SYLLABUS & COURSE INFORMATION

SCHOOL OF PUBLIC HEALTH
UNIVERSITY OF MINNESOTA

PUBH 6160

Principle of Toxicology II
Spring 2019

Grading Option A/F

COURSE & CONTACT INFORMATION

Credits: 3
Meeting Day(s): Tuesdays and Thursdays
Meeting Time: 3:35 pm – 4:50 pm
Meeting Place: Mayo 1155

Instructors: Lisa Peterson and Irina Stepanov
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Office Hours: by appointment
Office Location: 2-126 CCRB

COURSE DESCRIPTION

This second part of the Principles of Toxicology course is focused on toxicodynamics. In this course, students will learn to apply their knowledge of basic toxicokinetic principles and metabolic systems to elucidate mechanisms of toxicity induced by xenobiotic compounds. In addition, they will learn basic principles of omics-based approaches and methodologies, and how such data can be integrated to assess and predict adverse effects of chemical exposures across multiple levels of biological complexity. At the end of the course, students will give a scientific presentation on a published article of their choice (approved by instructors) that explores the mechanism of a toxicodynamic process.

Acknowledgments
The contents of PubH 6160 have been developed with the contributions of the Toxicology Advisory Board comprised of toxicology experts from Minnesota Department of Health, Environmental Protection Agency and various companies and organizations, including Cargill, Medtronic, 3M, Ecolab, Upsher-Smith, Covestro, and Proximagen. The Board members provided input on the conceptual development of the current course, and are acknowledged for their contributions.

COURSE PREREQUISITES

Biochemistry and PubH 6104 or permission of the instructor

COURSE GOALS & OBJECTIVES

Students will: 1) learn basic principles of signaling pathways and mechanisms of cell death; 2) understand gene-environment interactions; 3) examine the application of genomics, proteomics, and metabolomics data in determining how xenobiotics disrupt normal cellular processes; 4) understand mechanisms of systemic and organ toxicity induced by xenobiotics; and 5) learn how to analyze and interpret complex data sets in toxicological research and deliver a scientific presentation.

METHODS OF INSTRUCTION AND WORK EXPECTATIONS

Course Workload Expectations
PubH6160 is a 3 credit course. The University expects that for each credit, you will spend a minimum of three hours per week attending class or comparable online activity, reading, studying, completing assignments, etc. over the course of a 15-week term.

The primary method of instruction will be classroom lecture and discussions. 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.

Learning Community
In this course, students are expected to engage with each other in respectful and thoughtful ways.

In group discussion, this can mean:

- Respecting the identities and experiences of your classmates.
- Avoid broad statements and generalizations. Group discussions are another form of academic communication and responses to instructor questions in a group discussion are evaluated.
- Consider your tone and language.

Like other work in the course, all student to student communication is covered by the Student Conduct Code (https://z.umn.edu/studentconduct).

COURSE TEXT & READINGS

Books

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

Comprehensive Toxicology, Second Edition, Editor Charlene McQueen, 2010; available online through the biomedical library website

Molecular and Biochemical Toxicology, Fourth Edition, Editors: R.C. Smart and E. Hodgson, 2008; available online through the biomedical library website.

International Agency for Research on Cancer: IARC Monographs on the Evaluation of Carcinogenic Risk to Humans, available online through the IARC website.

Examples of journals for scientific presentation (online access through UMN library)

- Annual Reviews in Pharmacology and Toxicology
- Chemico-Biological Interactions
- Chemical Research in Toxicology
- Critical reviews in toxicology
- Regulatory Toxicology and Pharmacology
- Toxicology letters
- Environmental toxicology
- Food and chemical toxicology

