Course syllabus for Chemistry 162B / 262B

Drug Design (Spring 2012)

Class meets: Mon, Wed, Fri **8:00 – 8:50 AM** **PHELPS 1508**

Instructor: Professor *Kalju Kahn*, Office: PSB-N 2623
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Office Hours: Mon 10:30–11:30 and Tue 4:30–5:30 or by appointment
Course website: http://www.chem.ucsb.edu/~kalju/chem162

Lecture Textbook: Richard B. Silverman, The Organic Chemistry of Drug Design and Drug Action, 2nd edition

***The Course*:** In Chem 162, students learn principles that govern the process of modern drug discovery and development. Students will follow a path similar to that taken by real-life drug developers by learning important elements of the drug design process in a logical order. Some topics that we focus more extensively in 162B are:

- Principles of molecular recognition
- Mechanism of enzymes and enzyme inhibition
- Structure based drug design
- Drug metabolism and prodrugs

Expectations of Students:

- Attendance and taking good lecture notes is expected. Submitting completed assignments in time is required.
- The textbook provides some necessary background material. Furthermore, students are expected to read modern drug design-related research literature. Required literature will be available on the course website.
- Honesty and academic integrity must be always preserved. While discussing your ideas with others is encouraged outside the classroom, you must answer the assignment questions individually. No supplemental material should be used during an exam.
- Your grade in the course is based on points you collect from the weekly assignments (10 points each), the mid-term (40 points), the final exam (50 points), the poster (10 points), and the written research proposal (50 points). This has often been a small class in which participating students historically have earned grades between A+ and B-.
- The course requires that you have a solid understanding of organic chemistry; good background in biochemistry and physical chemistry will be helpful.
- No student shall give, sell, or otherwise distribute to others or publish any electronically available course materials or recordings made during any course presentation without the written consent of the instructor.

Study tips:

- I am posting lecture note slides on-line before the class meets so that you can focus on following my talk. The slides are mainly illustrative and you need to follow the lecture in order to fully understand the topics I cover.
- Come in class prepared. Read the relevant textbook material and required reading **before** the class meets. I like to interact with students during our meetings and you enjoy the lectures more if you can think along.
- Review (or rewrite) your class notes the same day and supplement them with material from the textbook and other resources (optional reading, Internet). Ask for help if something remains unclear.
- This course is not about memorization of names, reactions, or facts. It is about understanding the process, its principles and methods. You should demonstrate good understanding of the material when answering assignment questions and the exam problems. Your creativity and originality are highly important for getting a high score in the final written proposal.

Good luck! — Kalju

Chem162B/262B Schedule for Spring 2012

Apr 2	M	Introduction to enzymes; enzymes as drug targets	
Apr 4	W	General features of enzyme catalysis	
Apr 6	F	Principles of enzyme catalysis; TS stabilization	
Apr 9	M	Classification of enzymes; specific mechanisms	
Apr 11	W	Tutorial: Modeling of chemical reactions and transition state analogs	
Apr 13	F	Enzyme kinetics	
Apr 16	M	Enzyme inhibition. Reversible inhibitors; Transition state analogs.	
Apr 18	W	Enzyme inhibition. Irreversible inhibitors.	**HW1 due**
Apr 20	F	Mechanism-based inactivators	
Apr 23	M	Molecular recognition: Electrostatic interactions between molecules	
Apr 25	W	Tutorial: Chemical databases and visualization of macromolecules	**Milestone 1**
Apr 27	F	Molecular recognition: Polarization and dispersion; halogen bonding	
Apr 30	M	Molecular recognition: Entropy of binding; hydrophobic effect	
May 2	W	Structure-based drug design: Virtual screening	**HW2 due**
May 4	F	Tutorial: Structure-based drug design: docking (UCSF DOCK)	
May 7	M	Structure-based drug design: Virtual screening	
May 9	W	Structure-based drug design: Modeling protein flexibility	**HW3 due**
May 11	F	Midterm Exam	
May 14	M	Introduction to pharmacokinetics	
May 16	W	ADMET as a challenge in drug discovery	**Milestone 2**
May 18	F	Open (visit to AMGEN?)	
May 21	M	Tutorial: Structure-based drug design: docking (Schrödinger's Glide)	
May 23	W	Drug metabolism	**HW4 due**
May 25	F	Drug metabolism	
May 28	M	Memorial Day	
May 30	M	Drug toxicity and drug-drug interactions	**Milestone 3**
June 1	W	Prodrugs	
June 4	M	Nucleic acid drugs	
June 6	W	Discussion on individual drug design projects	**HW5 due**
June 8	F	Poster Session	

Written proposals due on June 10th.

Assignments

1. Transition state analogs as enzyme inhibitors
2. Mechanism-based enzyme inhibition
3. Structure-based drug design: visualization & docking
4. Pharmacokinetics, ADMET challenges
5. Drug metabolism and toxicity and prodrugs