

The biology of cancer

Yale University Summer Session 2017

Mondays, Wednesdays and Fridays 9:00 to 11:15

Office hours: Wednesday 1-4PM SSS room 26

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Prerequisites: successful completion of the Biology 101-104 sequence, or AP biology score of 5

Learning objectives: The main purpose of this course is to introduce to students the concept that cancer as a genetic disease, with particular emphasis on landmark discoveries in cancer biology that offer insights into the molecular biology of cancer. Students will emerge from this course with a firm understanding of the molecular pathways perturbed in various cancers and the therapeutics currently used to exploit these pathways for cancer treatment. The other goals of this course are that students will learn to (1) read primary scientific literature, (2) discuss this material in class and (3) write a short grant proposal. These skills are essential for any successful scientist or physician, and it's important to master them early.

Papers: All students are expected to read the assigned journal articles and be prepared to discuss them in class. All students will be divided into teams and assigned specific parts of a given paper to discuss. I am happy to work with students prior to paper discussion sessions over lunch to address any questions they might have.

Problem sets: these will serve to guide you in understanding important points in the assigned papers. You might have to do some internet sleuthing to answer the questions. Do not spend a lot of time on these! One succinct sentence demonstrating your understanding of the question is sufficient. I DO NOT want a 20-page paper! Problem sets are scored in a 1 (worst) to 10 (best) scale. Late P-sets will be penalized. You can work in groups, but I want **your** insights into the papers, not a group distillation.

Grant proposal: Understanding how to write fundable research proposals is an essential skill that all Yale undergrads interested in pursuing STEM majors need to master, but is never formally taught at Yale. In this class, students will be expected to produce a 8-10 page original research proposal on a specific topic related to cancer. This piece will be in the format of a grant proposal that is used by the Yale College Summer Research Fellowship in the Sciences and Engineering committee to select fundable undergraduate summer research fellowships. The student chooses a topic from a list of research papers posted in the Resources folder. The student is expected to find and read at least two additional papers of their choice (one additional primary paper, one review paper) to gain a better understand the chosen research topic. The student will then write a grant proposal on this topic, and propose two **original** research aims to investigate. If you were a student in the lab that generated the paper, what two experiments would you want to do and why? Please consult past grant proposals, as well as the scoring rubric in the Canvas Resources folder to guide your writing. You need to know how to use PubMed to find papers online. **Remember, proper citations are essential!**

Exams: two exams and a quiz will consist mostly of short answer essay questions that will test your understanding of the subject, NOT how well you memorize facts. I will ask you to design experiments, interpret experimental data, etc. You will be given a number of questions to choose from, and partial credit will be given for short answer question answers.

Grades: Grades will be based on the performance on the final paper (25%), two exams (15% each), 1 quiz (5%), problem sets (2% each, total 20%) and class participation (20%). Each student will be assigned a numerical score. The modal score (most common score) will be assigned a “B+”. Scores of 90-94% and above will be assigned an “A-“ and anything above a 94% will be an “A”. A score above 65% is considered passing.

Textbooks: the first is available at the Yale bookstore

Required: The Emperor of All Maladies: A Biography of Cancer, Siddhartha Mukherjee, New York: Scribner, November 2010. ISBN-10: 1439107955, \$10.80 paperback on Amazon (abbreviated as “EOAM”). This is one amazing book and really gives the reader an excellent, global view of cancer. It is divided into sections that we will read out of order to track more closely with the lectures. Now also a must-see 3 part PBS series which I highly recommend.

Suggested: Cancer: A Beginners Guide, Paul Scotting. London: Oneworld Publications, 2010. ISBN 9781851687558, \$13.46 paperback on Amazon. This short book offers a good general overview to the topics discussed in much greater detail in class.

Suggested: One Renegade Cell. Robert Weinberg. Basic Books, 1999. ISBN-13: 978-0465072767, \$12.71 on Amazon. The contents of this book are a bit outdated but Dr. Weinberg is the master of cancer biology, so it’s a worthwhile read if you have time.

