Bi426/526 Genetics of Cancer

Instructor
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Office hours: Tuesday, 9:00-10:30

Course overview and learning outcomes
This course will focus on selected topics in modern cancer biology that illustrate some of the fundamental mechanisms of cancer initiation and progression. The complexity of the genetic interactions that take place in all aspects of cancer biology is daunting; hundreds of genes have been identified, and most have multiple interconnections; furthermore, new associations and cancer-related genes are continually discovered. We will examine in detail only a few genes and their interactions in several broad areas of cancer biology. However, even such a limited scope will provide students with an understanding of important genetic systems in cancer cells, the tools and techniques of cancer research, and how those methods are applied to elucidate the genetic and biochemical phenomena behind the aberrant behavior of cancer cells. The course relies heavily upon information provided in primary research papers. Students will thus develop or hone skills in critically evaluating experimental design, data analysis and interpretation. The base of knowledge acquired in this course will enable students to further their studies in many areas of cancer biology should they so choose.

The prerequisites for Bi426 are a passing grade in either Bi214 or Bi282, and in either Bi320 (*Molecular Genetics*) or Bi322 (*Cell Biology*).

Class format
We meet twice each week for 1 hour and 20 minutes. My goal is to make class sessions mixtures of lecture and discussion. With such a small class size we can fashion our meetings as more dialogue than monologue. For most weeks the content on Mondays will be primarily background material, and that on Wednesdays will be from research articles. The images I will use for each class will be available (as pdf files) on Canvas under *Modules>Lecture Slides* the day before each class session.

Reading materials
Readings will be come from two sources. The background material is largely from *The Biology of Cancer*, 2nd edition (Garland Science), by Robert Weinberg. It is available for purchase at the UO Bookstore and the usual on-line outlets. It is available also as an e-book for purchase or rental through Amazon:
http://www.amazon.com/Biology-Cancer-Second-ebook/dp/B00D2J17GW/ref=sr_1_1?ie=UTF8&qid=1370442159&sr=8-1&keywords=the+biology+of+cancer+2nd+edition

and through VitalSource:
https://www.vitalsource.com/textbooks?utf8=%E2%9C%93&sort=&term=The+Biology+of+Cancer

The other reading source is from the primary literature in the form of research papers and reviews. These articles (as pdf files) will be available through Canvas under *Modules>Week N articles*. In many cases supplemental articles will be provided for additional background (they will be indented in the article list); there is no requirement that students read these, but are included if you wish to explore a topic further or get a deeper understanding of some of the technical aspects of the work. In addition, a "techniques" page will be provided that describes some of the experimental techniques used in the main article, as well as defines some terms.

Assignments and Grading

- Attendance (5%). Active participation in class is a vital component of your learning, and of the success of this course, so attendance is mandatory. If you arrive more than 10 minutes late you will be considered absent (this does not mean that 5 minutes late is acceptable!). You are expected to come to class having read and thought about the assigned materials. Thoughtful questions and good efforts are more important than are correct answers.

- Homework (55%). The homework sets are intended to guide you through the assigned readings. The format for these assignments will be as short-answer types of questions, usually 2-3 pages worth, based upon the background material and the research articles (in blue in the course schedule). Each assignment will be posted as a Word document on Canvas under *Modules>Homework* by the Friday preceding the week in which it is due. You are encouraged to discuss the articles and questions with your peers, but all responses must be your original work. Answers must be written with correct syntax, grammar, and punctuation, and should be concise but complete. Assignments must be typed in 12 point font and, if more than one page (they should be more than one page), stapled. You may include the questions on your assignments, but make clear separations between the questions and your answers. Homework is due at the beginning of Wednesday classes, except for students presenting that week (see below); these students have a deadline of 5:00 on that Thursday. Late homework will not be accepted.

- Quizzes (15%). A brief quiz will be given at the end of most Monday classes to test your grasp of the main concepts of the background reading in *The Biology of Cancer* for that week. You may use notes that you have taken from the text reading and from Monday's lecture. The low score will be dropped.

