

ENV H 593 A Wi 19: Current Topics In Risk Assessment

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SCHOOL OF PUBLIC HEALTH · UNIVERSITY of WASHINGTON
Environmental & Occupational Health Sciences

ENV H 593 A: Current Topics in Risk Assessment

Winter Quarter 2019: Novel Techniques for Evaluation of Reproductive and Developmental Toxicity

Credits: 2



Instructor:

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Office Hours: By appointment

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Course Times and Locations:

Day/Time: Wednesday, 2:30 pm - 4:20 pm

Location: 4225 Roosevelt Way NE in Roosevelt 2228

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Course Description:

Reproductive and developmental toxicity assessments are typically expensive and time-consuming. Because of this, there is a huge gap in availability of reproductive and developmental toxicity data for chemicals already on the US Market. In vitro and in silico approaches to model reproductive and developmental toxicity are being developed and beginning to show promise for incorporation in to risk management. In this course, we will review reproductive and developmental toxicity mechanisms, traditional assessment techniques and innovative new methods for alleviating data gaps. We will discuss the implications of these new methods for risk assessment.

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Winter 2019 Learning Objectives:

1. Review mechanisms of developmental and reproductive toxicity
2. Understand current standards for reproductive and developmental toxicity assessment (e.g. OECD guidelines)
3. Learn about new in vitro and in silico models of assessment of reproductive and developmental toxicity
4. Identify instances where novel techniques may be able to reduce or replace specific reproductive and developmental toxicity assessments

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Additional Generic Learning Objectives:

1. Think critically about risk assessment by completing reading assignments and participating in class discussions.
2. Communicate the concept of integrated risk assessment and risk communication.
3. Explain the risk assessment framework as it relates specifically to the current quarter topic.
4. Analyze assigned readings and interpret their relevance to not only the quarter topic but also their applicability and generalizability to risk assessment topics at large.
5. Summarize key points from assigned journal articles or other required readings.
6. Prepare and deliver an oral presentation(s) discussing the required reading.
7. Critique risk assessment applications as they relate to the current quarter topic.
8. Identify risk assessment strengths and challenges, as well as the role of uncertainty.
9. Develop skills to think critically about the methods and tools used for assessment, management, and communication of risk.

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Grading:

- **50% Weekly Discussion Participation and Related Assignments:** Weekly summations and presentation of key points from readings and respectful engagement in substantive in-class discussions.
- **25% FIVE Article Reports** - See the template at the end of the syllabus and limit your responses to 2 pages double spaced. Reports will be graded for completeness and thoughtfulness. Reports should be submitted each week before class starts. You will need to submit five Article Reports throughout the quarter.

- **25% In-Class Presentation and report** - Presentation or demonstration of the applications to your own research or interest area. Please use the Research Relevancy Report Template at the end of this syllabus and limit your response to 3 pages double spaced. You will be required to submit ONE research relevancy report for the quarter. In addition to the report, please prepare a brief presentation (about 10 minutes) with 2-3 figures/tables to support your observations.

Academic Integrity Statement:

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.

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 (<mailto:uwdrs@uw.edu>) or disability.uw.edu (<http://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

Course Schedule:

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<u>Session #</u>	<u>Date</u>	<u>Topic</u>	<u>Readings</u>
Session 1	01/09/19	Introduction to the course and reproductive and developmental toxicology	
Session 2	01/16/19	Introduction to reprotox assessment and the philosophy behind in vitro and 3D models	References [1-25]
Session 3	01/23/19	Models for Developmental Toxicology Introduction to male reprotox models (Dude	

Session 4	01/30/19	on a chip) and female reprotox models (Video of NIEHA Council) (Dude on a chip)	References [26-28]
Session 5	02/06/19	High throughput tools: ToxCast for endocrine disruption	References [-]
Session 6	02/13/19	Quantitative In Vitro Risk Assessment (Examples for IVIVE and Benchmark Doses)	References [-]
Session 7	02/20/19	Application to TSCA Applications to MOA and AOPs	References [29, 30]
Session 8	02/27/19	Student Presentations- Research Relevancy	
Session 9	03/06/19	Student Presentations- Research Relevancy	
Session 10	3/13/19	NO CLASS – Society of Toxicology Annual Meeting	N/A

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Current Topics in Risk Assessment

Article Report Form Template:

**PLEASE LIMIT RESPONSES TO 2 PAGES DOUBLE SPACED*

Date:

Reviewer Name:

Title of Paper:

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What was the purpose of this paper?

