Biol/Chem 444 - Drug Discovery and Development - Spring, 2008

Chem - class nos. 14591, 14595; Biol - class nos. 14599, 14600

Lec	**MW**	**11:40-12:55pm**	**Biological Sciences 246**
Lab	**M**	**1:00-3:30pm**	**BioSci 236 computer room**

Instructors:

Dr. Patrick Krug
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BioSci 327, 3-2076

Dr. Alison McCurdy
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Office Hours: M 3:30-4:30 PM, W 1:30-2:30 PM (Dr. Krug); MT 10:30-11:30AM (Dr. McCurdy)

Course Page URL: http://instructional1.calstatela.edu/pkrug/

Prerequisite: Chem 301C AND one of: Biol 380 or Chem 431A or Chem 435

Required Materials: Required text available at the Student Book Mart (323-262-5571)
All handouts given in class
Molecular Conceptor: software installed in BS 236

Additional Resources for CSLA students:

Article and Reference Databases available through the library:
ACS Publications (http://pubs.acs.org/about.html);
ScienceDirect (http://www.sciencedirect.com/)

Reserve: Background and other materials may be placed on the course web site (given above).

University Add/Drop Policy (no exceptions)

1. Deadline to add classes - April 7, 2008
2. Deadline to drop class with no record - April 1, 2008
3. "W" drop period begins - April 2, 2008 (see Spring, 2008 Catalog p 10 for conditions).

Policy on Plagiarism:

Students are expected to abide by the University's Academic Honesty Policy, which can be downloaded at http://www.calstatela.edu/univ/stuaffrs/jao/. Students who violate this policy will be subject to disciplinary action, and will receive a failing grade in the course for a single violation. Plagiarism includes downloading text verbatim from internet sites for inclusion in presentations or papers; a zero-tolerance policy will be strictly enforced by the instructors.

Course Description:

This course will provide an overview of drug discovery and development for advanced biology and chemistry students, combining academic and industrial research perspectives. As an upper-level course, it assumes basic knowledge of organic chemistry and biochemistry. The course will begin with some background information, including a discussion of pharmaceutical industry, natural products chemistry and folk medicine, aspects of molecular binding, and common drug target biomolecules. The two approaches to rational drug design will be examined: pharmacophore-based (small molecule) and receptor-based (macromolecular binding site). Some of the modern tools used in drug discovery will be highlighted, and will include the use of microarrays to probe small molecule/protein interactions, combinatorial versus engineered biosynthesis of chemical libraries, and chemical genetics. Practical and ethical aspects of pharmaceutical R&D will be covered, with emphasis on roadblocks to successful drug development. For instance, the molecular basis for resistance, a major hurdle in the effective management of microbial pathogens, will be considered in depth. This course will be team-taught by biology and chemistry faculty, reflecting the diverse fields brought together in the endeavor to design effective pharmaceutical drugs.

Student learning will be assessed through a variety of assignments and classroom activities, designed to promote group work through active learning exercises. Chemistry and biology students will work together using a software package (Molecular Conceptor) designed to walk students through all steps in the drug discovery process, from hit to lead compound, clinical trial to marketplace. Small groups will work through case studies in the software, identifying how changes in the chemical structure of lead compounds affected protein binding, ultimately determining the success or failure of candidate drugs. Student groups will make an in-class presentation on a selected medicinal drug, describing its discovery and development, its mechanism of action, and problems such as the molecular basis for resistance to the compound. Additionally, each student will write a final paper to isolate or design a drug for a target protein or gene selected from the recent literature.

Learning Objectives:

(1) Understand major biosynthetic pathways for secondary metabolism, classes of compounds used as drugs.

(2) Understand molecular forces involved in the binding of small molecules and proteins, understand how binding constants are measured. Know major classes of protein targets. Use Molecular Conceptor software to visualize how structural changes to drugs affect binding interactions with cellular targets.

(3) Learn how drugs are developed from a lead compound (pharmacophore-based analysis); become familiar with theories for optimizing activity and synthetic methodologies used.

