

**PUB HLTH 529**  
**CANCER CHEMOPREVENTION**  
**Fall Quarter 2007**  
**October 29 – November 28, 2007**  
**0.5 credit course**

**Time:** Mondays and Wednesdays 6:00-7:30 pm  
**Location:** Department of Preventive Medicine  
680 N. Lake Shore Drive, Suite 1102, Large Conference Room  
**Course Instructor: (office hours by appointment)**  
Raymond Bergan, MD  
Associate Professor  
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**Guest Lecturers:**

Borko Jovanovic, PhD, Research Associate Professor, Dept. of Preventive Medicine  
Michael Avram, PhD, Associate Professor, Dept. of Anesthesiology; Director, Cancer Center  
Clinical Pharmacology Core

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**I. Course Description**

The purpose of this course is to review the basic concepts and issues relevant to cancer chemoprevention. Specifically, this course will focus on describing the current state of knowledge regarding the molecular pharmacology of therapeutic intervention, targeted to early stages of carcinogenesis, for the major cancer sites. In addition, issues related to the function of a specific target, characteristics of a drug, choice and characteristics of an endpoint biomarker, and research design and interpretation, as they relate to molecular and cellular carcinogenesis, will be discussed. The course is appropriate for students who have an introductory knowledge of epidemiology and statistics. Students should also have an understanding of cancer biology – per approval of the instructor.

**II. Prerequisites**

- Introduction to Epidemiology – PH 304 (or Medical Decision Making II)
- Introduction to Biostatistics – PH 302
- Permission of Instructor

**III. Course Objectives**

After completion of the course, students will be able to:

- Identify cell and molecular changes associated with carcinogenesis, and critically evaluate their potential as therapeutic targets.
- Define what a biomarker is, and critically evaluate the utility of a specific biomarker for investigating the relationship between a specific therapeutic intervention and its effect upon the targeted disease process.

- Describe the general principals of clinical and cellular pharmacology, and explain how they relate to the therapeutic modulation of a specific molecular target.
- List the characteristics of an ideal drug, and describe common characteristics of a chemopreventive drug.
- Describe the multiple steps involved in drug development
- Describe common assays used in measurement of endpoints
- Critically evaluate the impact of tissue processing methods upon the outcome of specific assay types, and list common quality control methods.
- Define the relationship between the prevalence of a specific biomarker in target tissue, the variability of the associated assay, and the size of a clinical trial.
- Define the different types of clinical trials, and describe their primary endpoints.
- Describe common problems associated with individual types of trials
- Design a research study, which investigates the relationship between a specific drug and its effect upon cell and molecular alterations associated with disease specific carcinogenesis.

#### IV. Teaching Format

New and supplementary material will be presented in formal lectures. Students will be expected to read the assigned reading material prior to the lecture or the discussion. Following formal lectures, students will be assigned a thought problem. Students will be responsible for researching and finding possible solutions to the thought problem. They will also be responsible for leading a discussion about the thought problem in the class dedicated to problem-based learning. Participation in-group discussion is mandatory. One of the problem based learning classes will take place in the laboratory, and will involve the practical interpretation of immunohistochemical-based assays.

#### V. Student Evaluation

- a) Class participation: Students are expected to have completed the assigned reading prior to each class. Students are expected to come to class with knowledge of the assigned reading, and be prepared to ask informed questions related to this or other issues they have identified, in the context of formal lectures, and in response to questions posed by the instructor during lectures. Following didactic lectures, the instructor will assign subject related thought problems. Students are expected to come to the following class prepared to lead an informed discussion, in a problem based learning format, about the assigned problem. Participation will count towards 50% of the total grade. If you will miss a class, you must notify the Instructor in advance.
- Presentation – Each student will be expected to prepare a presentation on the underlying rationale, design, and implementation of a cancer prevention trial, for a specific drug and a specific cancer site. This assignment will count towards 50% of the student evaluation.

#### VI. Class Material

- **Textbooks:**
  - CANCER: Principals and Practice of Oncology, DeVita, V.T., Hellman, S., Rosenberg, S.A. (editors). Lippincott Williams and Wilkins. 2001.
  - Cancer Chemoprevention, Bergan, R.C.. (editor). Kluwer Academic Publications. 2001.
  - Cancer Precursors: Epidemiology, Detection and Prevention, Franco, E.L., Rohan, T.E. (editors). Springer. 2002.
  - Biostatistical Applications in Cancer Research, Beam, C. (editor). Kluwer Academic Publications. 2002.

- **Other supplementary readings will be provided by the Instructor.**

## **VII. Course Evaluation**

The MPH Program administers web-based course evaluations to students for each course near the end of the quarter. ***Your completion of both the unit (course) and faculty evaluation components is required; failure to complete either of the evaluations will result in an incomplete grade until the evaluations are submitted.*** You will be sent the web link and instructions via email later in the quarter. You will have about two weeks time to complete the evaluations before grades are submitted.



