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When: Tuesdays, Time: 1:45pm—3:45pm

Where: BRB 601

Goals:

- 1) Become familiar with the major principles of how the cell cycle machinery operates and is regulated by DNA damage checkpoints, examine how these and other processes are utilized to facilitate DNA repair and govern telomere maintenance, and learn how viral mimicry can be studied to better understand these mechanisms. The ways in which perturbation of the cell cycle, DNA damage checkpoints, and repair machinery can both promote cancer and be capitalized upon for cancer treatment will be illustrated.
- 2) Develop and practice the key academic skills that you will need throughout your careers: critical analysis of the literature, oral presentation of scientific information, writing reviews of the literature, proposing experiments, listening actively to and digesting scientific presentations, meeting professional deadlines, and providing critical/constructive criticism.

Structure:

This is a seminar course, with an additional requirement for a short (review) paper. Each week one or two students will present a seminal paper in the field. The student will first present a brief history of the topic (see list of topics below) and establish why the work was done. The paper will then be analyzed, figure by figure, through student participation. A summary will be made of the important findings. Unanswered questions and directions for future work will be presented, accompanied by a class discussion. A designated faculty member (coach) will meet with the student before the presentation to offer advice and help ensure that the topic is addressed well, for the benefit of the presenter and the rest of the students. The same faculty member will attend the presentation and provide feedback. A short review of recent important papers on a topic germane to the course will be written and turned in at the end of the course.

Content:

The course topics are chosen to familiarize the student with the key principles, the most productive experimental systems, and the seminal studies from an exciting past twenty years of cell cycle and DNA damage/repair research. Primary literature will be used to illustrate the impact of perturbations in both cell cycle regulation and genome surveillance mechanisms on neoplastic growth. The topics will unfold by focusing on major classes of cell cycle regulatory proteins, mechanisms of their regulation, critical cell cycle transitions, and their importance for normal cell proliferation. We will subsequently consider surveillance/checkpoint mechanisms that are activated by perturbation in genome integrity and determine cell fate.

<u>Date</u>	<u>Topic</u>	<u>Faculty coach</u>
09/06/22	Course orientation	David Feldser
09/13/22	CDK/Cyclins	Luca Busino
09/20/22	No Class	
09/27/22	Mitosis and the spindle assembly checkpoint	Michael Lampson
10/04/22	Molecular basis of tumor suppressor function	Ronen Marmorstein
10/11/22	Oncogenic stress and the DDR	Donita Brady Yes
10/18/22	CDK Inhibitors	Kelly Jordan-Sciotto
10/25/22	Homologous Recombination and Cancer	Roger Greenberg
11/01/22	Secreted factor responses to DNA damage	Andy Minn
11/08/22	Genotoxic stress and clonal evolution	Bobby Bowman
11/15/22	Chromatin and DNA repair	Paul Lieberman
11/22/22	Transcription and Genome Stability	Irfan Asangani
11/29/22	Synthetic lethality and Genetic screening	Junwei Shi
12/06/22	DNA damage responses to viruses	Matt Weitzman
12/13/22		
12/20/22		

Grading:

Presentation	25%
Oral participation	25%
Problem sets	25%
Attendance at PCGI Talks	25%

Presentation:

- a) Copies of all papers for presentation will be available on Canvas. Once the enrollment is finalized, students will be assigned presentation topics covering the rest of the course. If the date confers an unusual hardship, you may ask the directors to switch. Presentations should be in the form of a PowerPoint presentation.
- b) We will supply you with a short list of suggested references and reviews for each topic by the 2nd class meeting. Your presentation will focus on one paper, or in rare cases two (related) papers. If you would like to present a paper that is not on the list, please obtain approval from the faculty coach well in advance of your presentation date. With the exception of the presentation in the course (week two), one should choose a paper no less than three weeks before your presentation date, which gives guest lecturers (coaches) time to write a problem set and work with the presenter on the paper topic. In addition, your fellow students will then have ample opportunity to read and evaluate the chosen paper.
- c) Please feel free to chat with presentation coaches at any point as you choose or try to understand the chosen paper. Your final discussion with coaches should be no later than the Monday prior to your presentation date. You should have specific questions in mind, and you

may wish to discuss your presentation and PowerPoint slides. The more you prepare beforehand, the better the guest lecturer can help you.

