

BIO 475-001: THE BIOLOGY OF CANCER

Spring 2009: T at 7:00 PM – 9:30 PM

Room: Sowa Hall 233

Credit Hours: 3.00



PROVIDENCE
COLLEGE

INSTRUCTOR:

Name: Fr. Nicanor Pier Giorgio Austriaco, O.P., Ph.D.

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I am generally in my office (Sowa 229B) or in my laboratory (Hickey 181) from 9:00 AM - 5:00 PM daily and am easily available with a prior appointment. To make an appointment, you may call me on my telephone or email me. I'll keep Tuesday afternoons from 2:00 P.M. to 4 P.M. for drop-in appointments. I will either be in my office or in my laboratory. Please feel free to talk to me about any issue relating either to the course or to your life as a student here at Providence College.

A PRAYER BEFORE STUDY **St. Thomas Aquinas, O.P.**

O God, Creator of all things, true source of light and wisdom, graciously let a ray of your light penetrate the darkness of my understanding. Give me a keen intellect, a retentive memory, and the ability to grasp things correctly and fundamentally. Give me the talent of being exact in my explanations and the ability to express myself with thoroughness and charm. Point out the beginning, direct the progress, and perfect my work. We ask you this through Jesus Christ Our Lord. Amen.

COURSE DESCRIPTION:

What is cancer? In this advanced topics seminar, we will answer this question by focusing on the six hallmarks that define cancer cells: evasion of apoptosis, insensitivity to anti-growth signals, self-sufficiency in growth signals, sustained angiogenesis, tissue invasion and metastasis, and a limitless replicative division potential (cf. Hanahan and Weinberg, 2000). The seminar will involve extensive student-led discussions based upon the very best research papers in contemporary cancer biology. As a capstone course in biology, this seminar will also strive to help students to develop those skills needed by professional biologists including the ability to read, analyze, and critique scientific papers, and the craft of writing an NIH grant. Students will be expected to write five Methods & Logic Analyses of five published papers and to write an abbreviated NIH grant.

REQUIRED TEXTS:

- All the primary papers we will discuss and critique in this course can be downloaded from the course website on ANGEL. Please print out and bring the papers to class for discussion.
- Robert Weinberg, *The Biology of Cancer* (New York: Garland Science, 2006)

ACADEMIC EXPECTATIONS:

This is an upper-level seminar course, and I will expect active participation from all students. Thus, every student should come to class prepared to critically engage each scientific paper and each other. This means that you should read, take notes, and think about all the assigned readings before class. Each week, different students will take the lead and present the papers to the class before we discuss them.

During the course of the semester, each student will be expected to submit four (4) methods & logic analyses that critically engage one of the scientific papers we will discuss in class. A method & logic analysis for any one paper is due on the day that the paper is discussed in class. A detailed guide to writing a methods & logic analysis is available on the class website on ANGEL.

At the end of the semester, each student will submit a short 5-10 page grant proposal in the biology of cancer based on the format of National Institutes of Health Grant, PHS 398. (For details and for a template for the NIH grant, please refer to the NIH website, <http://grants.nih.gov/grants/funding/phs398/phs398.html>). Throughout the semester, students will work on different portions of the NIH grant. Please see the syllabus for a schedule of deadlines for each portion of the grant.

Since this is a course that requires active student participation, regular attendance is expected. Please email the instructor in advance if you expect to miss a class. Only one absence is permitted barring exceptional circumstances. More than one unexcused absences during the semester may lead to a final grade reduction of a full letter grade (e.g., B+ to C+).

GRADING POLICY:

Grades will be calculated as follows:

Grant Proposal	50%
Methods & Logic Analyses	40%
Paper Presentations	10%

In the world of science, grants have to be submitted to the funding agency by a particular deadline. There are no exceptions to this rule. Thus, in this class, I expect all work to be

handed in on time. Late assignments will be penalized 10% of their point value per calendar day late (not per class day).

Academic dishonesty and plagiarism (“the stealing and passing off of the ideas or words of another as one’s own without crediting the source”) is not tolerated in the professional world of science and will not be tolerated in this class. Plagiarism on any written submission will result in an F for that assignment. Please consult the current Providence College Undergraduate Catalogue for its statement on “Academic Honesty.”

SCHEDULE OF READINGS

Week 1: The Nature of Cancer [January 20, 2009]

C. Murgia et al., "Clonal origin and evolution of a transmissible cancer," *Cell* 126 (2006): 477-487.

H.R. Christofk et al., "The M2 splice isoform of pyruvate kinase is important for cancer metabolism and tumour growth," *Nature* 452 (2008): 230-233.

Week 2: Tumor Viruses and the Discovery of Cellular Oncogenes

[January 27, 2009]

H.K. Arnold et al., "The Axin1 scaffold protein promotes formation of a degradation complex for c-Myc," *EMBO J* Epublished ahead of print on January 8, 2009.

C.A. Maher et al., "Transcriptome sequencing to detect gene fusions in cancer," *Nature* Epublished ahead of print on January 11, 2009.

Week 3: Growth Factors Receptors, Cell Signaling, and Cancer [February 3, 2009]

Q. Feng et al., "Cool-1 functions as an essential regulatory node for EGF receptor- and Src-mediated cell growth," *Nat Cell Biol* 8 (2006): 945-956.

