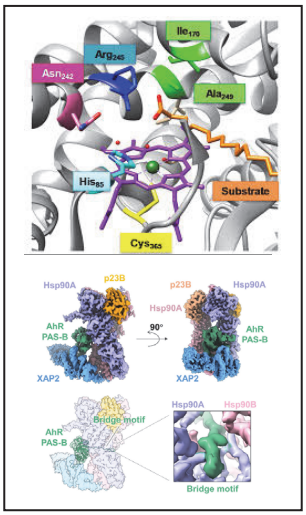
TOXICOLOGY 575: ADVANCED XENOBIOTIC METABOLISM AND DISPOSITION
FALL TERM 2024



Elective Course for Graduate Students (alternate years)

Useful for students in the fields of:

Toxicology
Biochemistry
Chemistry
Botany
Integrated Biology
Microbiology
Food Science
Pharmacy
Vet Medicine
Public Health
CBEE
BE
Forestry
Entomology
Plant Pathology
MSI
F&W

Students outside the Toxicology Program are encouraged to register.

TOX 575 (2 credits) Graduate Elective

TIME: M/W 11-11:50 am (Pacific Time Zone)
LOCATION: **ALS 1019 / Hybrid**
Prerequisite: Consent of Instructor

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Register for: TOX 575 CRN 20862; 2 credits

Essentially *ALL* living organisms have evolved specialized defensive pathways mediated by proteins designed to metabolize a myriad of *foreign chemicals* and transport them into and out of cells. These proteins both protect cells from xenobiotics as well as synthesize and metabolize *endogenous molecules* with important cell growth and developmental functions. Thus, this course will be highly useful and interesting to almost all graduate students in the life sciences. Although the emphasis of this course is metabolism of foreign chemicals and the transport of foreign chemicals and their metabolites within cells and between tissues in vertebrates, the concepts apply to metabolism and transport of both xenobiotics and endogenous compounds in all organisms, including *insects*, *plants, fish,* and *microorganisms*.

This course will focus on: 1) the structure, function and regulation of xenobiotic metabolizing enzymes (Cytochromes P450 and flavin monooxygenase enzymes), and 2) (xenobiotic) transmembrane transport proteins. These processes are key for understanding the pharmacokinetics and toxicokinetics of xenobiotics, including but not limited to: therapeutic drugs and environmental contaminants. The course will also cover; 3) synthesis, metabolism, & transport of important endogenous molecules in living organisms by these pathways and the role of xenobiotics in causing or mediating environmental diseases.

The course consists of student-centered discussions and readings from book chapters, review articles, and primary research papers accompanied by didactic lectures on classical as well as emerging topics relating to metabolism, included but not limited to:

- Structure/Function/Regulation of P450s and other metabolic enzymes.
- Bioactivation reactions resulting in chemical toxicity, adverse drug reactions, chemical carcinogenesis, environmental diseases.
- Intracellular vectorial transport by macrovesicles and exosomes.
- Metabolomics.
- Microbiome and Metabolism.
- Nuclear Receptor structure, binding by xenobiotics and endobiotics.
- Alternative splicing and other mechanisms of adaptive responses to xenobiotics and environmental stress.

Advanced Drug Metabolism and Disposition: Toxicology 575
DRAFT COURSE SYLLABUS – FALL 2024

Instructors: Drs. Marcus, Annalora, Iversen, Sharpton, Garcia-Jaramillo, Perdew, Smith

LECTURE SCHEDULE

	Date	Instructor	Topic
1	W 9/25	Annalora	Xenobiotic Disposition I ADME,
2	M 9/30	Annalora	Xenobiotic Disposition II ADME Toxicokinetics
3	W 10/2	Marcus	Phase I Xenobiotic Metabolism I (Biotransformation; structure/function of P450s)
4	M 10/7	Marcus	Phase I Xenobiotic Metabolism II (structure/function/regulation of P450s/FMOs)
5	W 10/9	Marcus	Phase I Xenobiotic Metabolism III (function/XME mediated regulation of P450s)
6	M 10/14	Sharpton/ Alexiev	Microbiome: Analysis of the functions of gut microbiome and the role it plays in defining exposure outcomes, how it is studied, the impact it has on human physiology and health, and the emerging understanding or the role of the gut microbiome mediates exposure outcomes.
7	W 10/16	Marcus	Phase II Xenobiotic Metabolism 1 (Conjugation/synthetic reactions)
8	M 10/21	Marcus	Phase II Xenobiotic Metabolism 2 (Coordinate evolution with Phase I and XME receptors; Pleiotropic defense pathways)
9	W 10/23	Marcus	Xenobiotic Uptake (Transporters: OCTI, OATS, ASBT, Epithelium, xenobiotic uptake in small intestine (enterocytes)
10	M 10/28	Marcus	Xenobiotic Excretion I (ATP binding cassette proteins)
11	W 10/30	Marcus	Xenobiotic Excretion II (Structural biology of P-glycoprotein/transporters) (**Midterm Exam (Take Home**)
12	M 11/4	Garcia-Jaramillo	Metabolomics: Mass spectrometry-based metabolomics analysis as a tool for the assessment of the effects of contaminants exposure on metabolic pathways.
13	W 11/6	Perdew	NR and AHR
	M 11/11		**Veterans Day**
14	W 11/13	Iversen	Role of CYP and other oxidases and oxygenases (heme and non-heme) in immune responses, metabolism of xenobiotics and cellular signaling.
15	M 11/18	Iversen	Broad discussion of gene expression and relevance to xenobiotic metabolism - gene promoter regions, introns with a focus on miRNA, alternate translation start sites, and post-translational modifications.
16	W 11/20	Iversen	Alternative Splicing of Xenobiotic Metabolizing Enzymes, Receptors and Transporters
17	M 11/25	Annalora	Exosomes: Role for intercellular transport of xenobiotic metabolizing enzymes and cellular signaling regulating xeno- and endobiotic metabolism.
18	W 11/27	Smith	Activity-based substrate probes as an approach to profile active CYP enzymes and practical applications for metabolic pathway determinations
			Thanksgiving Break
19	M 12/2	Annalora	Nuclear Receptor Signaling and the Chemical Immune System (Xenobiotics and Environmental Disease)
20	W 12/4	Annalora	New Frontiers in Phase 2 and 3 Drug and Xenobiotic Metabolism (Xenobiotics and Environmental Disease)
	Dec. 9		**Finals week – Final Exam (Takehome?)**