COURSE OUTLINE/WEEKLY SCHEDULE

Week	Topic	Readings	Activities/Assignments
Week 1 **1/21-1/25**	• **Lecture 1 (1/22): Introduction to the course** **Irina Stepanov**	• Chapter 3 Casarett & Doull's Toxicology	**Learning objectives:** • Understand the course content, structure, and expectations for the course project
	• **Lecture 2 (1/24): Signaling pathways** **Thu Truong**	• Chapters 5-6, The Biology of Cancer, RA Weinberg or Chapters 4-6, The Biology of Cancer, 2nd Ed., RA Weinberg	**Learning objectives:** • Understand how signaling molecules bind to receptors • Understand how interaction of cell with its environment can influence cell morphology, behavior, division, or survival • Understand how exposure to chemicals may affect these interactions
Week 2 **1/28-2/1**	• **Lecture 3 (1/29): Mechanisms of cell death – apoptosis, necrosis, autophagy** **Lisa Peterson**	• Comprehensive Toxicology 2nd Edition, Volume 1 Chapter 12 Cytolethality • Chapter 3 Casarett & Doull's Toxicology. • Chapter 16, Molecular and Biochemical Toxicology • Shen, S., & Codogno, P. (2016). The Role of Autophagy in Cell Death. In Autophagy: Cancer, Other Pathologies, Inflammation, Immunity, Infection, and Aging (pp. 139-154). https://www.sciencedirect.com/science/article/pii/B9780128029374000077	**Assignment: Compare and contrast discussion of assigned reviews (cell death)** **Learning objectives:** • Understand basic mechanisms of apoptosis, necrosis, and autophagy • For each cell death mechanism, understand: mediators of process; effects of environmental exposures; clinical implications
	• **Lecture 4 (1/31): Genomics** **Colin Campbell**	• Reading: Comprehensive Toxicology 2nd Edition, Volume 1 Chapter 18 • Pinker, S. (2009). My Genome, My Self. New York Magazine • https://www.npr.org/sections/health-shots/2018/01/22/578293890/my-grandmother-was-italian-why-arent-my-genes-italian	**Learning objectives:** • Understand genetic variation and its impact on the toxic response • Understand methodologies: hybridization, molecular cloning, gene sequencing
Week 3 **2/4-2/8**	• **Lecture 5 (2/5): Epigenomics** **Lisa Peterson**	• Comprehensive Toxicology 2nd Edition, Volume 1 Chapter 18 • Comprehensive Toxicology 2nd Edition, Volume 2 Chapter 4 • Skinner, M. L. (2014 August). A New Kind of Inheritance. Scientific American	**Learning objectives:** • Understand epigenetics and its importance in gene regulation and disease • Understand how chemical exposures and other environmental stressors affect DNA methylation • Understand methodologies for the analysis of DNA methylation and histone modifications
	• **Lecture 6 (2/7): Paper discussion** **Lisa Peterson**	• C. Weinhouse, et al. (2016) Environmental and Molecular Mutagenesis 57: 435-446.	**Prepare for paper discussion**