- Class discussion and presentation (10%). On one Wednesday during the term, you will be one of 4 students who will be discussion leaders for that session. Each leader will guide a small group of peers in a discussion of a portion of a research paper, and then present their portion of the paper to the class. The primary articles for discussion and presentation are listed in green in the course schedule, and are related to the topic of that week.

  Before the small group discussions begin, the group leaders should present a brief overview to the entire class so that essential background information is provided. Any style of presentation will be acceptable (projected slides, document camera figures, whiteboard drawings).

  In the small group discussions, each leader will focus on 1-3 experiments (and the figures accompanying them) from the article. Leaders should provide background information that explains the context in which the specific experimental question is placed, and also describe

the techniques in enough detail to allow the group members to follow the experiments. Leaders are expected to formulate original questions for their groups to stimulate discussion.

Following the discussion, the group leaders will summarize their sections to the entire class. Again, any style of presentation will be acceptable.

All students in the class will be expected to have read the abstract and the introduction of the paper. A brief (~5 minute) quiz with three or four questions on the introduction will be administered at the beginning of these discussion sessions. Students are expected to bring a copy of the paper to class that day.

During the second week I will ask each student to rank their topic preferences (see the "Group presentations" in the lecture schedule); I will do my best to match students with their first or second choices, but I cannot guarantee everyone will be so matched. Please do not contest topic assignments once I make them. All students will be assigned to a "discussion group" of 7 members; these same groups will form each Wednesday for that week's discussion.

The group leaders must arrange to meet with me on the Friday or Monday before their presentation.

- Analysis paper (15%). You will submit a short paper summarizing two or three current research papers (published within the last four years) on same topic. You are encouraged to use additional articles, including reviews, for background information. The topic may be related to your class presentation, but need not be. Focus on molecular genetic phenomena rather than clinical work, tests of inhibitors, or therapeutic trials. The "previews" that accompany many of the papers we cover in class provide good examples of the type of paper that I want you to write.

  - Papers must be double-spaced and five to seven pages in length. Do not include figures of data (gels, histological sections, etc.), but you may include one diagram as a summary of the phenomenon under study (see those in the *Cancer Cell Previews*). In your text do not refer to specific figures in papers. A title must be included; if relevant, section headings may be used.

  - The target audience comprises your peers in this course, that is, a group well educated in cancer genetics. Thus, broad or basic descriptions of genes, proteins, or phenomena that we have covered in class are not appropriate.

  - As smart as this audience is, they need to have new acronyms defined, unfamiliar experimental techniques described, relevant genetic backgrounds of cell lines and organisms explained, etc.

  - If you include a conclusions section, make it short and direct. Do not restate all of the findings or go on at length about myriad therapeutic applications.

  - Avoid directly quoting passages from papers; that indicates laziness on the part of the writer. You should be able to summarize or paraphrase in your own words.

  - References must be from peer-reviewed literature; websites are not acceptable citation

resources, though you can certainly use them as starting points in your research. In the body of the paper references should be cited in parentheses as close to the relevant passage as possible, with the last name of the first author, followed with "et al." if the article has more than two authors, followed by the year of publication. For example: (Knight, et al., 2000). If there are just two authors both names should be in the citation, such as (Bierie and Moses, 2006).

All references cited must be listed in a separate reference section at the end of the paper. References must follow this format:

Author names (year) Article title. *J. Name* **volume**:page range.

For example:
Knight B, Yeoh GCT, Husk KL, Ly T, Abraham LJ, Yu C, Rhim JA, Fausto N (2000) Impaired preneoplastic changes and liver tumor formation in tumor necrosis factor receptor type 1 knockout mice. *J. Exp. Med.* **192**:1809-1818.

<u>Do not include web-related information</u>, such as the doi number or on-line publication date.

A short (less than one double-spaced page) summary of your intended topic will be due during the 7th week. It is simply an overview of the main idea that you are investigating, and includes one or two references that will likely be featured in the final paper.

Completed papers will be submitted electronically on Canvas as Word documents (doc or docx) or pdf files during the last week. As with homework assignments and the oral presentation, all text must be your original work. Papers will be screened through *Vericite*; suspected cases of plagiarism (this includes uncited passages) will be forwarded to the Office of Student Conduct and Community Standards.

