learn to present and critically evaluate scientific literature.

Grading: Students are expected to attend all classes and actively participate in discussions. At the end of the course, students will write a paper (~1000 words) discussing future avenues of research in the field of in vivo brain imaging. The final paper will constitute 80% of the grade and participation in class will be 20% of the grade.

ANDY SINGSON: *GENETICS & CELL BIOLOGY OF FERTILIZATION (16:695:622:13062)*

Description: The union of sperm and egg is required for the propagation of all sexually reproducing species. The underlying molecular mechanisms of fertilization are also paradigms for other important cell cell interactions during development. After successfully completing this course, students will have gained a broad perspective of the field of fertilization that will include a historical point of view as well as an understanding of the current challenges in reproductive biology.

KAREN SCHINDLER & SHUO XIAO: *HOW TO MAKE A GOOD EGG: A MOLECULAR PERSPECTIVE (16:695:623:13063)*

Description: Production of high-quality gametes is essential for sexual reproduction. In females this process takes place within the follicle, a supporting structure and functional unit of the ovary. This process is highly error prone, affected by aging exposure to reprductve toxicants and many disease states. Students will learn about the latest technological advances that clinicians use to select quality eggs, developments in contraception and in fertility preservation.

Structure: The course will provide a mixture of lecture, active learning and primary literature discussion.

Outcome: After taking this course, students will have a working knowledge of the ovarian processes involved in generating developmentally competent eggs, understand exposures and disease states that impact egg quality. They will be able to synthesize biomedical findings to communicate the implications of these finds in writing to an audience with broad scientific knowledge.

Grading: Students will be graded on attendance and participation (10%) and production of 2 "News and Views" style writing assignments (90%).

DAVID AXELROD: *MODELS OF HUMAN CANCER (16:695:624:13064)*

Description: Model systems have provided information about aspects of human cancer not available directly from humans. Models include viruses, bacteria, yeast, cell lines, organoids, worms, flies, fish, mice, microfluidic systems, mathematical, and computational models, etc. The information includes molecular and cellular aspects about tumor initiation, progression, evolution,

invasion, metastasis, prevention, and therapy. The instructor will introduce unmet challenges of human cancer, and a survey of model systems, with references to published review articles. Each student will select any model system that has been used to illuminate a cancer problem. Each student will make a presentation reviewing experimental articles about the selected model system, lead a discussion, and write a two-page letter of intent arguing for the use of their selected model system to illuminate a particular cancer problem.

Grading: Grades will be based upon each student's presentation (40%), participation in discussion of other students' presentations (10%) , and each student's two-page letter of intent (40%).

SUBHAJYOTI DE: ***APPLICATION OF NEXT-GENERATION SEQUENCING TECHNIQUES (16:695:625: 17574)***

Description: Next generation sequencing (NGS) technologies allow us to sequence DNA and RNA quickly and cheaply than that was previously possible, revolutionizing the study of genomics and molecular biology, ultimately guiding clinical decision making in Precision Medicine. The mini-course will comprise of 6 instructed sessions and one hands-on tutorial session, and a mini-essay will be due in the last session. In an instructional session, first I will give an overview of the topic, guided by a classic review paper. Then, one (or two depending on the class strength) student(s) will present a research paper engaging the class in a scholarly group discussion. The students will learn about the emerging applications of the next generation sequencing technologies, best practice guidelines, key considerations during design of experiments, and interpretation of results.

Grading: Grading will be based on (i) participation in the discussion during the instructed sessions, and (ii) a mini proposal (~1000 words) due in the last class. The proposal will describe a possible NGS-based investigation the student might conduct in their area of research interest outlining Significance, Approach, and Expected Results and potential pitfalls in ~1000 words. Grading will be relative, and will be based on intuitive thinking in classroom setting (rather than domain knowledge).

KIRAN CHADA: ***REGENERATION – ALL CUT UP TO BE (16:695:626:13065)***

Description: Regeneration involves the replacement of missing organs, appendages, or large body regions and has always been fascinating at the gross and morphological level. The course will detail the recent tremendous advances that have been made at the cellular and molecular level using highly regenerative model organisms. These studies will identify principles that explain how regeneration can occur so as to provide an understanding into this biological phenomenon. Additionally, these insights have also revealed common molecular pathways that are used in non-regenerating systems.

Grading : During each session, 1-2 students will give a presentation of the cellular and molecular basis of the regenerative capacity of a single organism. It is expected that all the students will have read the paper that forms the basis of the presentation and will participate in the discussion after the presentation. Students are expected to attend all classes. The presentation will constitute 50% of the grade, class participation 25% and 25% on a 3-5 page paper on regeneration in mammals.

