

ENVH 532

Reproductive and Developmental Toxicology

3 Credits, Winter 2017

Tuesdays (12:30-1:20pm) and Wednesdays (4:30pm-6:20pm)

Instructor

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Course Description

This class will cover basic principles of normal reproduction and development and then focus on how and when environmental chemicals induce adverse reproductive and developmental outcomes. Discussion topics include identification and characterization of specific classes of reproductive and developmental toxicants, mechanisms of action of these agents at the molecular and cellular level, and risk assessment and regulatory issues relevant for reproductive health. The course will include discussions of recent literature as well as in-class demonstrations of laboratory-based assessments for reproductive and developmental toxicology. A key focus will be on understanding gene-environment issues. Practical approaches for communicating developmental and reproductive risk issues will be given. As a base for this course we will use a free Primer from the Teratology Society, an electronic copy of which will be made available to all students. This course provides an in depth immersion for these important endpoints in public health.

Learning Objectives

At the end of the course, students shall be able to:

- 1) Describe the main themes of reproductive and developmental toxicology and Identify new emerging issues for reproductive public health.
- 2) Discuss current research issues in these topics.
- 3) Summarize in-class laboratory demonstrations assessing reproductive and developmental toxicology. Characterize strengths and limitations in applying these approaches for assessing reproductive and developmental impacts.
- 4) Apply approaches for data integration for evaluating these complex and dynamic endpoints.
- 5) Demonstrate skills for synthesis and oral and written reporting of research.
- 6) Share in the excitement of this area of study

Assignments

- 1) Become familiar with background material
- 2) Read, critique and report on current literature. You are expected to read 6 articles and write a review as described below.
- 3) Fill out a brief report (1-2 pages) for each paper review assignment. Come to class prepared to share your points orally in front of the class for your papers. Prepare copies of all of your assignments so we can share with your classmates. Remember that your fellow students will not have read every paper so you will need to prepare the equivalent of 1-3 slides with key points, figures, and tables from the paper to familiarize everyone.
- 4) Required Paper (see details below): Option 1- Propose a research study based on an evaluation of the shortcomings of the research in a reproductive or developmental toxicology area of your choice that will improve upon existing data. Option 2- Propose a Mechanism or Proposed Adverse Outcome Pathway (AOP) for your agent of interest. Use the outline to support your proposed MOA or AOP and to identify additional research you would like to do to confirm your mechanism or AOP. The short proposal (3-5 page max) must be organized as follows:
 - A. Abstract containing Hypothesis or Proposed Mechanism and list of 2 Specific Aims
 - B. Background & Significance
 - C. Preliminary Data (based on the literature)
 - D. Experimental Design & Methods
Note: One Specific Aim must contain
 - 1.) rationale
 - 2.) short experimental design
 - 3.) expectations & pitfalls
 - E. References

An example proposal will be provided as a guide.

Required Paper

Students will be required to write a 3-5 page proposal, expanding one of the course topics. Examples include but are not limited to endocrine disruptors, stress and pregnancy outcome, nutrition (prevention versus prescription), pesticides, drugs, radiation, mechanisms of normal and perturbed development, 17 pathways of evolutionary conserved cell signaling, lifestage models for children, autism, neural tube defects, fetal basis of adult disease, and epigenetics and development. Papers will require a framework of problem/issue formation, analysis and science integration, characterization and finally steps forward. Dependent on student background and interest, a research application or risk assessment AOP framework will be employed.

Course Grade

Students are required to constructively participate in class discussions and to synthesize scientific literature and key issues into discussions, presentations, and written materials (short manuscripts reviews, and required paper). Students who miss a session will be responsible for preparing the overheads and key points and sending these to the instructor prior to class.

Students will be graded as follows:

<u>Graded Assignments</u>	<u>Percentage of Grade</u>
Short Written Literature Reviews (6 total reviews)	30%
Brief Presentation of Literature Reviews	20%
3-5 Page Proposal	40%
<u>Credit/No Credit</u>	
Lab Demonstration Forms (5 completed forms)	10%
<hr/>	
100%	

Academic Integrity (<http://sph.washington.edu/students/academicintegrity>)

Students at the University of Washington (UW) are expected to maintain the highest standards of academic conduct, professional honesty, and personal integrity. The UW School of Public Health (SPH) is committed to upholding standards of academic integrity consistent with the academic and professional communities of which it is a part. Plagiarism, cheating, and other misconduct are serious violations of the University of Washington Student Conduct Code (WAC 478-120). We expect you to know and follow the university's policies on cheating and plagiarism, and the SPH Academic Integrity Policy. Any suspected cases of academic misconduct will be handled according to University of Washington regulations. For more information, see the University of Washington Community Standards and Student Conduct website.