Week 4 **2/11-2/15**	• **Lecture 7 (2/12): Transcriptomics** **Kevin Silverstein**	• Comprehensive Toxicology 2nd Edition, Volume 1 Chapter 18 • Comprehensive Toxicology 2nd Edition, Volume 2 Chapter 4	**Learning objectives:** • Understand gene regulation and how chemical exposures affect gene expression • Methodologies: hybridization, PCR
	• **Lecture 8 (2/14): Proteomics** **Yue Chen**	• Chapter 4, Molecular and Biochemical Toxicology • Titz, B., et al (2014). Computational and Structural Biotechnology Journal, 11, 73-90.	**Learning objectives:** • Chemical exposures and post-translational protein modifications • Analytical tools and platforms for studies of protein expression and modifications
Week 5 **2/18-2/22**	• **Lecture 9 (2/19): Metabolomics** **Lisa Peterson**	• Bouhifd, M., et al. (2013). Toxicometabolomics. Journal of Applied Toxicology, 33(12), 1365-1383. • Chapter 5, Molecular and Biochemical Toxicology	**Learning objectives:** • The principles of metabolomics • Analytical tools and platforms for metabolomics studies • Selection of appropriate experimental designs • Analysis and interpretation of metabolomics data
	• **Lecture 10 (2/21): Systems Toxicology paper discussion** **Lisa Peterson**	Gao, B.et al. (2017). Multi-omics reveals that lead exposure disturbs gut microbiome development, key metabolites, and metabolic pathways. Chemical Research in Toxicology, 30(4), 996-1005.	**Assignment:** Prepare for paper discussion
Week 6 **2/25-3/1**	• **Lecture 11 (2/26): Endocrine Disruption** **Bill Toscano**	• Chapter 10 Casarett & Doull's Toxicology.	**Learning objectives:** • Mechanisms and effects of endocrine disruption by environmental contaminants • Complexities, knowledge gaps, and limitations in identifying the causes of endocrine disruption • Impact of environmental exposures on male and female reproductive capability.
	• **Lecture 12 (2/28): Developmental Toxicology** **Bill Toscano**	• Chapter 34, Molecular and Biochemical Toxicology	**Learning objectives:** • Impact of environmental exposures on in utero development and birth outcomes
Week 7 **3/4-3/8**	• **Lecture 13 (3/5): Paper discussion** **Irina Stepanov**	X. Jiang et al (2018) Toxicology and Applied Pharmacology 355: 247 – 256.	**Assignment (3/5): Prepare for paper discussion on developmental toxicology**
	• **Lecture 14 (3/7): Neurotoxicity** **Lisa Peterson**	• Chapter 16 Casarett & Doull's Toxicology. • Chapters 30 and 31, Molecular and Biochemical Toxicology	**Learning objectives:** • Mechanisms of neurotoxicity • Environmental neurotoxicants • Neurotoxicity assays
Week 8 **3/11-3/15**	• **Lecture 15 (3/12): Paper discussion** **Lisa Peterson**	Teismann Pet al. (2003) Proc Natl Acad Sci U S A. 100: 5473-5478.	**Assignment: Prepare for paper discussion on neurotoxicity**

	• **Lecture 16 (3/14): Immunotoxicology – cytokine networks** **Devavani Chatterjea**	• Chapter 12, Casarett & Doull's Toxicology. • Chapter 32, Molecular and Biochemical Toxicology • Germolec, D., et al. (2017). Current Opinion in Toxicology, 5, 55-59.	**Learning objectives:** • The immune system, major functions, levels and types of immune regulation • Immune pathologies and mechanisms of immunotoxicology by environmental agents • Methodologies and tools for the assessment of immunotoxicological effects
	3/14: receive take home mid-term exam	**Due 3:30 pm 3/26**	
Spring break 3/18-3/22			
Week 9 **3/25-3/29**	• **Lecture 17 (3/26): Oxidative stress and inflammation** **Irina Stepanov**	• Comprehensive Toxicology 2nd Edition, Volume 1 Chapter 14 • Comprehensive Toxicology 2nd Edition, Volume 5 Chapter 16	**Learning objectives (3/26):** • Mechanisms of oxidative stress and inflammation, and their interaction • Environmental exposures and stressors contributing to oxidative stress and inflammation • Biomarkers of oxidative damage, inflammation, and tools for their analyses
	• **Lecture 18 (3/28): Paper discussion** **Irina Stepanov**	Shah A, et al. (2018) Toxicol Appl Pharmacol. 350: 52-63	**Assignment:** Prepare for paper discussion on immunotoxicity and inflammation
Week 10 **4/1-4/5**	• **Lecture 19 (4/2): Chemical carcinogenesis and the foundations of multi-stage carcinogenesis** **Elizabeth Wattenberg**	• Chapter 8 Casarett & Doull's Toxicology. • Chapter 24, Molecular and Biochemical Toxicology • https://www.ncbi.nlm.nih.gov/pubmed/26600562 • https://www.ncbi.nlm.nih.gov/pubmed/15660110 • https://www.ncbi.nlm.nih.gov/pubmed/25302469	**Learning objectives:** • Multistage carcinogenesis model of cancer • Mechanisms of cancer promotion and progression • Environmental agents that facilitate cancer promotion and progression • In vitro and animal models of carcinogenesis
	• **Lecture 20 (4/4): Carcinogenesis – DNA damage and mutagenesis** **Silvia Balbo**	• Chapter 9 Casarett & Doull's Toxicology • Chapters 22, 23 and 25, Molecular and Biochemical Toxicology	**Learning objectives:** • Formation of DNA adducts and other DNA modifications by environmental agents • DNA repair mechanisms and impact of chemical exposures on DNA repair • Types and consequences of mutations • Methodologies for the analysis of DNA damage, repair, and mutagenesis
Week 11 **4/8-4/12**	• **Lecture 21 (4/9): Paper discussion** **Irina Stepanov**	**Paper for discussion:** • Weng, et al. (2007). Cancer Research, 67(16), 7825-7832. https://www.ncbi.nlm.nih.gov/pubmed/17699788	**Assignment:** Prepare for paper discussion on carcinogenesis
	• **Lecture 22 (4/11): In class workshop**		**Assignment:** Prepare a draft presentation of the course project

