Chemistry 671: Receptor Pharmacology

Instructor: Dr. Kelly Drew
Office/office hrs: Murie 223F 10:00am-4:00pm, stop by or call for an appointment
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Lecture: Time: Tuesday and Thursday 9:40-11:15
Location:

Homework: Due at the end of class when indicated. **Late HW is not accepted.**

CRN# 76678 CHEM F671 F01 Receptor Pharmacology

Blackboard Access All Powerpoint slides used in class as well as reading material will be posted on UAF Blackboard at https://classes.uaf.edu
UAA and UAS students who register for the class will be assigned a username and password to login to UAF Blackboard. Contact our computer help desk at helpdesk@alaska.edu, 800 478-8226 or 907 450-8300 to ask about your user ID and password.

Course Description: This course will teach students to: 1) understand basic drug receptor theory; 2) be familiar with assays to assess affinity and efficacy of receptor ligands 3) work with and interpret functional assays and radioligand binding results 4) to critically evaluate original research regarding receptor pharmacology with an emphasis on ligand-gated ion channels and G-protein coupled receptors; 5) identify testable hypotheses and design experiments to test these hypotheses.

Prerequisite: Upper division or graduate biochemistry or neurochemistry course or permission of instructor. BIO 417 Neurobiology is recommended.

Learning Outcomes

1. Students will be able to defend the operational model of receptor function described by Black and Leff, 1983 and recognize concepts and equations from classical models that led to the operational model.
2. Students will be able to draw models of receptor function and receptor antagonism and derive equations that describe fractional occupancy or fractional response as a function of drug concentration.
3. Students will use Excel to calculate response as a function of drug concentration from expressions of fractional occupancy or fractional response derived from models of receptor function.
4. Students will use GraphPad (Prisim) software to perform nonlinear fits of simulated and actual data to equations derived from theoretical models of drug-receptor interaction.
5. Students will critically evaluate experimental design, detailed methods and data interpretation in peer-reviewed literature pertaining to receptor pharmacology and drug discovery.

Required Reading: **A Pharmacology Primer, Third Edition: Theory, Application and Methods**
Terry Kenakin, ISBN 978-0-12-374585-9

Original research and review articles to be assigned

Homework, and Grading: Homework (60%) will consist of approximately 10 take home assignments (3 points each). 3 points for excellent (complete and correct); 2 points for satisfactory (incomplete but correct or complete but partially correct; 1 unsatisfactory (partially correct and partially complete). Example assignments are as follows:

1. Draw a model and derive the equation that describes fractional receptor occupancy as a function of drug concentration.
2. Use published values for Kd and Ki to critically evaluate specificity and selectivity of drugs used in peer reviewed literature.
3. Use the operational model to describe the relationship between drug concentration and receptor occupancy, receptor occupancy and effect and drug concentration and functional response. Define τ and Ke and defend the advantages of the operational model over classical models of drug receptor interaction.
6. Discuss a peer reviewed paper on a topic related to course material. Identify limitations in experimental design, detailed methods and data interpretation
7. Use Excel to calculate response as a function of drug concentration from expression of fractional occupancy or fractional response derived from a given model of receptor function.
8. Fit simulated results to appropriate equation using Graph Pad (Prism) software.

Presentation of peer reviewed, original research paper (20%) to be graded on the basis of clarity and completeness in presentation of the following:

1. Introduction to problem and significance of problem
2. Explanation of experimental design and approach in the context of drug-receptor interaction models discussed in class.
3. Results
4. Critique of approach, methods, use of models and other aspects of the research.
5. Summary of significance noting caveats due to limitations of approach or experimental design.

Final exam (20%) will consist of a selection of modified homework assignments.

See schedule for when homework is due. Permission to hand-in HW via e-mail may be arranged in advance and will not be accepted without prior arrangements. Late homework will not be accepted unless arrangements are made before the homework is late. The letter grades assigned will be based on the overall performance of the class but will usually be in the range 90-100=A, 80-90=B, 70-79=C, 60-69=D, and below 60 is failing.

Published work must be cited to identify the source of the work and to acknowledge author's contributions. Evidence of plagiarism will lower the overall score on a homework assignment or project. Plagiarism includes the following:

- to steal and pass off (the ideas or words of another) as one's own
- to use (another's production) without crediting the source
- to commit literary theft
- to present as new and original an idea or product derived from an existing source.

Disabilities:

The Office of Disability Services implements the Americans with Disabilities Act (ADA), and insures that UAF students have equal access to the campus and course materials. Dr. Drew will work with the Office of Disabilities Services (*208 WHIT, 474-5655) to provide reasonable accommodation to students with disabilities.

Course Schedule (tentative)
Aug 29, 2016 - Dec 17, 2016

Date		Topic	Homework assignment
Aug	30	What is pharmacology	
Sept	1	Drug receptor theory	
	6	No class	
	8	Discussion of paper 1	
	13	Discussion of paper 1	
	15	Relationship between receptor occupancy and functional response	
	20	Kd and tau from functional assays	
	22	Pharmacological Assay Formats: Binding	Due 9/22 – sample data – operational model – results and graph
	27	Discussion of paper 2 – Kulkarni et al., 2016	Due 9/27 Take home message for each table and figure and 3 questions from Kulkarni et al., 2016
	29	IC50s and Ki's	Due 9/29 – Critical review of Kulkarni et al., 2016
Oct	4	IC50s and Ki's	Due 10/4 3 papers for discussion
	6	Displacement binding Section 4.2.2. and 13.1.1-13.1.2 Discuss Kim et al., 2007	
	11	Discuss Weltzin and Schulte 2010 Section 4.3 Complex binding phenomenon: agonist affinity from binding curves	Due 10/13 Excel file with data generated to Fit log ki Fit log Ki curves and results from Prism
	13		
	18		
	20		
	25		
	27		
Nov	1		
	3		
	8	Student led discussion of original research or selected paper	
	10	Student led discussion of original research or selected paper	
	15	Principles of pharmacokinetics absorption, distribution and elimination	
	17	Pharmacokinetics continued	
	22	Ligand gated channels (Maegan Weltzin)	
	24	Allosteric modulation of ligand gated channels (Maegan Weltzin	Critical review of paper 6
	29	Thanksgiving	
	1	Pharmacokinetics- DUI and blood alcohol concentration	
Dec	6	Pharmacokinetics- DUI and blood THC concentration	
	8	Student led discussion of original research or selected paper	
	13	Student led discussion of original research or selected paper	
	19	Take home final exam	
		Final exam due 10:00 am	