

## Chemistry 323/425: Medicinal Chemistry

**Spring Semester, 2014**  
**Mon/Wed 5:30-6:45 p.m.**  
**Flanner Hall 105**

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**Prerequisite:** Organic Chemistry 221/222 or Chem 223/224. This course is open to both undergraduate students (as CHEM 323) and graduate students (as CHEM 425).

**Required Text:** Medicinal Chemistry: The Modern Drug Discovery Process by Erland Stevens, Pearson Press 2014. ISBN 978-0-321-71048-2, ISBN 0-321-71048-7

**Sakai:** All Handouts that are given out in class will be posted on Sakai

**Office Hours:** Tuesday 3:30-5:00 or by appointment

**Course Description:** This course will provide an in-depth look at how novel, pharmacologically active molecules are designed to treat human diseases. We will follow the order of the Stevens text, and additional examples and applications will be drawn from the published literature. Selected case histories throughout the course will serve to illustrate the concepts. The course will include guest lecturers from practicing medicinal chemists.

Readings and problems will be assigned, both from the text and from the primary literature as handouts. There will be several 30-minute quizzes during the semester at the conclusion of the lecture period, and there will be a cumulative final examination during our scheduled final exam slot. Students enrolled in Chem 425 will be required to give a presentation on some aspect of drug discovery, from the recently-published literature, and folks in Chem 322 will submit notes from those presentations. This course is didactic only; there is no lab associated with this course.

**Goals of this course include the demonstration of proficiency in understanding:**

- risk/benefit aspect of medicines, understanding toxicity and therapeutic index
- pharmacodynamics of drugs with receptors, enzymes, and oligonucleotides
- pharmacokinetics of drug action, including ADME
- metabolism of drugs, and the role of metabolism in PK and drug safety
- strategies of lead discovery toward new drugs
- strategies of lead optimization
- synthesis of drug molecules using the reactions of synthetic organic chemistry
- patent process of protecting intellectual property
- ethical aspects of drug development and marketing
- relevance of the principles of drug discovery to environmental and dietary exposure

**Evaluation**

	<b>CHEM 323</b>		<b>CHEM 425</b>
Homework	150	Homework	150
Two Hourly Exams	200	Hourly Exams	200
Presentation Summaries	50	Presentations	100
Cumulative Final	100	Cumulative Final	100
<b>Total (ca.)</b>	<b>500</b>	<b>Total (ca.)</b>	<b>550</b>

### Selected Medicinal Chemistry Textbooks

- *An Introduction to Medicinal Chemistry*, 5<sup>th</sup> Edition, by Graham L. Patrick, Oxford University Press, 2013. **ISBN-10:** 0199697396; **ISBN-13:** 978-0199697397
- *The Organic Chemistry of Drug Design and Drug Action*, by Richard B. Silverman, 2nd Edition. Elsevier Academic Press, 2004, ISBN 0-12-643732-7.
- *Foye's Principles of Medicinal Chemistry*, 7th Edition, by David A. Williams and Thomas L. Lemke, Lippincott Williams & Wilkins, 2012.
- *Medicinal Chemistry: A Molecular and Biochemical Approach*, 3<sup>rd</sup> Edition, by Thomas Nogrady and Donald F. Weaver, 2005.
- *Medicinal Chemistry, An Introduction*, 2<sup>nd</sup> Edition, by Gareth Thomas, John Wiley & Sons, 2008.
- *The Practice of Medicinal Chemistry*, 3<sup>rd</sup> Edition, ed. Camille Wemuth, Academic Press, 1996.

### Fun Medicinal Chemistry Books

- *Molecules that Changed the World* by K.C. Nicolaou and T. Montagnon, 2008, Wiley-VCH. A lovely coffee table book and gift for the new medicinal chemist in the family.
- *Molecules and Medicine* by E. J. Corey, László Kürti and Barbara Czakó, 2007, Wiley. A remarkable little paperback describing the structures and mechanisms of action of over one hundred key pharmaceuticals organized by therapeutic area.

### Selected Medicinal Chemistry Journals

- *Journal of Medicinal Chemistry*
- *Journal of Medicinal Chemistry Letters* (starting with 2010, Volume 1)
- *Bioorganic & Medicinal Chemistry*
- *Bioorganic & Medicinal Chemistry Letters*
- *European Journal of Medicinal Chemistry*
- *ChemMedChem*

### Additional Resources

- *Annual Reports in Medicinal Chemistry*
- The U.S. Patent and Trademark Office at <http://www.uspto.gov/>
- Free patent pdf files are available at: <http://www.freepatentsonline.com/>

**Academic Honesty:** For this course, all exams are closed book and closed note unless otherwise prescribed. Academic dishonesty includes using notes or books during exams, looking at another student's test during the exam period, talking during an exam, and plagiarizing in written assignments. Punishment for academic dishonesty is failure of the course, and the incident will be reported to the Chemistry Department Chair and the Office of the Dean. Additional sanctions, including expulsion from the university, may be imposed. The Undergraduate Handbook (pp 12-13) contains a complete description of the University policy regarding academic dishonesty.

**Chemistry 395/425 Med Chem Tentative Outline – updated 1-13-14**

Wk	Dates	Topics	Reading Due	Handouts	Due
1	1-13	Intro		Intro Ch 1-2 History & Modern Drug Disco Process	
	1-15	Brief History of Drug Disco	Ch 1	Quickie Orgo Rev, Functional Groups, & Lead Optimization Strategies; Pharma Promenade	
2	1-20	<b>MLK Holiday</b>			ACDLabs ChemSketch draw & min
	1-23	Modern Drug Disco Process; orgo review	Ch 2		Ch 2 probs 1-5
3	1-27	Trip Through the Body	Ch 3		Orgo Synthesis Problems
	1-29				Ch 3 probs 1-10
4	2-3	Enzymes	Ch 4	neuraminidase inhibitors – Tamiflu	
	2-5	neuraminidase inhibitors – Tamiflu			Ch 4 probs ###
5	2-10	Receptors	Ch 5		
	2-12	<b>Exam I Ch 1-3</b>			Ch 5 probs ###
6	2-17	Oligonucleotides	Ch 6		
	2-19				Ch 6 probs ###
7	2-24	PK (pharmacokinetics)	Ch 7		
	2-26				Ch 7 probs ###
8	3-3	<b>Spring Break</b>			
	3-5	<b>Spring Break</b>			
9	3-10	Metabolism	Ch 8		Ch 8 probs ###
	3-12	<b>Exam II Ch 4-7</b>			
10	3-17	Molecular Structure & Diversity	Ch 9		
	3-19				Ch 9 probs ###
11	3-24	Lead Discovery	Ch 10		
	3-26	Docking: Autodock VINA			Ch 10 probs ###
12	3-31	Lead Optimization - traditional	Ch 11		
	4-2				Ch 11 probs ###
13	4-7	Lead Optimization - Hansch	Ch 12	Vaccines, Vioxx & Viagra	
	4-9	Dr. Tom Penning: Celebrex; Veliparib, PARP inhibitor for cancer		Breaking the Seal on Drug Research; Economist: How Science goes wrong	Ch 12 probs ###
14	4-14	Pharmaceutical Sciences	Ch 13		
	4-16	Dr. Hillary Peltier - Abbott			Ch 13 probs ###
15	4-21	Top \$\$ Oral Drugs	App A		
	4-23	Presentations			
Fin	4-28	Cumulative			