Week 12 **4/15-4/19**	• **Lecture 23 (4/16): Hepatotoxicity** **Rob Roy**	• Chapter 13, Casarett & Doull's Toxicology. • Chapter 28, Molecular and Biochemical Toxicology	**Learning objectives:** • Mechanisms of hepatotoxicity and hepatotoxic agents/metabolites • In vitro and animal models of hepatotoxicity
	• **Lecture 24 (4/18): Nephrotoxicity** **Catherine Jacobson**	• Chapter 14 Casarett & Doull's Toxicology. • Chapter 29, Molecular and Biochemical Toxicology	**Learning objectives:** • Mechanisms of nephrotoxicity and nephrotoxic agents/metabolites • In vitro and animal models of nephrotoxicity
Week 13 **4/22-4/26**	• **Lecture 25 (4/23): Respiratory toxicity** **Rob Roy and Catherine Jacobson**	• Chapter 15, Casarett & Doull's Toxicology. • Chapter 27, Molecular and Biochemical Toxicology	**Learning objectives:** • Mechanisms of respiratory toxicity, respiratory irritants, inflammatory agents • In vitro and animal models of respiratory toxicity
	• **Lecture 26 (4/25): Cardiovascular toxicity** **Nicole Soucy**	• Chapter 18, Casarett & Doull's Toxicology	**Learning objectives:** • Mechanisms of cardiovascular toxicity and cardiovascular toxicants • In vitro and animal models of cardiovascular toxicity
Week 14 **4/29-5/3**	• **Lecture 27 (4/30): Toxicity testing** **Kelly Coleman**	• https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2746847/ • https://www.ncbi.nlm.nih.gov/pubmed/27351633 • http://www.scopemed.org/?mno=217140 • https://www.ncbi.nlm.nih.gov/pubmed/18186670 • https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4594046/ • https://www.ncbi.nlm.nih.gov/pubmed/29371136 • Alternative Methods Validated for Regulatory Use. PETA International Science Consortium, UK.	**Learning objectives:** • Toxicity testing in regulatory and industry settings • Predictive capacity and limitations of in vitro and in vivo data • Novel alternative testing methods
	• **Lecture 28 (5/2): Student presentations**		**Assignment: Final presentation of the selected papers**
5/2	**Receive take home final**	**Due 12 pm on 5/7**	

Course project
Course project will consist of giving a 15-minute scientific presentation (plus 5 min Q&A) on a published article that explores the mechanism of a toxicodynamic process. Each student will be required to select three papers which will be evaluated by instructors so that at least one can be approved for presentation. If more than one paper is approved, the student will choose which one to present. If none of the papers is acceptable, student will have to select additional paper options for approval. At the end of the semester, students will give a scientific presentation of their selected papers as if this is their own research project. Specific guidelines and grading rubrics for presentations will be reviewed at the beginning of the course and posted on the Canvas site.

SPH AND UNIVERSITY POLICIES & RESOURCES

The School of Public Health maintains up-to-date information about resources available to students, as well as formal course policies, on our website at www.sph.umn.edu/student-policies/. Students are expected to read and understand all policy information available at this link and are encouraged to make use of the resources available.

