

Cancer Biology, Biol 1290, Section 2

Spring, 2009; Tuesdays 3-6 PM

Course Director - Anatoly Zhitkovich, Ph.D.

Contact information: tel. (401) 863-2912, e-mail: anatoly_zhitkovich@brown.edu

Course Description and Objectives:

BIO1290 is designed to provide a conceptual understanding of molecular events underlying development of human cancer. The main focus of the course will be on the genetic changes leading to the neoplastic transformation of cells. The course will cover several major areas of cancer biology such as cell cycle control, DNA damage, tumor microenvironment, chemotherapy and drug resistance.

The ability to understand malignant transformation of cells on the molecular level and to critically evaluate existing literature in the field are two major goals of this course. The lecture materials will provide an overview of each topic whereas discussions of original research articles will be used as a tool for developing critical thinking in the analysis of cancer-related research.

Specific Objectives:

1. To develop a conceptual understanding about how a misbalance between cell death and cell proliferation leads to cellular transformation.
2. To understand principal mechanisms of DNA damage and DNA repair and how these processes can be linked to variability in individual susceptibility to cancer.
3. To learn molecular mechanisms that allow transformed cells to progress into malignant tumors by avoiding immune surveillance and activating angiogenesis.
4. To learn how understanding of the molecular basis of cancer can be used for the development of new treatment strategies.

Exams and Grading:

- | | | |
|---------------------|---|----------------------|
| 1. Midterm exam - 1 | - | 30% |
| 2. Midterm exam - 2 | - | 30% |
| 3. Final exam | - | 30% (non-cumulative) |
| 4. Weekly quizzes | - | 10% |

Readings:

- 1) Weinberg R. A. The Biology of Cancer (2007)
- 2) Selected review and primary journal articles

Main topics:

Cellular transformation
DNA damage and mutagenesis
Genetic instability
Cell cycle
Cell death
Oncogenic viruses
Angiogenesis
Metastasis
Tumor immunology
Chemotherapy
Cancer stem cells

Class Schedule

Biol 1290, Section 2: *Cancer Biology*

Meeting time: 3-6 pm

Date	Topic	Faculty
2008		
December 17	Overview of Cellular Transformation	Zhitkovich
2009		
January 27	<i>No class</i>	
February 3	Genomic Instability <u>Quiz #1</u> – previous lecture	Zhitkovich
10	UV and Skin Cancer <u>Quiz #2</u> – previous lecture	Zhitkovich
17	<i>No class</i> – Long weekend	
24	Midterm Exam - 1	Zhitkovich
March 3	Cell Cycle	Zhitkovich
10	Cell Death <u>Quiz #3</u> – previous lecture	Zhitkovich
17	Metastasis <u>Quiz #4</u> – previous lecture	Dr. Jonathan Reichner
24	<i>No class</i> – Spring Recess	
31	Midterm Exam - 2	Zhitkovich
April 7	Tumor Immunology	Dr. Loren Fast
14	Oncogenic Viruses and Tumor Hypoxia <u>Quiz #5</u> – previous lecture	Zhitkovich
21	Chemotherapy and Drug Resistance <u>Quiz #6</u> – previous lecture	Zhitkovich
May 12	Final Exam	Zhitkovich

Reading List

Biol 1290, Section 2: *Cancer Biology*

2008

December 17 – *Overview of Cellular Transformation*

1. Textbook, Chapter 2: pp. 43-56
2. Textbook, Chapter 4
3. Salnikow K. Genetic and epigenetic mechanisms in metal carcinogenesis and cocarcinogenesis: nickel, arsenic and chromium. *Chem. Res. Toxicol.* 21: 28-44 (2008). *Read only Chapter 4: Chromium.*
<http://pubs.acs.org/cgi-bin/sample.cgi/crtoec/2008/21/i01/pdf/tx700198a.pdf>

2009

February 3 – *Genomic Instability*

1. Textbook, Chapter 12
2. Loeb L.A., Bielas J.H., Beckman R.A. Cancers exhibit a mutator phenotype: clinical implications. *Cancer Res.* 68(10): 3551-3557 (2008). <http://cancerres.aacrjournals.org/cgi/reprint/68/10/3551.pdf>
3. Fukasawa K. Oncogenes and tumour suppressors take on centrosomes. *Nature Reviews Cancer* 7(12): 911-924 (2007). <http://www.nature.com/nrc/journal/v7/n12/pdf/nrc2249.pdf>