UW Disability Statement (<http://depts.washington.edu/uwdrs/faculty-resources/syllabus-statement>)

Access and Accommodations: Your experience in this class is important to me. If you have already established accommodations with Disability Resources for Students (DRS), please communicate your approved accommodations to me at your earliest convenience so we can discuss your needs in this course. If you have not yet established services through DRS, but have a temporary health condition or permanent disability that requires accommodations (conditions include but not limited to; mental health, attention-related, learning, vision, hearing, physical or health impacts), you are welcome to contact DRS at 206-543-8924 or uwdrs@uw.edu or disability.uw.edu. DRS offers resources and coordinates reasonable accommodations for students with disabilities and/or temporary health conditions. Reasonable accommodations are established through an interactive process between you, your instructor(s) and DRS. It is the policy and practice of the University of Washington to create inclusive and accessible learning environments consistent with federal and state law.

Multi-cultural Inclusion Commitment from Environmental Health

The UW School of Public Health seeks to ensure all students are fully included in each course. We strive to create an environment that reflects community and mutual caring. We encourage students with concerns about classroom climate to talk to your instructor, your advisor, a member of the departmental or SPH Diversity Committee and/or the program director. DCinfo@uw.edu is a resource for students with classroom climate concerns.

We have the privilege of learning together and we have a responsibility to engage in dialogue in a way that supports learning for all of us. Many of the issues we will discuss in this course may concern issues of disproportionate risks, sensitivities, and impacts due to age, gender, race, and/or social inequalities. This is what public health hopes to address, however we know that these can be difficult topics to

address, hence we thus feel it is even more important to be sensitive to our colleagues' experiences and ideas. Here are some practices we as learning community members can strive to use in our learning process:

- My own viewpoint is important—share it. It will enrich others.
- My students' and colleagues' viewpoints are important—listen to them. Do not judge them.
- Extend the same listening respect to others I would wish them to extend to me. We all have room to grow to become better listeners in non-judgmental ways.
- Recognize that I might miss things others see and see things others might miss.
- Raise my views in such a way that I encourage others to raise theirs.
- Inquire into others' views while inviting them to inquire into mine.
- Ask questions when I don't understand something.
- Surface my feelings in such a way that we make it easier for others to surface theirs.
- Test my assumptions about how and why people say or do things.
- Challenge what was said or done, rather than make assumptions about the individual.
- Beware of either-or thinking.
- Be willing to take risks in moving outside my comfort zones.
- Affirm others.

ENVH 532 Winter 2017 Course Schedule

Reproductive & Developmental Toxicology

Date	Schedule	Session Leader
Jan. 3 rd Tuesday	<ol style="list-style-type: none"> 1. Introduction to Course and Participants 2. Review of Developmental and Reproductive Toxicology 3. Identification of Course Readings – Requested Interest Areas 	E. Faustman C. Tamaro
Jan. 4 th Wednesday	<ol style="list-style-type: none"> 1. Guidelines for Assessing Developmental Toxicity Studies 2. Risk Assessment and Risk Communication 3. Introduction of Case Studies 	E. Faustman C. Tamaro
Jan. 10 th Tuesday	<ol style="list-style-type: none"> 1. Female Reproductive Toxicology 2. Endocrine Disruption 	E. Faustman C. Tamaro
Jan. 11 th Wednesday	Lab: Estrogen Kinetics and Cycling Cortisol Cycling	S. Hong M. Smith
Jan. 17 th Tuesday	<ol style="list-style-type: none"> 1. Developmental Biology 2. Mechanisms of Developmental and Reproductive Toxicology 3. Conservation of Signaling Pathways 4. Windows of Susceptibility 	E. Faustman C. Tamaro
Jan. 18 th Wednesday	<ol style="list-style-type: none"> 1. National Children’s Studies (US and International Examples) 2. Life Course Concepts 3. Epidemiological Methods for Cohort Studies 	E. Faustman M. Smith C. Tamaro B. Griffith

Jan. 24 th Tuesday	Adverse Outcome Pathways (AOP)	E. Faustman C. Tamaro
Jan. 25 th Wednesday	Lab: Case Studies on Specific Chemical Examples Student Discussion	C. Tamaro
Jan. 31 st Tuesday	In Vitro Methods for Reproductive and Developmental Toxicity	E. Faustman S. Hong C. Tamaro
Feb. 1 st Wednesday	Lab: In Vitro Models Microfluidics, stem cells, Organotypic Cultures, Reporter Assays	E. Faustman S. Hong C. Tamaro
Feb. 7 th Tuesday	Case Studies in Reproductive and Developmental Toxicology	E. Faustman C. Tamaro
Feb. 8 th Wednesday	Lab: Teratology Examination	S. Pacheco Shubin S. Hong C. Tamaro
Feb. 14 th Tuesday	Male Reproductive Toxicology	E. Faustman C. Tamaro
Feb. 15 th Wednesday	Lab: Sperm Assessment	S. Pacheco Shubin E. Faustman S. Hong