**Fall 2007**  
**Cancer Chemoprevention**

<b>Session</b>	<b>Date</b>	<b>Lectures: reading, topics, instructor</b>
<b>1</b>	Mon 10/29	Assigned Reading <ul style="list-style-type: none"> <li>• CANCER: Principals: chapter 1</li> <li>• Cancer Precursors: chapters 1 and 4</li> <li>• Cancer Chemoprevention: chapter 2</li> </ul>
<b>1</b>	Mon 10/29 (6-7:30)	Nature of the biological target ( <b>Bergan</b> ) <ul style="list-style-type: none"> <li>• Theories of carcinogenesis</li> <li>• Theoretical and practical targets</li> <li>• Biomarkers</li> </ul>
<b>2</b>	Wed 10/31 (6-7:30)	Discussion of assigned problem: for a specific process involved in carcinogenesis, what would you target, and how would you measure the effects?
<b>3</b>	Mon 11/5	Assigned Reading <ul style="list-style-type: none"> <li>• Cancer Chemoprevention: chapters 1 and 4</li> </ul>
<b>3</b>	Mon 11/5 (6-7:30)	Overview of therapy ( <b>Invited Lecturer: Avram; Bergan</b> ) <ul style="list-style-type: none"> <li>• Clinical pharmacology</li> <li>• Cellular pharmacology/pharmacodynamics</li> <li>• Drug characteristics and development</li> </ul>
<b>4</b>	Wed 11/7 (6-7:30)	Discussion of assigned problem: for a specific drug (against a given target), how would you give it to humans, and what would you measure?
<b>5</b>	Mon 11/12 (6-7:30)	Assigned Reading <ul style="list-style-type: none"> <li>• Cancer Precursors: chapter 3</li> <li>• Biostatistical Applications: chapter 5</li> <li>• Assay methodology: prepared and provided by instructor <ul style="list-style-type: none"> <li>• Histology a Text and Atlas: chapter 1, pages 1-13</li> <li>• Essentials of real time PCR</li> </ul> </li> </ul>
<b>5</b>	Mon 11/12 (6-7:30)	Endpoints ( <b>Bergan</b> ) <ul style="list-style-type: none"> <li>• Types: clinical Vs non-clinical</li> <li>• Tissue processing</li> <li>• Quality control</li> <li>• Assays: types, variables, and methods</li> </ul>
<b>6</b>	Wed 11/14 (6-7:30)	Implementation of assigned problem: develop and discuss a potential method to evaluate a tissue biomarker. Evaluate the effectiveness of your approach on pre-prepared stained tissue. Class to meet in the Bergan lab.
<b>7</b>	Mon 11/19 (6-7:30)	Assigned Reading <ul style="list-style-type: none"> <li>• CANCER: Principals: chapter 21</li> <li>• Disease specific examples <ul style="list-style-type: none"> <li>• (prostate) Cancer Chemoprevention: chapter 5</li> <li>• (lung) Ca. Epi. Biomarkers and Prev, 14(4):892-9, 2005</li> <li>• (breast) Cancer Chemoprevention: chapter 6</li> </ul> </li> </ul>
<b>7</b>	Mon 11/19 (6-7:30)	Trial design ( <b>Invited Lecturer: Jovanovic; Bergan</b> ) <ul style="list-style-type: none"> <li>• Types of trials (<b>Jovanovic</b>)</li> <li>• Statistics (<b>Jovanovic</b>)</li> <li>• Discuss specific examples (<b>Bergan</b>)</li> </ul>

<b>8</b>	Wed 11/21	Discussion of assigned problem: for a specific drug and disease combination, what endpoints would you measure, and how would you measure them?
<b>9</b>	Mon 11/26 (6-7:30)	Student Presentations
<b>10</b>	Wed 11/28 (6-7:30)	Student Presentations

## Format for Student Presentations

- 1) Each student will select a unique cancer type and drug that were not presented in class. They will then prepare a presentation, which will provide a description of the underlying rationale, design, and implementation of a cancer prevention trial.
- 2) To assure no overlap, we will discuss which cancer site each of you have selected in class on **November 7th**.
- 3) Each student will prepare a 20-25 minutes presentation for their selected cancer type/drug combination. The presentation should be prepared in power point. Following each presentation will be a discussion so please be prepared to both ask questions as well as to address potential questions.
- 4) Each presentation should include:
  - a) Describe rationale for choice of drug and cancer type: define biological process(s) being targeted, its relationship to disease specific carcinogenesis, evidence supporting the use of the chosen drug to target that process.
  - b) Describe rationale for trial design: provide data to support choice of dose and length of administration, discuss rationale of choice of primary endpoint (including assay type and supportive statistics)
  - c) Describe how you will implement the trial: how will you accrue, monitor individuals, acquire samples/data, and what methods will you use to analyze samples/data.
  - d) Describe the new information, which will be gained once the trial is complete: what important question will your primary endpoint address. Will secondary endpoints answer specific secondary questions, or will they be hypothesis generating. What is their importance, and expected outcome?
  - e) Describe potential problems: common versus unexpected, how will they be dealt with
- 5) If you have question or need direction, please contact Dr. Bergan who might refer you to someone who has more experience with that cancer site.
- 6) Please email a complete copy of your presentation to Dr. Bergan ([r-bergan@northwestern.edu](mailto:r-bergan@northwestern.edu)) no later than **12 noon, Monday November 26<sup>th</sup>**.
- 7) The presentation counts towards 50% of total class evaluation.

**"Academic Integrity**

Academic integrity at Northwestern University is based on a respect for individual achievement that lies at the heart of academic culture. Every faculty member and student, both graduate and undergraduate, belongs to a community of scholars where academic integrity is a fundamental commitment. The Programs in Public Health abides by the standards of academic conduct, procedures, and sanctions as set forth by The Graduate School at Northwestern University. Students are responsible for knowledge of the information provided by The Graduate School on their Web page at <http://www.tgs.northwestern.edu/studentsvcs/ethics/>.

Additionally, faculty reserve the right to use the "Safe Assignment: Plagiarism Detection Tool" that is part of the Course Management System. Info about this tool is found at <http://course-management.northwestern.edu/tipsheets.html>."