PubH PubH 6160-001
Metabolomics
Spring 2007

Credits: 3
Meeting Days: Mondays and Wednesdays
Meeting Time: 3:35-4:50 pm
Meeting Place: Mayo 1155
Instructor: Lisa Peterson
Office Address: CCRB 760D
Office Phone: 612-626-0164
Fax: 612-626-5135
E-mail: peter431@umn.edu
Office Hours: by appointment

I. Course Description
In this course, students will learn to apply information regarding basic pharmacokinetic principles and metabolic systems to elucidate mechanisms of toxicity induced by xenobiotic compounds. In addition, they will learn basic principles of metabolomic methods and their application to determine how environmental chemicals disrupt normal cellular processes.

II. Course Prerequisites
Biochemistry and PubH 6104 or permission of the instructor

III. Course Goals and Objectives
Students will: 1) learn basic pharmacokinetic principles of absorption, distribution, and elimination; 2) investigate biochemical mechanisms by which xenobiotics are bioactivated and detoxified by Phase I and Phase II enzymes; 3) examine genetic and environmental factors that affect these enzymes and influence the biochemical fate of xenobiotics; 4) learn how xenobiotics can influence endogenous pathways; and 5) formulate logical hypotheses about the biochemical basis of toxicity of xenobiotics.

IV. Methods of Instruction and Work Expectations
The primary method of instruction will be classroom lecture. The students are expected to attend each class and participate in classroom discussions. It is expected that the students have read and are capable of discussing any assigned readings in class.

Exams: There will be a midterm and final examination (each worth 100 points).

Homework: There will be graded homework assignments (each worth up to 20 points).

Report: There will be one research paper on a toxicant or pharmaceutical compound of the student's interest (200 points).
The ten page report (double spaced, 12 point) containing the following:

1. The physical chemical properties of the compound
2. The toxicological and/or pharmacological properties of the compound (parts 1 and 2: 2 page total).
3. A description of the known pharmacokinetic parameters for the compound, which includes major sites of how the compound is absorbed, distributed and excreted. Include in this description, how the physical chemical properties of the compound influence these parameters and how they relate to the toxicology and/or pharmacology of the compound. (2 page).
4. A scheme showing a physiologically based pharmacokinetic model for the compound
5. A description of the major routes of metabolism including a discussion of enzymes involved. Compare what is known about humans vs animal models (2 page).
6. A discussion of factors (endogenous, environmental, chemical and genetic) that affect the toxicological and/or pharmacological properties of the compound (4 pages). This discussion should include interactions of the compound and/or its metabolites with endogenous pathways.

Subsequent pages may be used for references. All resources should be appropriately referenced.

Timeline for submission of parts:
Monday, January 28, 2008: Let Dr. Peterson know the topic of your paper.
Monday, February 13, 2008: Turn in a draft document containing parts 1 and 2 (no more than 2 pages).
Monday, March 10, 2008: Turn in draft document containing parts 3 and 4 (no more than 2 pages for part 3; part 4 is a figure)
Monday, April 9, 2008: Turn in draft document containing part 5 (no more than 2 pages).
Friday, May 16, 2008: Turn in final document containing parts 1-6 to Dr. Peterson’s office by 12 noon. This document will contain all requested changes to parts 1-5 and part 6.

While the only final product will be graded (150 points), the students will receive 10 points for turning in each draft on time (for a total of 200 points).

Oral Presentation.

On the last three days of class, each student will make a 20 min oral presentation of their research report. This is worth 50 points.

V. Course Text and Readings
The following books are on reserve at the Biomedical Library

Casarett & Doull’s Toxicology. Available at the Biomedical Library Reserve Desk as well as online through the biomedical library website.


