USC School of Pharmacy

RXRS 407: The Discovery, Development and Marketing of Modern Medicines

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Course Weight: 4 Units (two 1.5 hour sessions; plus 1 hour outside activities)

Day/Time/Location: TTH 9:30-10:50 Location: VKC 157

Introduction

This course introduces the student to the biomedical community as it relates to current strategies undertaken to move research discoveries from the laboratory (bench) into clinical practice (bedside) to diagnose and treat patients. This concept is commonly referred to as Translational Science or Translational Medicine. The tenets of this course will be defined and explained in terms of promoting focused multidisciplinary interactions between science and medicine to enhance disease research and drug development. In addition, the wider inter-relationships with regulatory, ethical and societal sectors will be presented.

Objectives

This course is designed for undergraduates of both scientific and non-scientific majors with an interest in learning about principles and concepts underlying drug discovery and development of medicines. Chapters from the required textbook will be supplemented with a variety of source materials including articles from scientific journals and public websites. Selected cases studies will be critically reviewed and emerging "hot" topics discussed.

Upon successful completion of this course, the student should be able to demonstrate a working knowledge of:

- The importance of a team effort in the drug discovery/drug development process as seen through the eyes of the pharmaceutical industry.
- The many challenges faced by a start-up pharmaceutical company.
- The importance of intellectual property (IP); critical IP issues and timing.
- The preclinical drug development process from therapeutic target to marketable drug.
- The basic terminology used in characterizing a new drug (e.g. potency, EC_{50}, IC_{50}, MTD, efficacy, selectivity, ADME, etc.…).
- The importance of properly designing a scientific experiment (Scientific Method).
- The importance of identifying potential genotoxicity, carcinogenicity and reproductive/developmental toxicology issues during the course of a drug discovery campaign and how to test for them.
- The difference between a small molecule drug and a biopharmaceuticals and understand the advantages and disadvantages of each therapy.

- The importance of good laboratory practices (GLP), good manufacturing practices (GMP) and good clinical practices (GCP).
- The role of clinical trials in drug development.
- Why so many experimental compounds fail to ever reach the market.

Assignments and Grading:

Class participation:	10 pts (5 %)
5 quizzes @ 10 pts each	50 pts (25%)
2 midterm exams @ 40 pts each:	80 pts (40 %)
1 final exam (partially cumulative):	60 pts (30 %)
Total:	200 pts.

Class Participation and Attendance (10 pts): On a scale of 10, 0-indicating no participation, 10-indicating best participation. You can therefore increase the probability of getting a higher mark by being proactive in terms of asking (relevant) questions in class and/or contributing to discussions.

Attendance at all classes is expected. Participation will include asking and answering questions and being actively involved in the discussion. It is expected that the students read the assigned papers prior to the lecture and be prepared to discuss background, current understanding, treatments, and gaps in knowledge for the topic in each lecture.

There will be 5 quizzes over the course of the semester that will primarily be based on questions pulled from the text book and lectures. The midterms (40 points each) will include multiple choice questions T/F questions fill-in the blank questions, and short answers.

Instead of a final exam, a 6-page double-spaced essay (deliverable) will be due by email to ddavies@usc.edu by 5pm on the day of the final (May 8). The deliverable will focus on the discovery, development and use of cancer therapies based on Car-T Therapies.

Within the assignment, you will present the background and history of CAR-T therapies. Briefly, how they work, what are the target cells, etc. I don't expect you to be a molecular biologist, but as future clinician's this is a therapy that is gaining momentum and it is one that you need to start reading about. Also discuss the advantages (and challenges) for CAR-T therapies. What are the current drug companies that are working on CAR-T therapies? What cancers are they trying to address with these therapies? What is the alternative to these therapies? How would you address the cost factor of the therapy? Who will pay?

Proper references to the literature (this excludes Wikipedia and the like) are required but do not count against the page limits.

Notes, books, calculators, electronic dictionaries, regular dictionaries, cell phones or any other aids are not allowed during exams.

Students will be asked to complete an anonymous critical evaluation of the course at its

completion.

Course Readings

Required Readings

Drug Discovery and Development: Technology in Transition, 2nd Edition
Raymond G. Hill & Humphrey P. Rang; **ISBN-13:** 978-0702042997

Although not mandatory, it is strongly suggested that the students purchase the textbook for this course as it will greatly improve the students grasp on the Drug Discovery/Development process. The students will be able to use identified chapters in the text to support their learning process throughout the semester.