N.A. Riobo et al., "Phosphoinositide 3-kinase and Akt are essential for Sonic Hedgehog signaling," *PNAS* 103 (2006): 4505-4510.

NIH Grants: An Introduction to Writing an NIH Grant Proposal

Week 4: Tumor Suppressors [February 10, 2009]

B.H. Kang et al., "Regulation of Tumor Cell Mitochondrial Homeostasis by an Organelle-Specific Hsp90 Chaperone Network," *Cell* 131 (2007): 257-270.

A. Bagchi et al., "*CHD5* Is a Tumor Suppressor at Human *1p36*," *Cell* 128 (2007): 459-475.

Week 5: pRb and the Control of the Cell Cycle Clock [February 24, 2009]

I. Ajioka et al., "Differentiated Horizontal Interneurons Clonally Expand to Form Metastatic Retinoblastoma in Mice," *Cell* 131 (2007): 378-390.

H. Varma et al., "Functional Ablation of pRb Activates Cdk2 and Causes Antiestrogen Resistance in Human Breast Cancer Cells," *PloS ONE* 2 (2007): e1256.

Week 6: p53 and Apoptosis – Master Guardian and Executioner of Apoptosis
[March 3, 2009]

R. Cui et al., “Central role of p53 in the suntan response and pathologic hyperpigmentation,” *Cell* 128 (2007): 853-864.

J. Hitomi et al., “Identification of a Molecular Signaling Network that Regulates a Cellular Necrotic Cell Death Pathway,” *Cell* 135 (2008): 1311-1323.

Week 7: Cell Immortalization and Tumorigenesis [March 17, 2009]

J.M. Pinkston et al., “Mutations that increase the life span of *C. elegans* inhibit tumor growth,” *Science* 313 (2006): 971-975.

L. Hao et al., “Short Telomeres, even in the Presence of Telomerase, Limit Tissue Renewal Capacity,” *Cell* 123 (2005): 1121-1131.

NIH Grant Draft: Specific Aim, Background, and Research Significance Section Due

Week 8: Tumorigenesis and the Microenvironment [March 24, 2009]

C.A. O’Brien et al., “A human colon cancer cell capable of initiating tumour growth in immunodeficient mice,” *Nature* 445 (2007): 106-110.

E. Quintana et al., “Efficient tumour formation by single human melanoma cells,” *Nature* 456 (2008): 593-598.

C.R. Walkley et al., “A Microenvironment-Induced Myeloproliferative Syndrome Caused by Retinoic Acid Receptor γ Deficiency,” *Cell* 129 (2007): 1097-1110.

Week 9: Maintenance of Genomic Integrity and the Development of Cancer
[March 31, 2009]

R. Di Micco et al., “Oncogene-induced senescence is a DNA damage response triggered by DNA hyper-replication,” *Nature* 444 (2006): 638-642.

R. Rai et al., “BRIT1 regulates early DNA damage response, chromosomal integrity, and cancer,” *Cancer Cell* 10 (2006): 145-157.

NIH Grant Draft: Experimental Design Section Due

Week 10: Angiogenesis [April 7, 2009]

C. Fischer et al., "Anti-PlGF Inhibits Growth of VEGF(R)-Inhibitor-Resistant Tumors without Affecting Healthy Vessels," *Cell* 131 (2007): 463-475.

J. Ridgway et al., "Inhibition of DII4 signaling inhibits tumour growth by deregulating angiogenesis," *Nature* 444 (2006): 1083-1087.

I. Noguera-Troise et al., "Blockade of DII4 inhibits tumour growth by promoting non-productive angiogenesis," *Nature* 444 (2006): 1032-1037.

Week 11: Invasion and Metastasis [April 14, 2009]

K. Podsypanina et al., "Seeding and Propagation of Untransformed Mouse Mammary Cells in the Lung," *Science* 321 (2008): 1841-1844.

G. Hu et al., "MTDH Activation by 8q22 Genomic Gain Promotes Chemoresistance and Metastasis of Poor-Prognosis Breast Cancer," *Cancer Cell* 15 (2009): 9-20.

NIH Grant: Final Draft Due with Form Page 1, Form Page 2, Biographical Sketch, Specific Aim, Background and Significance, and Experimental Design Sections. Proposals sent out for Peer Review

Week 12: Tumor Immunology and Immunotherapy [April 21, 2009]

J. Qiao et al., "Purging metastases in lymphoid organs using a combination of antigen-nonspecific adoptive T cell therapy, oncolytic virotherapy and immunotherapy," *Nat Med* Epublished ahead of print on December 9, 2007.

P. Juszczynski et al., "The AP1-dependent secretion of galectin-1 by Reed Sternberg cells fosters immune privilege in classical Hodgkin lymphoma," *Proc Natl Acad Sci USA* 104 (2007): 13134-13139.

NIH Grant: Peer Reviews Due

Week 13: The Rational Treatment of Cancer [April 28, 2009]

W. Xue et al., "Senescence and tumour clearance is triggered by p53 restoration in murine liver carcinomas," *Nature* 445 (2007): 656-660.

A. Ventura et al., "Restoration of p53 function leads to tumour regression in vivo," *Nature* 445 (2007); 661-665.

S.W. Lowe et al., "p53 status and the efficacy of cancer therapy in vivo," *Science* 266 (1994): 807-810.