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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 involvement. 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.

<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Faculty coach</th>
<th>Student(s)</th>
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<tbody>
<tr>
<td>9/5/12</td>
<td>Orientation</td>
<td>Alan and Eric</td>
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<tr>
<td>9/12/12</td>
<td>CDK/Cyclins</td>
<td>Alan Diehl</td>
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<tr>
<td>9/19/12</td>
<td>G1/S-RB-E2F</td>
<td>Kelly Jordan-Sciutto</td>
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<tr>
<td>9/26/12</td>
<td>CDK inhibitors</td>
<td>Andrew Wells</td>
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<td>10/3/12</td>
<td>S-phase</td>
<td>Paul Lieberman</td>
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<td>10/10/12</td>
<td>Mitosis/Spindle assembly checkpoint</td>
<td>Michael Lampson</td>
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<td>10/17/12</td>
<td>Cell cycle and proteolysis</td>
<td>Serge Fuchs</td>
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<tr>
<td>10/24/12</td>
<td>DNA damage checkpoints</td>
<td>Eric Brown</td>
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<td>10/31/12</td>
<td>Chromatin and DNA repair</td>
<td>Roger Greenberg</td>
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<td>11/7/12</td>
<td>DNA damage responses and cancer</td>
<td>Craig Bassing</td>
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<td>11/14/12</td>
<td>Telomere biology and cancer</td>
<td>Brad Johnson</td>
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<td>11/21/12</td>
<td>Thanksgiving</td>
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<td>11/28/12</td>
<td>DNA repair and cancer treatment</td>
<td>Susan Domchek</td>
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<td>12/5/12</td>
<td>Tumor virology</td>
<td>Jim Alwine</td>
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<td>12/12/12</td>
<td>DNA damage responses to viruses</td>
<td>Matt Weitzman</td>
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<td>12/19/12</td>
<td>Papers Due</td>
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**Grading:**

- Presentation: 30%
- Oral participation: 30%
- Problem sets: 20%
- Paper/Proposal: 20%
Presentation:

a) A student will be asked to volunteer to give the first presentation and will receive, in turn, the gratitude of the directors and brownie points. Copies of all papers for presentation will be available on Blackboard. Once the enrollment is finalized, students will be randomly 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. Focus the presentation on one or two (related) papers depending upon topic. If you would like to present a paper that is not on the list, please get approval in advance from the faculty coach. You must choose your paper more than a week before your presentation to provide your fellow students with ample opportunity to read and evaluate the chosen paper.

c) You can talk to us at any point as you choose your paper or try to understand the paper. However, your final discussion with us should be no later than Friday prior to your presentation date, at a mutually agreed upon time. You must have your talk and slides (PowerPoint) prepared prior to going into this meeting. The more you prepare yourself first, the more you learn, and the more we can help you and ensure good coverage of the field for the class.

d) Students will anonymously evaluate each presentation. This feedback will be given directly to the presenter and will not be used in grading. On the day you present, you are to stay after class and meet with the assigned faculty member for feedback.

We encourage students to make a handout for the class on their presentation topic.

Participation

Oral participation: 30%. 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: 20%. To facilitate discussion and a more thorough understanding of the material presented in the weekly paper, students will be provided with 2-4 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!
Papers:

Use a ‘preview’ format (follow instructions to authors Cancer Cell or Cell journals)

A. Choosing a topic: The topic must be different from your lab research and from your own presentation and should not focus primarily on a paper presented in class, but can be on the same topic.

The review should focus on articles from journals of the highest quality (Cell, Cancer Cell, Developmental Cell, Molecular Cell, Genes & Development, Nature, Science, Nature Genetics, Nature Cell Biology, Current Biology, and EMBOJ. Any other journals must first be approved by the Course Directors.)

Read several primary papers and focus your review on one or two of the most recent publications that address the topic, controversy or question you have chosen. You can also read recent reviews to help you recognize which questions are unanswered or controversial. Write the paper discussing these papers in the paper format outlined below.

B. Format (Preview for Cancer Cell or Molecular Cell): Use format instructions for preview found under instructions to authors on the Cancer Cell or Molecular Cell website.

In general, you should provide a brief introduction for the topic citing the paper or papers previewed in the first paragraph. Discuss the primary paper or paper(s) (that cover the same topic and should have been published within the same time frame). You can read and cite reviews, but you may not simply rewrite a review: exercise your own scholarship. Critically analyze the results. Formulate an opinion on whether the conclusions are scientifically supported, what is the significance of the paper in the context of the field, and what issues remain. Lastly, propose experiments that will address open issues. This is designed in part to give you practice for your preliminary exams.

C. Due date: 12/19.

Note that papers (available for presentation) will be available on Blackboard.