Reference only: The Biology of Cancer, Robert Weinberg, New York: Garland Science, 2014. ISBN-13: 978-0815342199, \$149.09 on Amazon (hard cover). This is the definitive textbook on cancer biology, but you are not required to purchase it or even to read it. Most of the images presented in the lectures will be from this book. You can borrow this book from the Yale library if you need to clarify specific points not covered in class.

Primary scientific articles to be discussed in class and corresponding problem sets will be posted in the Resources section.

Comment on academic integrity: academic integrity is the pursuit of scholarly activity free from fraud and deception. All University policies regarding academic integrity apply to this course. Academic dishonesty includes, but is not limited to, cheating, plagiarizing, having unauthorized possession of examinations, submitting work of another person or work previously used without informing the instructor, or tampering with the academic work of other students. All homework and exam answers and research papers must be the student’s own work.

May 28 (M) Session 1: **Introduction; oncogenes 1-tyrosine kinases**

Reading: Weinberg Sci Am 1996, EOAM parts 5, 6

May 30 (W): Session 2: **Targeted therapeutics against tyrosine kinases**

Reading: Druker et al., NEJM 2001

Problem set 1 (due 6/1/17)

Class discussion: Weinberg Sci Am 1996, EOAM part 5

- June 1 (F): Session 3: **Oncogenes 2-Ras G-proteins**
Reading: Shi and Weinberg Cell 1982
Problem set 2 (due 6/4/17)
Class discussion: Druker et al., NEJM 2001 and EOAM 6
- June 4 (M) Session 4: Class discussion: Shi and Weinberg Cell 1982
QUIZ 1 (sessions 1-4, no EOAM)
Reading: EOAM parts 1-4
- June 6 (W) Session 5: **Carcinogens, DNA damage and genomic instability**
Reading: Brown et al., Cell 1986
Problem set 3 (due 6/8/17)
Class discussion EOAM part 4
- June 8 (F) Session 6: **Tumor suppressor 1: Retinoblastoma and defects in cell cycle control**
Readings: Friend et al., Science 1986
Problem set 4 (due 6/11/17)
Class discussion on Brown et al., Cell 1986, EOAM parts 1, 2
- June 11 (M) Session 6: **Tumor suppressor 2: p53, apoptosis and cellular senescence**
Reading: Malkin et al., Science 1990
Problem set 5 (due 6/13/17)
Class discussion of Friend et al., Science 1986, EOAM part 3
- June 13 (W) Session 7: **EXAM 1 (Sessions 1-6, EOAM 1-4)**
Class discussion of Malkin et al., Science 1990
Reading: finish EOAM
- June 15 (F) Session 8: **Telomeres, telomerase and cellular immortality**
Reading: Blasco et al., Cell 1997
Problem set 6 (due 6/18/17)
Class discussion EOAM part 4
- June 18 (M) Session 9: **Invasion, metastasis and angiogenesis**
Reading: Braun et al., NEJM 2000
Reading: EOAM p. 60-72, 193-201, 218-223, 305-333
Problem set 7 (due 6/20/17)
Class discussion on Blasco et al., Cell 1997
- June 20 (W) Session 10: **Tumor immunology**
Reading: Eggermont NEJM 2016
Problem set 8 (due 6/22/17)
Class discussion on Braun et al., NEJM 2000
- June 22 (F) Session 11: **Breast cancer genomics and therapeutics**
Reading: Wood et al., Science 2007
Reading: EOAM p. 384-392, 412-440, 448-459
Problem set 9 (due 6/25/17)
Class discussion on Eggermont NEJM 2016

June 25 (M) Session 12: **Novel technologies to combat cancer**

Class discussion on Wood et al., Science 2007

June 27 (W) Session 13: Review and discussion of grant proposal

June 29 (F) Session 15: **Final Exam (Sessions 8-15, EOAM part 6 and specific pages)**