The University of Minnesota has official policies, including but not limited to the following:

- Grade definitions
- Scholastic dishonesty
- Makeup work for legitimate absences
- Student conduct code
- Sexual harassment, sexual assault, stalking and relationship violence
- Equity, diversity, equal employment opportunity, and affirmative action
- Disability services
- Academic freedom and responsibility

Resources available for students include:

- Confidential mental health services
- Disability accommodations
- Housing and financial instability resources
- Technology help
- Academic support

EVALUATION & GRADING

Grading percentages will be based on points earned through the assignments and exams. A total of 415 points (100% of the total grade) can be earned as determined by the following:

Classroom activities and evaluations (115 points, 28% of the grade)

The purpose of these activities is to involve students in active learning process and to apply the gained knowledge to the analysis of case studies.

Paper discussions (105 points). Students will read assigned research papers and prepare for class discussion, focusing on the critique of issues relevant to the specific course topic (as indicated by the instructor). Points will be awarded for active discussion in the class. A total of seven papers will be discussed (15 points/paper). If a student is unable to attend the class, an opportunity will be offered to earn points by writing a summary of the assigned paper.

Lecture evaluations (10 points). Students will be required to evaluate lectures by using a provided template and upload the evaluations on Moodle site (https://moodle.umn.edu/). Points (0.5 point/evaluation) will be awarded for turning in the evaluation within 24 hours after the end of the class.

Exams (200 points, 48% of the grade)

Students can earn a maximum of 100 points for each exam – midterm and final – to a total of 200 points.

Paper presentation (100 points, 24% of the grade)

Each student will present their selected paper following guidelines provided by the instructors. Points will be awarded according to the rubric which will provided by the instructors at the time when the paper selection is approved.

Grading Scale
The University uses plus and minus grading on a 4.000 cumulative grade point scale in accordance with the following, and you can expect the grade lines to be drawn as follows:

% In Class	Grade	GPA
93 - 100%	A	4.000
90 - 92%	A-	3.667
87 - 89%	B+	3.333
83 - 86%	B	3.000
80 - 82%	B-	2.667
77 - 79%	C+	2.333
73 - 76%	C	2.000
70 - 72%	C-	1.667
67 - 69%	D+	1.333
63 - 66%	D	1.000
< 62%	F	

- A = achievement that is outstanding relative to the level necessary to meet course requirements.
- B = achievement that is significantly above the level necessary to meet course requirements.
- C = achievement that meets the course requirements in every respect.
- D = achievement that is worthy of credit even though it fails to meet fully the course requirements.
- F = failure because 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 (Incomplete).
- S = achievement that is satisfactory, which is equivalent to a C- or better
- N = achievement that is not satisfactory and signifies that the work was either 1) completed but at a level that is not worthy of credit, or 2) not completed and there was no agreement between the instructor and student that the student would receive an I (Incomplete).

Evaluation/Grading Policy	Evaluation/Grading Policy Description
Scholastic Dishonesty, Plagiarism, Cheating, etc.	You are expected to do your own academic work and cite sources as necessary. Failing to do so is scholastic dishonesty. Scholastic dishonesty means 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; altering, forging, or misusing a University academic record; or fabricating or falsifying data, research procedures, or data analysis (As defined in the Student Conduct Code). For additional information, please see https://z.umn.edu/dishonesty The Office for Student Conduct and Academic Integrity has compiled a useful list of Frequently Asked Questions pertaining to scholastic dishonesty: https://z.umn.edu/integrity. If you have additional questions, please clarify with your instructor. Your instructor can respond to your specific questions regarding what would constitute scholastic dishonesty in the context of a particular class-e.g., whether collaboration on assignments is permitted, requirements and methods for citing sources, if electronic aids are permitted or prohibited during an exam. Indiana University offers a clear description of plagiarism and an online quiz to check your understanding (http://z.umn.edu/iuplagiarism).
Late Assignments	Late work will be penalized by reduction in points: 5% of the total points for every late day.
Attendance Requirements	Students are expected to attend all classes and actively participate in class discussions. When approved absences occur (see University of Minnesota policy https://policy.umn.edu/education/makeupwork), the students should work with the faculty to develop a plan to make up for missed class discussion points.
Extra Credit	Extra credit is not offered in this course.

CEPH COMPETENCIES

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Resources for filling out the CEPH competencies grid are available on isph:
http://www.isph.umn.edu/sph/instructor-resources/

Competency	ssment Strategies