(4) Learn how drugs are developed to target a specific protein (receptor-based analysis).

(5) Understand modern tools for drug development, including molecular modeling, chemical genetics, microarray screening, manipulation of biosynthetic genes, mechanism-based inhibitors, and antibodies targeting drugs to specific cells.

(6) Understand major roadblocks to successful drug development, including resistance of microorganisms or cancer cells, delivery and bioavailability of molecules that are effective *in vitro*, and the use of peptidomimicry to overcome obstacles inherent in the use of peptides as therapeutics.

(7) Develop a sense of the overall process of drug development, from hit to lead compound, clinical trial to marketplace. Students will learn the whole process through case studies in software exercises and lectures, guest speakers, and student presentations on major medicinal drugs.

(8) Seeing and understanding drug action on a molecular level

(9) Interpreting quantitative data in light of drug activity and structure-function relationships

(10) Understand some wet lab techniques (bioassays; combinatorial synthesis) used in drug discovery

(11) Apply what has been learned to case studies of drugs and/or drug targets that are new to the student.

Course Structure:

Grading: This course will be graded +/-. Grades will be determined on a curve, based on total points to be awarded as follows:

Quizzes (4)–	100 pts
Homework (4) –	100 pts
Presentation –	100 pts
Final Exam –	100 pts
Lab exercises –	100 pts
	500 pts total for course

There will be **4 quizzes** covering lecture material, each worth 25 pts, **4 homework assignments** to be completed outside of class, and **9 lab exercises** to be completed during lab. A missed quiz or lab can be made up only with prior approval by the instructor or an official excuse (doctor's note); a missed quiz or lab exercise must be made up before the next class period. You have 1 week from the time a quiz is returned to report errors in the grading or discuss alternative answers. Homework is due one week from the class when it is assigned, in class at the beginning of the class; late homework will not be accepted.

Group presentations: Students will work together in small groups to prepare and give a final presentation on a selected medicinal drug. Presentations will last for 20 min with 5 min for questions, and will be given at the end of the quarter. Groups will give their presentation in Powerpoint, then will receive feedback from instructors, and will revise and turn in their Powerpoint file for final grading **at or before the final exam**.

Spring 2008 Lecture Schedule

Date	Lecture Topic	Lab*
M 3/24	Intro and overview: pharmacophore-based vs. receptor-based approaches	Intro to MC** software, Background
W 3/26	Natural Products; historical perspective on medicinal chemistry	
M 3/31	UNIVERSITY CLOSED	
W 4/2	Natural products: terpenes, polyketides	
M 4/7	Binding phenomena: intermolecular forces	Wet lab: bioassay of extracts
W 4/9	Binding Quantification, examples	
M 4/14	Case study: Taxol	**Quiz 1.** MC 1
W 4/16	Closer look at Pharmacophore-based approach	
M 4/21	Closer look at Receptor-based approach	MC 2
W 4/23	Receptor-based approach (cont)	
M 4/28	Modern Tools: Molecular Diversity (Synthesis)	**Quiz 2.** Primary literature; MC 3
W 4/30	Modern Tools: Chemical Genetics	
M 5/5	Modern Tools: Computers in Drug Design	Wet lab: combinatorial synthesis and deconvolution
W 5/7	Enzymes as drug targets: pharmacophore and receptor-based approaches	
M 5/12	Engineered Biosynthesis	**Quiz 3.** Engineered biosynthesis
W 5/14	Speaker from Drug Discovery Industry (may move)	
M 5/19	Roadblocks: Antibiotic Resistance	MC 4
W 5/21	Roadblocks: Pharmacokinetics; primary literature **Quiz 4.** Engineered Biosynthesis	
M 5/26	UNIVERSITY CLOSED	UNIVERSITY CLOSED
W 5/28	Student Presentations	
M 6/2	Student Presentations	Speaker from Drug Discovery Industry
W 6/4	FINAL EXAM 10:45-1:15	

*Lab will be in different rooms depending on the activity
**MC = Molecular Conceptor Software