

ENV H 532: Reproductive and Developmental Toxicology

3 Credits, Winter 2023

Tuesdays (2:30-3:20pm, [HSEB 430](#)) and Thursdays (2:30-4:20pm, Roo 2228)

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. It will cover both male and female reproductive topics. 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. Problem Formulation
 - D. Preliminary Data (based on the literature)
 - E. Experimental Design & Methods
 - Note: One Specific Aim must contain
 - 1.) Rationale
 - 2.) Short experimental design
 - 3.) Expectations & pitfalls
 - F. 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 disrupters, stress and pregnancy outcome, nutrition (prevention versus prescription), pesticides, drugs, radiation, mechanisms of normal and perturbed development, 17 pathways of evolutionary conserved cell signaling, life stage 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%
	100%

Classroom Climate- Equity, Diversity and Inclusion

Diverse backgrounds, embodiments and experiences are essential to the critical thinking endeavor at the heart of University education. In SPH, students are expected:

- To respect individual differences, which may include, but are not limited to, age, cultural background, disability, ethnicity, family status, gender, immigration status, national origin, race, religion, sex, sexual orientation, socioeconomic status and veteran status.
- To engage respectfully in the discussion of diverse worldviews and ideologies embedded in course readings, presentations and artifacts, including those course materials that are at odds with personal beliefs and values.
- To encourage students with concerns about classroom climate to talk to their instructor, adviser, a member of the departmental or SPH EDI Committee, the Assistant Dean for EDI, or the program's director.

UW School of Public Health Equity Diversity and Inclusion Statement:

Our School of Public Health is committed to addressing the root causes of health inequities and promoting healthy and safe communities in our region and beyond. As the problem of racial and ethnic disparities in health outcomes continues to persist, policymakers and the general public increasingly look to health professional schools to address these urgent and unacceptable circumstances. As one of the few schools of public health in the Northwest, it is particularly important for us to be up to this challenge.

Underlying all public health research and training activities is an acknowledgement and deeper understanding of the effects that historical, cultural and socioeconomic factors have on the health of communities, especially those who are most underserved. Racism and race-based oppression is all too often a central driver of health disparities. We work to attract and retain students, faculty and staff from diverse backgrounds and perspectives, to build and sustain a positive climate for inclusion and community, and to engender multiple modes of approaching complex problems. We strive to create opportunities for education, research and collaboration that leverage our strengths, similarities and differences. We challenge ourselves to view problems and evaluate solutions through an equity lens. Through each of these efforts, we aim to foster a generation of public health professionals and academicians who are poised to transform health for the better in our communities.

Our historical logo, the SoulCatcher by Marvin Oliver, symbolizes the restoration of health and wellness and reminds us to align our work with the history, traditions, and practices while respecting and supporting the agency of individuals and communities to achieve their desired health outcomes. More information about our logo can be found [here](#).

The work of equity, diversity and inclusion is the work of Public Health. We are committed to a future that is free of health inequities, that promotes the highest level of wellness that our communities aim for, and a diverse and inclusive public health workforce that embodies humility, respect, leadership and service on behalf of the diverse communities we are privileged to serve.

Academic Integrity:

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 (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.

Land Acknowledgment:

Washington State is home to 29 federally recognized and five unrecognized tribes. The University of Washington acknowledges the Coast Salish people of this land, the land which touches the shared waters of all tribes and bands within the Duwamish, Suquamish, Tulalip and Muckleshoot nations. This is important for several specific reasons in the course not the least of which is that these nations develop their own recognized environmental risk assessment programs. Their framing is one which many can learn from as it in many cases will have recognition of cultural and wellbeing and temporal scales that our broader and more inclusive of environment. We will be honored to learn from these concepts in this course. The other reasons include the shared physical space both on land and sea that we experience and which impacts our populations.

Religious Accommodations:

Washington state law requires that UW develop a policy for accommodation of student absences or significant hardship due to reasons of faith or conscience, or for organized religious activities. The UW's policy, including more information about how to request an accommodation, is available at Religious Accommodations Policy (<https://registrar.washington.edu/staffandfaculty/religious-accommodations-policy/>). Accommodations must be requested within the first two weeks of this course using the Religious Accommodations Request form (<https://registrar.washington.edu/students/religious-accommodations-request/>).