Other course materials including but not limited to the syllabus, supplemental reading assignments and additional handouts will be posted on http://blackboard.usc.edu/. The students will also be encouraged to use the online discussions among students via Blackboard.

Recommended

- Adman Bernstein and Patricia Sullivan. "Frances Oldham Kelsey, FDA scientist who kept thalidomide off U.S. market, dies at 101." *Washington Post.* August 7, 2015 https://www.washingtonpost.com/national/health-science/frances-oldham-kelsey-heroine-of-thalidomide-tragedy-dies-at-101/2015/08/07/ae57335e-c5da-11df-94e1-c5afa35a9e59_story.html
- Christine M. Clovis, PhD and Christopher P. Austin, MD. The NIH-Industry New Therapeutic Uses Pilot Program: Demonstrating the Power of Crowdsourcing. *Drug Repurposing, Rescue and Repositioning.* VOL. 1 NO. 1 (March, 2015)

- Cynthia Fox, Reading Leaves a Dramatic Imprint on the Brain: http://www.biosciencetechnology.com/articles/2014/12/reading-leaves-dramatic-imprint-brain?location=top

- Stephanie Guzowsk, FDA Approves Addyi (Flibanserin) for Low Libido in Women http://www.dddmag.com/news/2015/08/fda-approves-addyi-flibanserin-low-libido-women

- Dr. Timothy Scott discusses some of the history of the FDA and how it shaped the industry today. https://youtu.be/TXAVCaOSi-s

- Free magazine "Translational Science" https://www.youtube.com/watch?v=9Cw9v-LnrRU&feature=youtu.be

Course Outline

This course will be in the format of a directed seminar/lecture under the guidance of the instructor for the specific session. During each weekly session the instructor will engage the students with questions and draw comments or interpretations primarily based on the assigned reading. Students are expected to ask questions and participate in an interactive fashion.

Week & Date	Topic	Subtopics to be Included	Assigned and Supplemental Reading
		Introduction and Background	
Week 1 Jan. 9, 11	Introduction: expectations and goals of this class. General overview of drug development process from therapeutic target to marketable drug.	Pharmacological principles and definitions: Efficacy (EC_{50}), potency, MTD, ADME, etc. Market Strategies Case studies illustrating why we have the FDA.	Hill/Rang, Chapter 22. Additional readings to enrich subject matter will be posted on Blackboard.
Week 2 Jan. 16, 18	Development of Pharmaceutical Industry-	History of drug development (where and how it all got started).	Hill/Rang , Chapter 1 What is Translational Science? https://www.youtube.com/watch?v=rAblbUmyQgk
Week 3 Jan 23, 25	Nature of Disease Quiz 1	Etiology, pathology, research highlights, current drug treatments and future drug development. Therapeutic Interventions; Therapeutic modalities	Hill/Rang , Chapters 2-3
		Drug Discovery	
Week 4 Jan. 30, Feb. 1	Introduction to Drug Discovery	General Principles; Case Histories,	Hill/Rang , Chapter 4
Week 5		**In Class Midterm 1 Feb. 6**	
Weeks 5-6. Feb. 8, 13, 15	Project Management of Drug Discovery Where does it all start. Feb 15 Dr. Robert Pacifici from CHDI	Identifying the Project; Identifying the Target	Hill/Rang , Chapters 5-6
Weeks 7-8 Feb. 20, 22, 27	Quiz 2 The Components of Drug Discovery	The role of genomics/bioinformatics in the drug discovery process; Role of high-throughput screening and in vitro assay development in the drug discovery process	Hill/Rang , Chapters 7-9
Week 8 Mar. 1	The Components of Drug Discovery Mary Ellen Cosenza Components of Drug Discovery	Biopharmaceuticals;	Hill/Rang , Chapter 12
Weeks 9 Mar. 6, Mar 8	Quiz 3 The Components of Drug Discovery Mary Ellen Cosenza	Understand the role of drug metabolism and pharmacokinetics (DMPK) and early stage toxicology studies as major hurdles in the drug discovery process; Role of pharmacology (specifically confirmation *in vitro* assays, target selectivity testing and *in vivo* pharmacological profiling) in the drug discovery process; Assessing Drug Safety; cGLP, cGMP	Hill/Rang , Chapters 10-11;13-14
		Drug Development	
Week 10 Mar. 13, 15	No Class	Spring Break	
Week 11 Mar. 20, 22	Dr. Ashutosh Kulkarni, Allergan	Understand the role of drug metabolism and pharmacokinetics (DMPK) and early stage toxicology studies as major hurdles in the drug discovery process; Role of pharmacology (specifically confirmation *in vitro* assays, target selectivity testing and *in vivo* pharmacological profiling) in the drug discovery process; Assessing	Hill/Rang , Chapters 10-11;13-14

