MDCM 950. Industrial Medicinal Chemistry: Practices and Concepts
Spring Semester 2015 (2 credit hours)

Instructor: Michael Rafferty
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The aim of this course is to provide an overview and understanding of the process of drug discovery, and exposure to the issues and challenges of drug discovery. This is an attempt to create a true-to-life experience requiring strategic thinking, interpretation of complex and often inconclusive data, overcoming common problems encountered in the course of drug discovery, and appreciation of the complexities of contemporary drug discovery and preclinical/clinical development. Students who enroll in this course will be assigned to a team consisting of 3-5 students. Each team will be assigned a molecular target of current interest in pharmaceutical drug discovery, and a list of hypothetical compounds representing the typical outcome of a screening campaign. Teams will be expected to research the target, decide on a therapeutic application, develop a target profile for a development candidate, and select a lead from the list of hits provided within the first 3 weeks of class. Teams will also propose a comprehensive testing sequence consistent with current practices in industry, and will apply contemporary tools such as efficiency metrics in analogue design and SAR interpretation. As projects progress, students will encounter issues related to data interpretation, potency, physical properties, pharmaceutical and ADME issues, and toxicity/side effect concerns that inevitably impact lead optimization. Each team will be assigned to an external mentor who is a current or former expert in pharmaceutical drug discovery and who will be available throughout the semester to help guide the team and address any specific issues or questions that might arise from their project. The mentors for the upcoming 2015 Spring semester include Dr. John McCall, former vice president of chemistry with Pharmacia; Dr. Paul Galatsis, CNS Design Fellow with Pfizer in Cambridge MA; and Dr. Arthur Romero, Research Professor at Washington University in St. Louis and former Research Fellow with Pfizer. It is expected that students will utilize online literature databases such as SciFinder, PubMed, and any other resources at their disposal including modeling tools.

Course requirements: This course is open to all graduate students who have completed at least three full semesters of their graduate program in medicinal chemistry, chemistry (organic and bioorganic), pharmaceutical chemistry, molecular biosciences, bioinformatics, or pharmacology. There are no set prerequisites for this course, although many of the concepts discussed in MDCM 710 will be applied during execution of the projects. Auditing the course is acceptable on the condition that auditing students and postdocs agree to participate fully in as a project team member.

Course schedule and content: The class will meet Monday on Wednesday, 10:00 AM. Class sessions will consist of lectures on topics of relevance to drug discovery given by the instructor or occasional guest lectures. Topics of these lectures will include

HTS triage and hit selection; hit-to-lead strategies; property-based drug design and the application of property metrics; interpretation of biological data and basic statistics; methods for measurement of physical properties including solubility, permeability, and pKa,; and patents and patent law basics. We will also discuss team behaviors and team dynamics, since for most of the students this course will be their first experience in a team setting. This aspect of the course is particularly important and in this context students will be asked to self-administer the Myers-Briggs assessment tool and discuss their profiles with their teammates. Beginning approximately week 4 of the semester, every other week will be devoted to in-class presentations by the teams, by which they will discuss and interpret recent results, changes in strategy, or any other issues including requests for special studies where warranted. These presentations will follow a standard format, but the content is entirely the responsibility of the teams.

Grading: There are no exams in this course. Grades will be based on the level of engagement and participation, the quality of organization and delivery of presentations, and occasional feedback from team mentors and teammates.

For further information, contact Dr. Michael Rafferty at raffe01@ku.edu.

Date	time	Topic
21-Jan	9-9:50	1. Class introduction
26-Jan	9-9:50	2. Statistical methods and data analysis
2-Feb	9-9:50	3. Teams and team behaviors (Briggs-Myers)
4-Feb	9-9:50	4. Drug discovery organizations and process
9-Feb	9-9:50	5. HTS analysis andlead selection
11-Feb	9-9:50	6. Introduction to property based drug design
16-Feb	9-9:50	first project team presentations
18-Mar	9-9:50	7. Property metrics, uses and limitations
23-Feb	9-9:50	8. Fragment based lead discovery and strategies
25-Feb	9-9:50	project team presentations
2-Mar	9-9:50	9. Membrane permeability: methods and interpretation
4-Mar	9-9:50	Lecture/case study
9-Mar	9-10:50	project team presentations/discussion
11-Mar	**no class**	
16-Mar	**no class**	Spring Break-
18-Mar	**no class**	Spring Break-
23-Mar	9-9:50	10. allometry and biomarkers
25-Mar	9-9:50	project team presentations
30-Mar	9-9:50	11. Bioisosterism
1-Apr	9-9:50	12. Pharmacokinetics
6-Apr	9-9:50	project team presentations
8-Apr	9-9:50	13. animal models and experimental design
13-Apr	9-9:50	14. Patent law and patenting srategies
15-Apr	9-9:50	project team presentations
20-Apr	9-9:50	15. Candidate selection and preclinical development
22-Apr	9-10:50	16. Case studies
27-Apr	no class	17. Case studies

29-Apr	9-10:50	project team presentations
4-May		Final project presentations
6-May		Final class: project and team after action reviews

18 Lectures, 8 in-class project team presentations