PAUL MANOWITZ: ***MEDICAL MYSTERIES (16:695:627:13066)***

Description: This mini-course will pose unique problems in genetics, metabolism, and/or biochemistry of seven human diseases in order to explore recent advances in their causes and treatments. These diseases are severely debilitating and in some cases fatal. During each session, one or two students will discuss a scientific paper that presents recent advances on an aspect of the disease. The class will work as a team during the session to better understand these diseases. In addition, each student will be asked to write a 3-5 page critique of the paper he/she presented in class with emphasis on the questions that this paper poses.

HONGHUA LI: ***APPROACHES TO GENE THERAPY (16:695:628:13067)***

Description: Gene therapy is a fast-growing field in biomedicine with major impact on treatment of many diseases that are not limited to genetic disorders. The proposed course covers the major concept (one hour), approaches (four hours) and clinical applications (two hours) with emphasis on approaches. The course completes with a brief summary and an essay exam (one hour).

Structure: A combination of reputable review articles and primary literature will be used as reference handout. Students are required to read the assigned handout for each class. One student will give a brief presentation to the class followed by comments of all other students. The amount of time for each student will be allocated based on the number of students. Instructor will give a summary of the class and provide important supplementary information that is not covered by the reference and class discussion to conclude the class.

Outcome: The class will expose students to the major aspects of the fast advancing field of gene therapy which will become one of the powerful tools in clinical practice and involves both basic research and clinical practice. Knowledge and training in gene therapy may let students gain advantage and become a great option in their career development. In addition, gene therapy can be used as a powerful tool in research and many other applications in biomedicine, for example, combatting deadly viruses including COVID-19.

Grading: Three aspects will be taken into consideration to determine the grades: 1. quality of presentation, 35%; (2). participation of class activities, 25% and (3) essay, 40%.

RANDY MCKINNON: ***STEM CELL THERAPY (16:695:629:13068)***

Description: Stem cells are important source for healthy tissue regeneration. This course will examine the primary literature detailing the identity and function of both pluripotent and tissue specific stem cells. The emphasis will focus on molecular mechanisms of signal transduction processes and their nuclear regulatory factor targets that dictate stem cell identity. Students will also gain skill sets necessary to critically read, evaluate and present scientific data from the biomedical literature.

WENWEI HU AND ZHAOHUI FENG: P53 ***(16:695:630:13069)***

Description: p53, which was discovered in 1979, is the most frequently mutated tumor suppressor gene in human cancer. In the past 30 years, the function of p53 has been the subject of intensive research, and new revelations about p53 function have not declined with age. p53 functions as a node in numerous signaling pathways to regulate many important biological activities. In addition to its pivotal role in tumor suppression, recent studies have shown that p53 is critically involved in many other physiological and pathological processes. Furthermore, it is clear that p53 is therapeutically important and many approaches are being taken to reconstitute its function in tumors. In this course, we will introduce some of our current understanding of p53

function by giving 1 lecture and using 7 examples from the current literature. Students that successfully complete this course will gain a rich knowledge of tumor suppressor p53 and its signaling pathway on cancer and other diseases. This knowledge and concepts will be also very useful for their future research on cancer research and molecular biology. In addition, students will learn the skills to critically evaluate the literature and scientifically present a paper.

Grading: Students will primarily be graded on active participation and scholarly presentation of their assigned papers within each class session. No exam will be given.

KIRAN MADURA: ***NUCLEOTIDE EXCISION REPPAIR: MOLECULAR MECHANISMS & CLINICAL RELEVANCE (16:695:631:13070)***

Description: Nucleotide Excision Repair (NER) is an evolutionarily conserved DNA repair mechanism that targets bulky, DNA distorting lesions; a central feature that permits the repair of a diverse range of damage. Notably, this mechanism is largely error free. The molecular mechanism of NER has been determined at the atomic level, and the critical steps observed in bacteria and yeast are fully conserved in human. Mutations in NER cause a number of diseases in human, including xeroderma pigmentosum (XP), Cockayne Syndrome (CS), and trichothiodistrophy.

This mini-course will summarize the key findings discovered in E. coli and yeast, and proceed to illuminate the greater complexity observed in humans. The underlying biochemical details and primary experimental approaches will be discussed.

Each lecture will cover an important element of this repair pathway and will be accompanied by 1-2 papers. Although Dr. Madura will discuss each paper during the lecture, it is expected that the participants will be familiar with the material so that we can engage in a productive discussion.

Organization: Dr. Madura will present all the lectures. Relevant publications pertinent to each lecture will be provided, and students are expected to review these studies before each lecture.

Grading: Attendance to all lectures is mandatory, and participation in discussion is expected. A final exam will be conducted during the last lecture period.