Bias Concerns:

The Office of the Dean has a student concern policy, a faculty concern policy and standard HR procedures for staff concerns. Our 2018 climate survey states that most people in SPH do not report bias incidents because they do not know where to go. Students are encouraged to report any incidents of bias to someone they feel comfortable with, including instructors, advisers or department staff. They can email dcinfo@uw.edu for immediate follow up. Bias concerns can be anonymously and confidentially reported at this link <https://sph.washington.edu/about/diversity/bias-concerns>. Data is collected by the Assistant Dean for EDI and the Director of Program Operations for Student and Academic Services and tracked for resolution and areas are identified for further training.

Pronouns:

According to the UW First Year Programs, being an ally is not just about intention, it is also about behavior. We share our pronouns because we strive to cultivate an inclusive environment where people of all genders feel safe and respected. We cannot assume we know someone's gender just by looking at them. We invite everyone to share their pronouns. To facilitate this in a non-zoom context and to help our colleagues learn our names, we will ask students to use name tags throughout the course. **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.

ENVH 532 Winter 2023 Course Schedule

Reproductive & Developmental Toxicology

Tuesdays (2:30-3:20pm, HSEB 430) and Thursdays (2:30-4:20pm, Roo 2228)

Date	Schedule	Session Leader	Readings
Jan. 3 rd Tuesday	<ol style="list-style-type: none"> 1. Introduction to Course and Participants 2. Identification of Course Readings, Interest Areas, and Case Studies 	Faustman	
Jan. 5 th Thursday	<ol style="list-style-type: none"> 1. Review of Developmental and Reproductive Toxicology 2. Windows of Susceptibility 	Faustman	
Jan. 10 th Tuesday	<ol style="list-style-type: none"> 1. Continue discussion of Developmental Toxicology 2. Introduction of Signaling pathways- Conservation during development 3. Selection of case studies 	Faustman	
Jan. 12 th Thursday	<ol style="list-style-type: none"> 1. Introduction to Computational Toxicology Dashboard (be prepared to id a case compound and understand setting of RfDs) 	Faustman	
Jan. 17 th Tuesday			
Jan. 19 th Thursday	<ol style="list-style-type: none"> 1. Case Studies on Specific Chemicals 2. Select paper discussions 	Faustman	
Jan. 24 th Tuesday	<p>Lab: Teratology Examination Continued Student Discussion of Developmental Toxicity Case Studies</p>	Hong	

Jan. 26 th Thursday	Male Reproductive Toxicology	Faustman	
Jan. 31 st Tuesday	<ol style="list-style-type: none"> 1. In Vivo and In Vitro Methods for assessing male and female Reproductive Toxicity 2. Case Studies on chemicals causing male reproductive toxicity 	Faustman Hong	
Feb. 2 nd Thursday	Lab: In Vitro Methods for Reproductive and Developmental Toxicity	Faustman Hong	
Feb. 7 th Tuesday	<ol style="list-style-type: none"> 1. National Children's Studies (US and International Examples), Echo, CHEAR 2. Life Course Concepts 3. Epidemiological Methods for Cohort Studies 	Faustman Smith Griffith	
Feb. 9 th Thursday	<ol style="list-style-type: none"> 1. Adverse Outcome Pathways (AOP) 2. Case Studies on Chemicals affecting reproductive health 	Faustman	
Feb. 14 th Tuesday			
Feb. 16 th Thursday	Lab: Sperm Assessment	Faustman Hong	
Feb. 21 st Tuesday	<ol style="list-style-type: none"> 1. Mechanisms of Developmental and Reproductive Toxicology (cont.) 2. Epigenetics 3. Multi-generational Inputs 	Faustman	

Feb. 23 rd Thursday	1. Female Reproductive Toxicology 2. Endocrine Disruption Lab: Estrogen Kinetics and Cycling Cortisol Cycling	Faustman Hong	
Feb. 28 th Tuesday	Consumer Product Safety Acts- National and International	Smith	
March 2 nd Thursday	Case Studies in reproductive and Developmental Toxicology	Faustman	
March 7 th Tuesday	Protective Practices for Reproductive and Developmental Endpoints in the Workplace and Environment	Faustman	
March 9 th Thursday	Lessons Learned and Identification of Research Needs	Faustman	

ENVH 532
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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: _____

Date: _____

Lab session: _____

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