Resources for the research paper:Books in the Library:

Books on Reserve at the Biomedical Library:
Biochemistry, Stryer

Journals:
Annual Reviews in Pharmacology and Toxicology http://pharmtox.annualreviews.org/
Cancer, Epidemiology, and Biomarkers-ejournal accessible through MNCAT
VI. Course Outline/Weekly Schedule

see attached document

VII. Evaluation and Grading

1. Grading Criteria - Letter grades and associated points are awarded in this course as follows below, and will appear on the student’s official transcript.
2. Grading Option (if applicable) – Students may change grading options during the initial registration period or during the first two weeks of the term. The grading option may not be changed after the second week of the term.

A -- 93 - 100 %
A- -- 90-92 %
B+ -- 87-89 %
B -- 83-86 %
B- -- 80-82 %
C+ -- 77-79 %
C -- 73-77 %
C- -- 70-72 %
D+-- 67-69 %
D -- 63-66 %
D- -- 60-62 %
F -- 0 - 60 %

F (or N) – Represents failure (or no credit) and signifies that the work was either (1) completed but at a level of achievement that is not worthy of credit or (2) was not completed and there was no agreement between the instructor and the student that the student would be awarded an I.

S – Achievement that is satisfactory will be expected to complete all assignments and receive a minimum of 70% to receive a passing score (achievement required for an S is at the discretion of the instructor but may be no lower than a 70%).

[If applicable, there should also be a statement on penalties for late work and/or a make-up exam policy.]

Procedure for contesting a grade:
If you disagree with the way an answer to an exam question has been graded, please do the following:

a. Make a photocopy of the exam question and your answer.

b. Write an explanation of why you disagree with the way your answer was graded.

c. Deliver the items mentioned in 1 and 2 to the office of the instructor within one week of receiving the grade from your exam.

d. Make an appointment with the instructor to discuss your question regarding the grading of the exam question.

Incomplete Grade
A grade of “I” (incomplete) will not be permitted except in the case of a documented emergency (e.g., medical). If an incomplete is deemed appropriate by the instructor, the student, in consultation with the instructor, will prepare a detailed written agreement specifying the time and manner in which the student will complete the course requirements. The written contract will give explicit details for every component of the course which remains to be completed. Extension for completion of the work will not exceed one year. The written agreement must be submitted to the instructor, major coordinator and the Student Services Center prior to the date by which grades must be entered at the end of the term.

After a review of transcripts (end of semester), instructors teaching School of Public Health courses will be contacted by the Student Services Center regarding assigned grades of “I” for students. If a written agreement exists between the student and instructor, the incomplete will remain on the transcript per the terms of the agreement. If a written agreement does not exist and an incomplete was submitted for the student without a written agreement, a grade of “F” or “N” will be officially submitted by the Student Services Center. If the student does not comply and meet the deadlines as determined in the written agreement, a grade of “F” or “N” will be officially submitted by the Student Services Center.

University of Minnesota Uniform Grading and Transcript Policy
A link to the policy can be found at onestop.umn.edu.

VIII. Other Course Information and Policies

Grade Option Change (if applicable)
For full-semester courses, students may change their grad option, if applicable, through the second week of the semester. Grade option change deadlines for other terms (i.e. summer and half-semester) can be found at onestop.umn.edu.

Course Withdrawal
Students should refer to the Refund and Drop/Add Deadlines for the particular term at onestop.umn.edu for information and deadlines for withdrawing from a course. As a courtesy, students should notify their instructor and, if applicable, advisor of their intent to withdraw.

Students wishing to withdraw from a course after the noted final deadline for a particular term must contact the School of Public Health Student Services Center at sph-ssc@umn.edu for further information.

Student Conduct, Scholastic Dishonesty and Sexual Harassment Policies
Students are responsible for knowing the University of Minnesota, Board of Regents’ policy on Student Conduct and Sexual Harassment found at www.umn.edu/regents/polindex.html.

Students are responsible for maintaining scholastic honesty in their work at all times. Students engaged in scholastic dishonesty will be penalized, and offenses will be reported to the Office of Student Academic Integrity (OSAI, www.osai.umn.edu).