What methods did the author use?

What were the key results?

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

How does this article contribute to today's discussion topic?

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Current Topics in Risk Assessment

Research Relevancy Report Form Template:

**PLEASE LIMIT RESPONSES TO 3 PAGES DOUBLE SPACED*

Date:

Reviewer Name:

Title of Paper:

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What was the purpose of this paper?

What were the key results?

Describe your research, briefly

How does the article relate to your research?

Based on your research area expertise, do you have any critiques (positive or negative) of the article?

Will the concepts or results presented in the article change or supplement how you think about your research? Why/how?

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References:

1. Hartung, T., et al., *An expert consortium review of the EC-commissioned report "alternative (Non-Animal) methods for cosmetics testing: current status and future prospects - 2010"*. Altex, 2011. **28**(3): p. 183-209.
2. Hayes, A.W., *Principles and methods of toxicology*. 2007: Crc Press.
3. Hales, B., A. Scialli, and M. Tassinari, *Teratology Primer*. 2010, The Teratology Society, Cincinnati, OH.
4. *Editorial Board*. *Toxicology and Applied Pharmacology*, 2018. **354**: p. ii.
5. Audouze, K., O. Taboureau, and P. Grandjean, *A systems biology approach to predictive developmental neurotoxicity of a larvicide used in the prevention of Zika virus transmission*. *Toxicology and Applied Pharmacology*, 2018. **354**: p. 56-63.
6. Bal-Price, A. and E. Fritsche, *Editorial: Developmental neurotoxicity*. *Toxicology and Applied Pharmacology*, 2018. **354**: p. 1-2.
7. Bal-Price, A., et al., *Strategies to improve the regulatory assessment of developmental neurotoxicity (DNT) using in vitro methods*. *Toxicology and Applied Pharmacology*, 2018. **354**: p. 7-18.
8. Delp, J., et al., *Stage-specific metabolic features of differentiating neurons: Implications for toxicant sensitivity*. *Toxicology and Applied Pharmacology*, 2018. **354**: p. 64-80.
9. Frank, C.L., et al., *Defining toxicological tipping points in neuronal network development*. *Toxicology and Applied Pharmacology*, 2018. **354**: p. 81-93.
10. Fritsche, E., et al., *Consensus statement on the need for innovation, transition and implementation of developmental neurotoxicity (DNT) testing for regulatory purposes*. *Toxicology and Applied Pharmacology*, 2018. **354**: p. 3-6.
11. Geier, M.C., et al., *Systematic developmental neurotoxicity assessment of a representative PAH Superfund mixture using zebrafish*. *Toxicology and Applied Pharmacology*, 2018. **354**: p. 115-125.
12. Harrill, J.A., et al., *Testing for developmental neurotoxicity using a battery of in vitro assays for key cellular events in neurodevelopment*. *Toxicology and Applied Pharmacology*, 2018. **354**: p. 24-39.








