PCEUT 502

DRUG DISPOSITION SCIENCE

Autumn Quarter, 2019 (2 credits)

Lectures: M, W (8:30-9:20), H-074

Course Organizer

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H272N

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Schedule

Lecture		Date	Instructor	Course Topic
1	W	9/25	KT	Drug Metabolism Processes – Phase 1
2	M	9/30	KT	Drug Metabolism Processes – Phase 2
3	W	10/2	LC	Drug Transport Processes – Efflux
4	M	10/7	LC	Drug Transport Processes – Uptake
5	W	10/9	KT	Subcellular Fractionation – Liver Tissue
6	M	10/14	KT	Enzyme Kinetics – Experimental Design ***(take home -1)***
7	W	10/16	LC	Transport Kinetics – Experimental Design
8	M	10/21	KT	Single Enzyme and Multi-Enzyme MM Kinetics
9	W	10/23	KT	Drug Disappearance Kinetics
10	M	10/28	KT	Enzyme Kinetics – Reversible Inhibition ***(take home-2)***
11	W	10/30	KT/TBN	**Exam-1** (9/25 – *10/23 material*)
12	M	11/4	KT	Enzyme Kinetics – Irreversible Inhibition
13	W	11/6	KT	DMET Variation – Protein Quantitation
14	M	11/11	KT	DMET Genotype – Activity Phenotype
15	W	11/13	EK	Isolation of Nucleic Acids, Quantitation and QC
16	M	11/18	EK	DMET Genotyping Methods
17	W	11/20	EK	DMET Variation – mRNA Quantitation ***(take home-3)***
18	M	11/25	LS	Rigor & Reproducibility – Management of Data
19	W	11/27	NI	Rigor & Reproducibility – Hypothesis Testing and p-Values
20	M	12/2	NI	Rigor & Reproducibility – Avoiding Bias in Study Design
21	W	12/4	NI	Rigor & Reproducibility – Research Integrity ***(take home-4)***
		6/9-12	NI/KT	**Exam-2** *(finals week; 10/25 – 12/6 material)*

Instructors

KT, Ken Thummel, Pharmaceutics, H272M, Thummel@uw.edu

EK, Ed Kelly, Pharmaceutics, H272K. edkelly@uw.edu

NI, Nina Isoherranen, Pharmaceutics, H272N, ni2@uw.edu

LC, Lindsay Czuba, Pharmaceutics, H-253/251, lczuba@uw.edu

LS, Laura Shireman, Pharmaceutics, 4225 Roosevelt, Rm 305B, shireman@uw.edu

Teaching Assistant

None

Course Goals:

The goals of the course are to provide the student with:

- Basic understanding of drug metabolism and transport (DMET) processes
- Detailed understanding of subcellular fractionation methods for isolation of in vitro kinetic systems
- Detailed understanding of in vitro experimental design for generating kinetic data
- Concepts relating Michaelis-Menten kinetics describing *in vitro* enzyme-catalyzed biotransformation and transport processes to pharmacokinetic principles, including *in vivo* drug clearance
- Mechanisms of DMET inhibition and induction and associated kinetic theories
- An understanding of methods for isolating and characterizing nucleic acids and proteins
- An understanding of common DMET genotype – activity phenotype relationships
- Principles underlying experimental rigor and reproducibility

Learning Objectives:

1. To describe metabolic and transport processes governing drug disposition
2. To understand basic models of drug biotransformation and transport
3. To understand how enzymatic and transport processes affect drug intrinsic clearance
4. To describe various perturbations of enzyme function or expression (DDIs, genetics) and how this translates into changes in intrinsic clearance
5. To understand the scientific method, hypothesis testing and the difference between objective vs subjective science
6. To understand and embrace research integrity

Performance Objectives:

Upon completing the course, the student should be able to:

1. Develop *in vitro* experimental designs to determine kinetic parameters that define metabolic and transport drug disposition
2. Use GraphPad to calculate in vitro kinetic parameters, including inhibition constants
3. Read and understand the literature pertaining to mechanisms of inter-individual variability in drug disposition kinetics, including drug-drug interactions and pharmacogenetics
4. Conduct research in a rigorous, reproducible and responsible manner

Text References: (Not required)

Clinical Pharmacokinetics and Pharmacodynamics, M. Rowland and T.N. Tozer (Eds), Wolters Kluwer/Lippincott Williams & Wilkins, 4th Edition, 2011.

Enzyme Kinetics, I.H. Segel, John Wiley & Sons (Wylie Classics Library Edition), 1993.

Drug-Drug Interactions: From Basic Pharmacokinetic Concepts to Marketing Issues, Second Edition. A.D. Rodrigues (Ed), Marcel-Dekker, New York, 2008.

Performance Evaluation:

Grades for the course will be assigned based on your take-home lab exercise performances and two written, in-class exams.

Take-home assignments (4 labs; 10% each)	40%
Written exams (2 exams; 30% each)	60%

Office Hours:

Arranged by each faculty member.

Accommodations:

If you would like to request academic accommodations due to a disability, please contact Disabled Student Services, 448 Schmitz, 543-8924 (V/TTD). If you have a letter from Disabled Student Services indicating you have a disability that requires academic accommodations, please present the letter to the instructors so we can discuss the accommodations you might need for the class.

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. Accommodations must be requested within the first two weeks of this course using the Religious Accommodations Request form."