February 10 – *UV and Skin Cancer*

1. Lin JY, Fisher DE. Melanocyte biology and skin pigmentation. *Nature* 445(7130): 843-850 (2007). <http://www.nature.com/nature/journal/v445/n7130/pdf/nature05660.pdf>
2. Cleaver J.E. Cancer in xeroderma pigmentosum and related disorders of DNA repair. *Nature Reviews Cancer* Jul;5(7): 564-573 (2005). <http://www.nature.com/nrc/journal/v5/n7/pdf/nrc1652.pdf>
3. Michaloglou C. BRAF^{E600}-associated senescence-like cell cycle arrest of human naevi. *Nature* 436: 720-724 (2005). <http://www.nature.com/nature/journal/v436/n7051/pdf/nature03890.pdf>

March 3 – *Cell Cycle*

1. Textbook, Chapter 8
2. Kastan MB, Bartek J. Cell-cycle checkpoints and cancer. *Nature* 432(7015): 316-323 (2004). <http://www.nature.com/nature/journal/v432/n7015/pdf/nature03097.pdf>
3. Xue W. Senescence and tumour clearance is triggered by p53 restoration in murine liver carcinomas. *Nature* 445: 656-660 (2007). <http://www.nature.com/nature/journal/v445/n7128/pdf/nature05529.pdf>

March 10 – *Cell Death*

1. Textbook, Chapter 9
2. Ashkenazi A, Herbst RS. To kill a tumor cell: the potential of proapoptotic receptor agonists. *J. Clin. Invest.* 118(6): 1979-1990 (2008). <http://www.jci.org/articles/view/34359/pdf>
3. Mathew R, Karantza-Wadsworth V, White E. Role of autophagy in cancer. *Nature Review Cancer* 7(12): 961-967 (2007). <http://www.nature.com/nrc/journal/v7/n12/pdf/nrc2254.pdf>

March 17 – Metastasis

1. Textbook, Chapter 14
2. Fidler I.J. The pathogenesis of cancer metastasis: the 'seed and soil' hypothesis revisited. *Nature Review Cancer* Jun;3(6): 453-458 (2003). <http://www.nature.com/nrc/journal/v3/n6/pdf/nrc1098.pdf>
3. Nguyen DX, Massagué J. Genetic determinants of cancer metastasis. *Nature Review Genet.* 8(5): 341-352 (2007). <http://www.nature.com/nrg/journal/v8/n5/pdf/nrg2101.pdf>

April 7 – Tumor Immunology

1. Textbook, Chapter 15
2. Zitvogel L. Cancer despite immunosurveillance: immunoselection and immunosubversion. *Nature Reviews Immunol.* 6: 715-727 (2006). <http://www.nature.com/nri/journal/v6/n10/pdf/nri1936.pdf>
3. Bhardwaj N. Harnessing the immune system to treat cancer. *J. Clin. Invest.* 117(5): 1130-1136 (2007). <http://www.pubmedcentral.nih.gov/picrender.fcgi?doi=10.1172/JCI32136&blobtype=pdf>

April 14 – Oncogenic Viruses and Tumor Hypoxia

1. Textbook, Chapters 3 and 13
2. Pouyssegur J., Dayan F., Mazure N.M. Hypoxia signalling in cancer and approaches to enforce tumour regression. *Nature* 441(7092): 437-443 (2006). <http://www.nature.com/nature/journal/v441/n7092/pdf/nature04871.pdf>

April 21 - Chemotherapy and Drug Resistance

1. Textbook, Chapter 16
2. Imai K, Takaoka A. Comparing antibody and small-molecule therapies for cancer. *Nature Review Cancer* 6(9): 714-727 (2006). <http://www.nature.com/nrc/journal/v6/n9/pdf/nrc1913.pdf>
3. Hurley L.H. DNA and its associated processes as targets for cancer therapy. *Nature Review Cancer* 2, 188-200 (2002). <http://www.nature.com/nrc/journal/v2/n3/pdf/nrc749.pdf>
4. DeVita V.T. A history of cancer chemotherapy. *Cancer Res.* 68(21): 8643-8653 (2008). <http://cancerres.aacrjournals.org/cgi/reprint/68/21/8643>