13. Hessel, E.V.S., Y.C.M. Staal, and A.H. Piersma, *Design and validation of an ontology-driven animal-free testing strategy for developmental neurotoxicity testing*. Toxicology and Applied Pharmacology, 2018. **354**: p. 136-152.
14. Masjosthusmann, S., et al., *A transcriptome comparison of time-matched developing human, mouse and rat neural progenitor cells reveals human uniqueness*. Toxicology and Applied Pharmacology, 2018. **354**: p. 40-55.
15. Myhre, O., et al., *Early life exposure to air pollution particulate matter (PM) as risk factor for attention deficit/hyperactivity disorder (ADHD): Need for novel strategies for mechanisms and causalities*. Toxicology and Applied Pharmacology, 2018. **354**: p. 196-214.
16. Pamies, D., et al., *Rotenone exerts developmental neurotoxicity in a human brain spheroid model*. Toxicology and Applied Pharmacology, 2018. **354**: p. 101-114.
17. Ruskiewicz, J.A., et al., *C. elegans as a model in developmental neurotoxicology*. Toxicology and Applied Pharmacology, 2018. **354**: p. 126-135.
18. Sachana, M., A. Rolaki, and A. Bal-Price, *Development of the Adverse Outcome Pathway (AOP): Chronic binding of antagonist to N-methyl-D-aspartate receptors (NMDARs) during brain development induces impairment of learning and memory abilities of children*. Toxicology and Applied Pharmacology, 2018. **354**: p. 153-175.
19. Spulber, S., et al., *Methylmercury interferes with glucocorticoid receptor: Potential role in the mediation of developmental neurotoxicity*. Toxicology and Applied Pharmacology, 2018. **354**: p. 94-100.
20. Terron, A. and S.H. Bennekou, *Towards a regulatory use of alternative developmental neurotoxicity testing (DNT)*. Toxicology and Applied Pharmacology, 2018. **354**: p. 19-23.
21. Vorhees, C.V., et al., *A better approach to in vivo developmental neurotoxicity assessment: Alignment of rodent testing with effects seen in children after neurotoxic exposures*. Toxicology and Applied Pharmacology, 2018. **354**: p. 176-190.
22. Wang, C., et al., *Lipid profiling as an effective approach for identifying biomarkers/adverse events associated with pediatric anesthesia*. Toxicology and Applied Pharmacology, 2018. **354**: p. 191-195.
23. Weldon, B.A., et al., *Using primary organotypic mouse midbrain cultures to examine developmental neurotoxicity of silver nanoparticles across two genetic strains*. Toxicology and Applied Pharmacology, 2018. **354**: p. 215-224.
24. Faustman, E.M. and G.S. Omenn, *Risk Assessment*, in *Casarett and Doull's Toxicology: The Basic Science of Poisons, 8e*. 2012, McGraw-Hill Education: New York, NY.
25. Council, N.R., *Toxicity Testing in the 21st Century: A Vision and a Strategy*. 2007, Washington, DC: The National Academies Press. 216.
26. Klaassen, C.D. and J.B. Watkins, *Casarett and Doull's toxicology: the basic science of poisons*. Vol. 5. 1996: McGraw-Hill New York.
27. Parks Saldutti, L., et al., *In vitro testicular toxicity models: opportunities for advancement via biomedical engineering techniques*. Altex, 2013. **30**(3): p. 353-77.
28. National Academies of Sciences, E. and Medicine, *Application of Systematic Review Methods in an Overall Strategy for Evaluating Low-Dose Toxicity from Endocrine Active Chemicals*. 2017, Washington, DC: The National Academies Press. 180.
29. Leung, M.C.K., et al., *Systems Toxicology of Male Reproductive Development: Profiling 774 Chemicals for Molecular Targets and Adverse Outcomes*. Environmental health perspectives, 2016. **124**(7): p. 1050-

1061.

30. Ankley, G.T., et al., *Adverse outcome pathways: a conceptual framework to support ecotoxicology research and risk assessment*. Environ Toxicol Chem, 2010. **29**(3): p. 730-41.

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Course Summary:

Date	Details	
Wed Feb 6, 2019	 Article Report 1 (https://canvas.uw.edu/courses/1255682/assignments/4637091)	due by 2:30pm
Wed Feb 13, 2019	 Article Report 2 (https://canvas.uw.edu/courses/1255682/assignments/4637092)	due by 2:30pm
Wed Feb 20, 2019	 Article Report 3 (https://canvas.uw.edu/courses/1255682/assignments/4637094)	due by 2:30pm
Wed Feb 27, 2019	 Article Report 4 (https://canvas.uw.edu/courses/1255682/assignments/4637095)	due by 2:30pm
Wed Mar 6, 2019	 Article Report 5 (https://canvas.uw.edu/courses/1255682/assignments/4637097)	due by 2:30pm
	 In-Class Presentation and Report (https://canvas.uw.edu/courses/1255682/assignments/4637116)	due by 2:30pm
	 Weekly Discussion Participation and Related Assignments (https://canvas.uw.edu/courses/1255682/assignments/4637117)	