BEATRICE HAIMOVICH: ***TOLL-LIKE RECEPTORS IN HEALTH AND DISEASE (16:695:634:13072)***

Description: All toll-like receptors (TLRs) family members are activated by signals produced by invading microorganisms. However, several TLRs also activated by signals derived from damaged host tissues and/or bacteria that live in the gut. In this course we will examine mechanisms by which TLRs regulate inflammatory responses, and link these processes to host homeostasis as well as human diseases. After successfully completing this course students will have a working knowledge of topics that extend from TLRs to cell signaling, host immunity, and immune cells interaction with the gut microbiome. The classes require active participation and will emphasize students-led critical evaluation and discussion of assigned current literature.

PAUL COPELAND AND TRACY ANTHONY: ***INTEGRATED STRESS RESPONSE – A PARADIGM FOR TRANSLATIONAL CONTROL (16:695:632:*****13071*****)***

Description: (taken in part from Costa-Mattioli and Walter, 2020): The integrated stress response (ISR) is an intracellular signaling program that is required for an organism to adapt to a variable environment and maintain health. In response to a variety of environmental and pathological conditions, including protein homeostasis (proteostasis) defects, nutrient deprivation, viral infection, and oxidative stress, the ISR restores balance by reprogramming gene expression. The

various stresses are sensed by four specialized kinases that converge on phosphorylation of a single serine on the eukaryotic translation initiation factor eIF2 (gene = EIF2S1). eIF2 phosphorylation blocks the action of eIF2's guanine nucleotide exchange factor termed eIF2B, resulting in a general reduction in protein synthesis. Paradoxically, phosphorylation of eIF2 also triggers the translation of specific mRNAs, including key transcription factors, such as ATF4. As such, the mechanistic underpinnings of this stress response network lie solidly in the world of post-transcriptional gene regulation at the translational level. This course will delve into the mechanism and methodology behind this essential stress response pathway, aberrations in which cause a myriad of diseases.

Grading: Student presentations of a paper will count toward 75% of the grade. The remaining 25% will be in the form of a concise (1-page) written project that requires answering a qualifying exam-type question based on a literature search and identification of lynchpin experiments.

JIM MILLONIG & EMANUEL DICICCO-BLOOM: ***NEURODEVELOPMENTAL DISORDERS (16:695:635:*****13073*****)***

Description: The goal of this course is to teach the molecular, developmental and genetic bases of autism spectrum disorder and related Mendelian diseases (e.g., Fragile X, Rett, Tuberous Sclerosis and Timothy syndromes). Each week seminal papers will be discussed by Emanuel DiCicco-Bloom MD, a developmental neurobiologist and child neurologist, and Jim Millonig PhD, a molecular geneticist. Papers will be selected that have led to greater understanding of the underlying pathology and the development of new treatments. A variety of cutting edge techniques such as immortalized pluripotent stem cells (iPSCs) will be introduced and the positives and negatives of these approaches will be discussed. Each week one disease will be examined with Dr Millonig leading the molecular genetic aspects while Dr DiCicco-Bloom will focus on the developmental studies. By the end of this minicourse students should have a greater understanding of these diseases, how scientific advances have led to the development of new treatments and the challenges facing the generation of new therapies.

BRIAN DANIELS: ***PROGRAMMED CELL DEATH AND INFLAMMATION (16:695:636:13074)***

Description: Cell death is a fundamental biological process that shapes diverse aspects of organismal health and disease. Programmed cell death (PCD) in the form of "apoptosis" is a widely known mechanism by which damaged, infected, or otherwise compromised cells are removed from tissues. However, recent work has described an ever-growing number of PCD modalities, including necroptosis, pyroptosis, and others, that represent distinct mechanisms of cellular demise. Importantly, we now understand that the manner in which a cell dies is a critical determinant of how the cell death event regulates the local tissue microenvironment, particularly as it relates to inflammation. In this course, we will explore the similarities and differences among different PCD types and discuss the role each plays in shaping the immune response in a variety of physiological settings.

Structure: We will alternate two primary session types each week. "Group Tutorial" sessions will include a brief lecture to provide background and context for each type of programmed cell death we cover in the course, supplemented by short presentations from students highlighting interesting or important aspects of that cell death program, taken from primary literature. In contrast, "Paper Discussion" sessions will be more traditional journal club style discussions of important recent papers in this area, with targeted discussion and critical analysis of experimental design, data analysis, etc.

Outcome: With the ongoing description of novel types of programmed cell death (PCD), there is an explosion of research interest in how PCD shapes human health and disease. Students will benefit from expanding their knowledge of cell death beyond textbook descriptions of apoptosis and gain exposure to the growing interdisciplinary field of PCD studies.

Grading: Students will primarily be graded on active participation and scholarly presentation of their assigned figures and/or topics within each class session. Rubrics will be provided to clarify grading criteria for all assignments. No exam will be given.