Feb. 21 st Tuesday	1. Mechanisms of Developmental and Reproductive Toxicology (cont.) 2. Epigenetics	E. Faustman C. Tamaro
Feb. 22 nd Wednesday	Lab: Epigenetics Case Examples- Student Discussions	E. Faustman C. Tamaro
Feb. 28 th Tuesday	Consumer Product Safety Acts- National and International	M. Smith C. Tamaro
March 1 st Wednesday	Lab: Demonstration of New Clinical Applications for Communications	J. Polifka E. Faustman C. Tamaro
March 7 th Tuesday	Protective Practices for Reproductive and Developmental Endpoints in the Workplace and Environment	E. Faustman C. Tamaro
March 8 th Wednesday	Lessons Learned and Identification of Research Needs	E. Faustman C. Tamaro

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Literature Review Form:

Date:

Reviewer Name:

Title of Paper:

What is the hypothesis?

What was the purpose of this paper?

What methods did the author use?

Were these methods appropriate? Explain.

What were the results?

Do you agree with the results? Explain.

What key issues does the author(s) cite in the discussion?

What do you think should be discussed?

On a scale of 1 - 5 (1 being lowest and 5 being highest rating for publication) what score would you give this paper for significance to the field

What would the most logical next steps be to expand your research?

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Reproductive and Developmental Toxicology
Lab Evaluation Form:

In order to facilitate and track learning at our lab sessions we would like you to complete the following form for each identified lab.

Name: _____

Lab session: _____ Date: _____

Topic: _____

What did you like most about the lab session?

What was the most novel or new information that you learned?

Can you identify how you might use this information?

What else would you like to know about this topic? (Please be specific as we will use this information to improve our next labs)

Selected Readings and Relevant Primer Chapters:

This course will primarily depend upon current literature and extensive suggestions for possible publications for student readings will be provided for each topic.

As a base for course we will use a free Primer from the Teratology Society:
All students will receive an electronic copy of the 2010 Teratology Society Primer.

Dependent upon student interests and expertise, tailored reading will be suggested and a current syllabus will be added for case studies.

1. General Development – Key References

- a) Alwan, S. et al., 2010. Teratology Primer. (Chapters 1, 2, 4)
- b) Experimental Approaches to Evaluate Mechanisms of Developmental Toxicity. Faustman EM, Gohlke JM, Ponce RA, Lewandowski TA, Seeley MR, Whittaker SG, Griffith WC. *Developmental and Reproductive Toxicology: A Practical Approach*, R. Hood (ed.), Boca Raton: CRC Press, Inc. 3rd Edition, 2011.
- c) Daston, G. et al., (2004). A framework for assessing risks to children from exposure to environmental agents. *Environ Health Perspect* 112(2): 238-56.
- d) World Health Organization et al., 2006. Principles for evaluating health risks in children associated with exposure to chemicals. *Environmental Health Criteria* 237. World Health Organization, Geneva.

2. Development Mechanisms

- a) Teratology Primer Chapters 6, 7, 8, 16
- b) Scientific Frontiers in Developmental Toxicology and Risk Assessment. National Research Council (NRC) 2000.

3. Development Toxicology Methods

- a) Teratology Primer Chapters 9, 12, 15

4. Epidemiology

- a) Teratology Primer Chapter 11

5. Case Studies – Examples (Final list to be chosen by class participants)

- a) Anticonvulsants - Teratology Primer Chapter 26
- b) Serotonin Reuptake Inhibitors
- c) Retinoids
- d) Pesticides - Teratology Primer Chapter 27
- e) Alcohol - Teratology Primer Chapter 23

- f) Endocrine Disruptors
- g) Fever/Infection - Teratology Primer Chapter 30
- h) Thalidomide
- i) Obesity - Teratology Primer Chapter 29
- j) Stress - Teratology Primer Chapter 24
- k) Radiation - Teratology Primer Chapter 21
- l) Nutrition - Teratology Primer Chapters 31, 32
- m) Herbal Supplements - Teratology Primer Chapter 28
- n) Anti Depressants - Teratology Primer Chapter 25

7. Developmental and Reproductive Conditions (final list will be chosen by class participants)

- a) Neural Tube Defects
- b) Autism
- c) Hypospadias
- d) Microcephaly
- e) Infertility
- f) Low Birth Rate
- g) Transplacental Carcinogenesis
- h) Male mediated teratogenesis
- i) Multigenerational impact

8. Risk Assessment

- a) Teratology Primer Chapters 13, 14, 17, 18, 19

9. Risk Communication

- a) Teratology Primer Chapter 10

10. Barker Hypothesis

- a) Teratology Primer Chapter 3, 33

11. Life Course