		Drug Safety; cGLP, cGMP	
Week 12 Mar. 27, 29	Quiz 4 Pharmaceutical Development Hovik Gukasyan, Allergan	Comprehend different drug delivery systems	Hill/Rang , Chapter 16
		Week 13 In Class Midterm 2 March 27	
Week 13 Apr 3, 5,	Clinical Development Apr 5 Dr. Robert Pacifici CHDI	Role of CROs in new drug development Identification of regulatory implications Development products for clinical testing and comparability Future research opportunities Scale-up /formulation challenges	Hill/Rang, Chapters 19-20
Week 14 Apr. 10, 12	Quiz 5 Market Expectations	Case studies of issues faced by a start-up pharmaceutical companies; Development of follow-on products	Hill/Rang , Chapter 21
Week 15 April 17,19	Development of BCR-ABL inhibitor Ponatinib for CML Sandra Kroll-Hellard, PhD Medical Science Liaison Ariad Pharmaceuticals Sandra.Kroll-Hellard@Ariad.com 440.666.2969	Case studies of issues faced by a start-up pharmaceutical companies; Development of follow-on products	
Week 16 April 24, 26	Wilmar Estrada: Regulation of Advertising and Promotion for Prescription Drugs		
	Anna Papinska, PhD	Regulation of Advertising and Promotion for Prescription Drugs	
Final Exam May 8 8:00- 10:00 am VKC 157			

Statement on Academic Conduct and Support Systems

Academic Conduct

Plagiarism – presenting someone else's ideas as your own, either verbatim or recast in your own words – is a serious academic offense with serious consequences. Please familiarize yourself with the discussion of plagiarism in *SCampus* in Section 11, *Behavior Violating University Standards* https://scampus.usc.edu/1100-behavior-violating-university-standards-and-appropriate-sanctions. Other forms of academic dishonesty are equally unacceptable. See additional information in *SCampus* and university policies on scientific misconduct, http://policy.usc.edu/scientific-misconduct.

Discrimination, sexual assault, and harassment are not tolerated by the university. You are encouraged to report any incidents to the *Office of Equity and Diversity* http://equity.usc.edu or to the *Department of Public Safety* http://capsnet.usc.edu/department/department-public-safety/online-forms/contact-us. This is important for the safety of the whole USC community. Another member of the university community – such as a friend, classmate, advisor, or faculty member – can help initiate the report, or can initiate the report on behalf of another person. *The Center for Women and Men* http://www.usc.edu/student-affairs/cwm/ provides 24/7 confidential support, and the sexual assault resource center webpage http://sarc.usc.edu describes reporting options and other resources.

Support Systems
A number of USC's schools provide support for students who need help with scholarly writing. Check with your advisor or program staff to find out more. Students whose primary language is not English should check with the *American Language Institute* http://dornsife.usc.edu/ali, which sponsors courses and workshops specifically for international graduate students. *The Office of Disability Services and Programs* http://sait.usc.edu/academicsupport/centerprograms/dsp/home_index.html provides certification for students with disabilities and helps arrange the relevant accommodations. If an officially declared emergency makes travel to campus infeasible, *USC Emergency Information* *http://emergency.usc.edu* will provide safety and other updates, including ways in which instruction will be continued by means of blackboard, teleconferencing, and other technology.

Emergency Preparedness/Course Continuity:
In case of emergency, and travel to campus is difficult, USC executive leadership will announce an electronic way for instructors to teach students in their residence halls or homes using a combination of Blackboard, teleconferencing, and other technologies. Instructors should be prepared to assign students a "Plan B" project that can be completed at a distance. For additional information about maintaining your classes in an emergency please access: http://cst.usc.edu/services/emergencyprep.html