The University’s Student Conduct Code defines scholastic dishonesty as “plagiarizing; cheating on assignments or examinations; engaging in unauthorized collaboration on academic work; taking, acquiring, or using test materials without faculty permission; submitting false or incomplete records of academic achievement; acting alone or in cooperation with another to falsify records or to obtain dishonestly grades, honors, awards, or professional endorsement; or altering, forging, or misusing a University academic record; or fabricating or falsifying of data, research procedures, or data analysis.”

Plagiarism is an important element of this policy. It is defined as the presentation of another’s writing or ideas as your own. Serious, intentional plagiarism will result in a grade of “F” or “N” for the entire course. For more
information on this policy and for a helpful discussion of preventing plagiarism, please consult University policies and procedures regarding academic integrity: http://writing.umn.edu/tww/plagiarism/.

Students are urged to be careful that they properly attribute and cite others’ work in their own writing. For guidelines for correctly citing sources, go to http://tutorial.lib.umn.edu/ and click on “Citing Sources”.

In addition, original work is expected in this course. It is unacceptable to hand in assignments for this course for which you receive credit in another course unless by prior agreement with the instructor. Building on a line of work begun in another course or leading to a thesis, dissertation, or final project is acceptable.

If you have any questions, consult the instructor.

**Disability Statement**

It is University policy to provide, on a flexible and individualized basis, reasonable accommodations to students who have a documented disability (e.g., physical, learning, psychiatric, vision, hearing, or systemic) that may affect their ability to participate in course activities or to meet course requirements. Students with disabilities are encouraged to contact Disability Services to have a confidential discussion of their individual needs for accommodations. Disability Services is located in Suite180 McNamara Alumni Center, 200 Oak Street. Staff can be reached by calling 612/626-1333 (voice or TTY).
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<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Lecturer</th>
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<tbody>
<tr>
<td>Wed, Jan. 23, 2008</td>
<td>Introduction</td>
<td>Lisa Peterson</td>
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<tr>
<td>Mon, Jan. 28, 2008</td>
<td>Toxicokinetics</td>
<td>Cheryl Zimmerman</td>
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<td>Wed, Jan. 30, 2008</td>
<td>Toxicokinetics</td>
<td>Cheryl Zimmerman</td>
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<td>Mon, Feb. 4, 2008</td>
<td>Physiologically based Pharmacokinetic Model</td>
<td>Cheryl Zimmerman</td>
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<td>Wed, Feb. 6, 2008</td>
<td>Turnover Concepts</td>
<td>William Elmquist</td>
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<td>Mon, Feb. 11, 2008</td>
<td>Transporters</td>
<td>William Elmquist</td>
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<td>Wed, Feb. 13, 2008</td>
<td>Xenobiotic metabolism</td>
<td>Lisa Peterson</td>
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<td>Mon, Feb. 18, 2008</td>
<td>Xenobiotic Metabolism</td>
<td>Lisa Peterson</td>
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<td>Wed, Feb. 20, 2008</td>
<td>Xenobiotic Metabolism</td>
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<td>Mon., Feb. 25, 2008</td>
<td>Factors that influence metabolism</td>
<td>Lisa Peterson</td>
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<td>Wed, Feb. 27, 2008</td>
<td>Species differences in xenobiotic metabolism</td>
<td>Lisa Peterson</td>
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<td>Mon, March 3, 2008</td>
<td>Genetic differences in xenobiotic metabolism</td>
<td>Lisa Peterson</td>
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<td>Wed, March 5, 2008</td>
<td>Lessons from transgenic animals</td>
<td>Lisa Peterson</td>
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<td>Mon, March 10, 2008</td>
<td>Systems Biology</td>
<td>Lisa Peterson</td>
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<td>Wed, March 12, 2008</td>
<td>PCA analysis</td>
<td>Francois Sanfort</td>
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<td>March 17-21, 2008</td>
<td>Spring Break</td>
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<td>Date</td>
<td>Topic</td>
<td>Instructor</td>
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<td>Mon, March 24, 2008</td>
<td>Oxidative Stress</td>
<td>Lisa Peterson</td>
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<td>Wed, March 25, 2008</td>
<td>Genomics methods</td>
<td>Lisa Peterson</td>
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<td><strong>Turn in take home mid-term exam</strong></td>
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<td>Mon, March 31, 2008</td>
<td>Genomics paper</td>
<td>Lisa Peterson</td>
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<td><strong>The following paper will be discussed in class:</strong> American Journal of Human Genetics (2007) 81: 427-437.</td>
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<td>Wed, April 2, 2008</td>
<td>Epigenomics</td>
<td>Heather Nelson</td>
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<td>Mon, April 7, 2008</td>
<td>Proteomics methods</td>
<td>Lisa Peterson</td>
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<td>Wed, April 9, 2008</td>
<td>Proteomics paper</td>
<td>Lisa Peterson</td>
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<td>Mon, April 14, 2008</td>
<td>Metabolomic methods</td>
<td>Lisa Peterson</td>
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<td><strong>Turn in draft part 5</strong></td>
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<td>Wed, April 16, 2008</td>
<td>Metabolomics paper</td>
<td>Lisa Peterson</td>
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<td><strong>The following paper will be discussed in class:</strong> Chem. Res. Toxicol. 16:295-303, 2003.</td>
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<td>Mon, April 21, 2008</td>
<td>Metabolomics paper</td>
<td>Lisa Peterson</td>
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<td><strong>The following paper will be discussed in class:</strong> NeuroToxicology (2008), 29, 1-12.</td>
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<td>Wed, April 23, 2008</td>
<td>Defining biochemical networks</td>
<td>Lisa Peterson</td>
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<td>Mon, April 28, 2008</td>
<td>Systems Toxicology paper</td>
<td>Lisa Peterson</td>
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<td><strong>The following paper will be discussed in class:</strong> J Proteome Res. 5: 1586-1601, 2006</td>
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<td>Wed, April 30, 2008</td>
<td>Student Presentations</td>
<td>Lisa Peterson</td>
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<td>Mon, May 5, 2008</td>
<td>Student Presentations</td>
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<td>Wed, May 7, 2008</td>
<td>Final Exam</td>
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<td><strong>Friday, May 16, 2008: Turn in final document containing parts 1-6 to Dr. Peterson’s office by 12 noon.</strong></td>
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The biochemistry/chemistry you need to know or learn for this course:

- **Functional Groups**
  - Carboxylic acids
  - Aldehydes
  - Ketones
  - Aromatic groups/heterocycles
  - Esters
  - Amides
  - Thiols (sulfhydryl)
  - Epoxide

- **Nucleophiles/Electrophiles**

- **Bonding**
  - Covalent bonds
  - Coordinate covalent bonds
  - Ionic bonds
  - Hydrogen bonds
  - van der Waal's interactions

- **Oxidation/reduction**

- **Thermodynamics and equilibria**

- **Acid/base chemistry**

- **Reaction kinetics and mechanism**
  - Zero-, First- and Second-order Reaction Kinetics
  - $S_N^1$ and $S_N^2$ nucleophilic substitution mechanisms
  - Michael Acceptors

- **Enzymes**
  - Kinetics
  - Co-factors/co-substrates: NAD$^+$/NADH, FAD/FADH; FMN, coenzyme A/acetyl CoA; UDP-glucuronic acid; ATP, 3'-phosphoadenosine-5'-phosphosulfate (PAPS); S-adenosylmethionine (SAM), glutathione

- **Lipids**
  - Membrane structure
  - Types of lipids: fatty acids (e.g. arachadonic acid), triglycerides, phospholipids

- **Mitochondrial structure and function**

- **Metabolism and ATP generation**

- **DNA structure**
  - Bases, nucleosides, nucleotides
  - Primary and secondary structure

- **Proteins/peptides**
  - Amino acid structure and side chain chemistry
  - Peptide bonds