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 (Essay Assignment): 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 5-page double-spaced essay (deliverable) will be due by email to ddavies@usc.edu by 5pm PST on the day of the final (Tuesday, May 7, 2019). The deliverable this year 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

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


- 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.bioscienctechnology.com/articles/2014/12/reading-leaves-dramatic-imprint-brain?location=top

- Stephanie Guzowsk, FDA Approves Addyi (Flibanserin) for Low Libido in 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

  • Newsletters such as: Drug Discovery Online Newsletter <info@DrugDiscoveryOnline.com>

  • Pharmaceutical Processing: https://www.rdmag.com/topics/pharmaceutical-processing

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.
<table>
<thead>
<tr>
<th>Week &amp; Date</th>
<th>Topic</th>
<th>Subtopics to be Included</th>
<th>Assigned and Supplemental Reading</th>
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<tbody>
<tr>
<td><strong>Introduction and Background</strong></td>
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<tr>
<td>Week 1 Jan. 8, 10</td>
<td>Introduction: expectations and goals of this class. General overview of drug development process from therapeutic target to marketable drug.</td>
<td>Pharmacological principles and definitions: Efficacy (EC50), potency, MTD, ADME, etc. Market Strategies Case studies illustrating why we have the FDA.</td>
<td>Hill/Rang, Chapter 22. Additional readings to enrich subject matter will be posted on Blackboard.</td>
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<tr>
<td>Week 2 Jan. 15, 17</td>
<td>Development of Pharmaceutical Industry-</td>
<td>History of drug development (where and how it all got started).</td>
<td>Hill/Rang, Chapter 1 What is Translational Science? <a href="https://www.youtube.com/watch?v=rAblbUmyQgk">https://www.youtube.com/watch?v=rAblbUmyQgk</a></td>
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<td>Week 3 Jan 22, 24</td>
<td>Nature of Disease Quiz 1</td>
<td>Etiology, pathology, research highlights, current drug treatments and future drug development. Therapeutic Interventions; Therapeutic modalities</td>
<td>Hill/Rang, Chapters 2-3</td>
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<td><strong>Drug Discovery</strong></td>
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<tr>
<td>Week 4 Jan. 29, 31</td>
<td>Introduction to Drug Discovery</td>
<td>General Principles; Case Histories,</td>
<td>Hill/Rang, Chapter 4</td>
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<td>Week 5 Feb 7</td>
<td>Defining a Market</td>
<td>Defining a Market for your Drug</td>
<td>Hill/Rang, Chapters 5-6</td>
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<td>Week 6 Feb. 12, 14</td>
<td>Project Management of Drug</td>
<td>Identifying the Project; Identifying the Target</td>
<td>Hill/Rang, Chapters 5-6</td>
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<td>Week 7 Feb. 19, 21</td>
<td>Translating your Science in academia Feb 22 --PPT presentations by Students</td>
<td>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</td>
<td>Hill/Rang, Chapters 7-9</td>
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<tr>
<td>Week 8 Feb 26, 28</td>
<td>Documentation Requirements The Components of Drug Discovery Mary Ellen Cosenza Components of Drug Discovery</td>
<td>Biopharmaceuticals;</td>
<td>Hill/Rang, Chapter 12</td>
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<tr>
<td>Weeks 9 Mar. 5, 7</td>
<td>Quiz 3 The Components of Drug Discovery Mary Ellen Cosenza Presentations by students</td>
<td>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</td>
<td>Hill/Rang, Chapters 10-11;13-14</td>
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<td><strong>Drug Development</strong></td>
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<td>Week 10 Mar.</td>
<td>No Class</td>
<td>Spring Break</td>
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<tr>
<td>Week 11 Mar. 19, 21</td>
<td>Dr. Ashutosh Kulkarni, Allergan</td>
<td>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</td>
<td>Hill/Rang, Chapters 10-11;13-14</td>
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### Week 12
**Quiz 4**
Pharmaceutical Development  
Hovik Gukasyan, Allergan  
Comprehend different drug delivery systems  
Hill/Rang, Chapter 16

<table>
<thead>
<tr>
<th>Week 13</th>
<th>In Class Midterm 2</th>
<th>April 3</th>
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<tbody>
<tr>
<td>Week 13</td>
<td>Apr 2, 4</td>
<td>Dr. Robert Pacifici CHDI</td>
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<td>Week 14</td>
<td>Apr. 9, 11</td>
<td>Quiz 5</td>
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<td>Week 15</td>
<td>April 16, 18</td>
<td>Anna Papinska, PhD</td>
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<td>Week 16</td>
<td>April 23, 25</td>
<td>Regulation of Advertising and Promotion for Prescription Drugs</td>
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| April 26 | 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 |

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**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 Part B, Section 11, “Behavior Violating University Standards” policy.usc.edu/scampus-part-b. 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](http://policy.usc.edu/scientific-misconduct).

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*The Discovery, Development and Marketing of Modern Medicines*
Support Systems:

*Student Counseling Services (SCS) – (213) 740-7711 – 24/7 on call*
Free and confidential mental health treatment for students, including short-term psychotherapy, group counseling, stress fitness workshops, and crisis intervention. engemannshc.usc.edu/counseling

*National Suicide Prevention Lifeline – 1 (800) 273-8255*
Provides free and confidential emotional support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week. www.suicidepreventionlifeline.org

*Relationship and Sexual Violence Prevention Services (RSVP) – (213) 740-4900 – 24/7 on call*
Free and confidential therapy services, workshops, and training for situations related to gender-based harm. engemannshc.usc.edu/rsvp

*Sexual Assault Resource Center*
For more information about how to get help or help a survivor, rights, reporting options, and additional resources, visit the website: sarc.usc.edu

*Office of Equity and Diversity (OED)/Title IX Compliance – (213) 740-5086*
Works with faculty, staff, visitors, applicants, and students around issues of protected class. equity.usc.edu

*Bias Assessment Response and Support*
Incidents of bias, hate crimes and microaggressions need to be reported allowing for appropriate investigation and response. studentaffairs.usc.edu/bias-assessment-response-support

*The Office of Disability Services and Programs*
Provides certification for students with disabilities and helps arrange relevant accommodations. dsp.usc.edu

*Student Support and Advocacy – (213) 821-4710*
Assists students and families in resolving complex issues adversely affecting their success as a student EX: personal, financial, and academic. studentaffairs.usc.edu/ssa

*Diversity at USC*
Information on events, programs and training, the Diversity Task Force (including representatives for each school), chronology, participation, and various resources for students. diversity.usc.edu

*USC Emergency Information*
Provides safety and other updates, including ways in which instruction will be continued if an officially declared emergency makes travel to campus infeasible. emergency.usc.edu

*USC Department of Public Safety – UPC: (213) 740-4321 – HSC: (323) 442-1000 – 24-hour*