Bi426 Class Schedule, Winter 2020

(Homework will be based upon articles in blue; discussions/presentations will be based upon articles in green)

Week	Date	Topic	Reading	Assignment
1	Jan. 6	The nature of cancer	*The Biology of Cancer*: 2.1-2.5	
	Jan. 8	The nature of cancer	*The Biology of Cancer*: 2.6-2.11	
2	Jan. 13	Overview of cancer genes	*The Biology of Cancer*: 3.1-3.12 Vogt (2012) *Nature Reviews Cancer* **12**:639-648	Quiz 1
	Jan. 15	Overview of cancer genes	*The Biology of Cancer*: 4.1-4.6; 5.1-5.6	
3	Jan. 20	MLK Day		
	Jan. 22	Growth factors and Receptors	*The Biology of Cancer*: 5.10 Perera and Bardeesy (2012) *Cancer Cell* **22**:281-282 Navas, et al. (2012) *Cancer Cell* **22**:318-330	HW1
4	Jan. 27	Tumor suppressor genes	*The Biology of Cancer*: 7.1-7.9	Quiz 2
	Jan. 29	Group 1 discussion	Will and Steidl (2014) *Cancer Cell* **25**:555-557 Chen, et al. (2014) *Cancer Cell* **25**:652-665 Weissmueller, et al (2014) *Cell* **157**:382-394	HW2
5	Feb. 3	Signal transduction	*The Biology of Cancer*: 6.1-6.6	Quiz 3
	Feb. 5	Group 2 discussion	Der and Van Dyke (2007) *Cell* **129**:855-857 Gupta, et al. (2007) *Cell* **129**:957-968 Castellano, et al (2013) *Cancer Cell* **24**:617-630	HW3
6	Feb. 10	Tumor suppressor-mediated apoptosis	*The Biology of Cancer*: 9.1-9.8; 9.10	Quiz 4
	Feb. 12	Group 3 discussion	Sharpless and DePinho (2007) *Nature* **445**:606-607 Martins, et al. (2006) *Cell* **127**:1323-1334 Li, et al (2012) *Cell* **149**:1269-1283	HW4
7	Feb. 17	Heterotypic interactions and angiogenesis	*The Biology of Cancer*: 13.1-13.8	Quiz 5 Summaries due
	Feb. 19	Group 4 discussion	Cully (2018) *Nature Reviews Cancer* **18**:136 Huelsken and Hanahan (2018) *Cell* **172**:643-644 Su, et al. (2018) *Cell* **172**:841-856 Rhim, et al (2014) *Cancer Cell* **25**:735-747	HW5
8	Feb. 24	The EMT and metastasis	*The Biology of Cancer*: 5.9; 14.1-14.6; 14.8-14.9	Quiz 6
	Feb. 26	Group 5 discussion	Brabletz (2012) *Cancer Cell* **22**:699-701 Alderton (2013) *Nature Reviews Cancer* **13**:3 Tsai, et al. (2012) *Cancer Cell* **22**:725-736 Krebs, et al (2016) *Nature Cell Biology* **19**:519-529	HW6
9	Mar. 2	Telomeres and genome integrity	*The Biology of Cancer*: 10.1-10.7; 10.9	Quiz 7
	Mar. 4	Group 6 discussion	Sedivy (2007) *Cancer Cell* **11**:389-391 Feldser and Greider (2007) *Cancer Cell* **11**:461-469 Wang, et al (2016) *Aging Cell* **15**:646-660	HW7
10	Mar. 9	Targeted cancer therapies (Dr. Christopher Corless)	*The Biology of Cancer*: 16.1-16.6; 16.11-16.13	Quiz 8
	Mar. 11	Group 7 discussion	Gazdar, et al. (2004) *Trends in Molecular Medicine* **10**:481-486 Pao, et al. (2004) *PNAS* **101**:13306-13311 Sordella, et al. (2004) *Science* **305**:1163-1167 Foster, et al. (2016) *Cancer Cell* **29**:477-493	HW8 Papers due on 3/13