- d) In general, the introduction (~30 minutes) should provide the appropriate context of the paper in the general field and highlight the underpinnings of the main question(s) addressed by the study. The introduction does not need to cover the whole area of research but should provide your fellow students with essential background information to evaluate the study and illustrate the reasons the authors investigated this biological question. Presentations should describe reasoning behind the experiments, the results and controls, and the interpretation of the findings by the authors. The experiments in the paper should be analyzed using the scientific method: observation, hypothesis, expectation if correct, experimentation, and conclusion. The logic and controls used should be discussed to determine the validity of the conclusions. At the end, each presentation should summarize the results for the class to evaluate the validity of each part of the paper. Finally, future directions and implications of the study should be discussed.
- e) After your presentation, faculty and the teaching assistant for the course will give you critical feedback to help you in the future.

Participation

Oral participation (25%): We seek to foster a supportive atmosphere in the class while maintaining scientific rigor, keeping people engaged, and learning as much as possible. Asking questions and making comments helps the presenter know if he/she is getting through. In addition, listening actively, assimilating scientific material, and asking questions that clarify or stimulate thought are useful scientific skills that can be honed by practice. There are no bad questions at this stage of your careers and admitting some ignorance is better in the long run. If you are unsure about something, chances are others are as well. To underscore these notions, we include participation as a significant part of the final grade. Students are expected to read each paper carefully in advance of the class. Everyone is expected to actively participate in the discussion each week; in other words, you should come prepared to ask questions, both philosophical and technical, each week. Grades will ultimately reflect your level of engagement each week. Active listening, assimilation of scientific material, and asking questions that clarify or stimulate thought are useful scientific skills that can be honed by practice.

Problem Sets (25%): To facilitate discussion and a more thorough understanding of the material presented in the weekly paper, students will be provided with 3-5 questions by the faculty coach/moderator, 1 week before the paper is presented/discussed. Students are expected to provide written answers (short answer) to be handed in for a grade. However, students are encouraged to use these questions (and their preferred answer) as a point of discussion when the papers are presented. In other words, the extra work here will facilitate better participation and contribute to oral participation!

Attendance at Penn Center for Genome Integrity (PCGI) Talks (25%):

PCGI holds weekly seminars from trainees around campus that are working in the broad field of genome integrity. Attendance at these project-update talks is intended to provide a broad overview of the ongoing research topics and approaches used by our colleagues. This is also an easy way to become immersed in the culture of the PCGI. Talks are held on Monday's at 4:00 PM—Location TBD. In the event that the series conflicts with the schedule of the student, an alternative research proposal is offered and described below.

Research Proposals (Alternative to attending PCGI Talks) (25%):

Each student will develop a research plan to investigate an unanswered question that overlaps with one or more of the areas described in this course. Students will be expected to identify this novel research question and propose how it will be answered experimentally. A two-page description of the proposal will be due after the final week of the course. This proposal should include 1) a title, 2) the question to be answered, 3) a rationale of why the question is novel and significant, 4) a hypothesis, and 5) a detailed experiment approach in the form of specific aims to address the research question. Students are encouraged to synthesize new perspectives from the diverse topics covered in the course and reveal underdeveloped research areas. Experimental methods described in the course and/or novel ones should be used to explore this new research area in the most definitive manner possible. Finally, the results that are expected to be observed if the hypothesis is correct should be described, and alternative outcomes and subsequent alternative hypotheses/models should be included. The goal should not be to write a grant proposal per se, but rather engage in a creative mission to identify an interesting/novel research area and develop an experimental approach with critical foresight to investigate it.