Drug Design and Development (BME 694/794)

Instructor: Moo-Yeal Lee, Ph.D.
Office: FH 439
Office hours: Friday 3:00 – 5:00 pm
Classroom: FH 268
Lecture hours: Tuesday & Thursday, 6:00 – 7:15 pm
Prerequisite(s): Graduate standing in chemical and biomedical engineering, chemistry or permission of instructor.

Course Description:

This course introduces students to the fundamental principles of drug design and development currently employed in pharmaceutical industries. Emphasis for this course will be drug discovery processes, which include disease target identification and validation, high-throughput screening for lead compound ("hit") generation, the optimization of lead compound structures, preclinical evaluations with animal models, clinical trials, regulatory applications for FDA approval, and drug manufacturing. This course will provide information on critical issues (e.g., efficacy vs. toxicity) in drug discovery and introduce diverse *in vitro* assays and animal tests used in drug discovery to enable more effective and safer drug candidates to enter clinical trials. The overall objective for this course is to have students understand broader implications of the drug discovery processes and complex real-world problems in the pharmaceutical industries. After completing this course, students should be able to appreciate critical issues in drug discovery, understand different phases of drug development processes, perform analysis between drug efficacy and toxicity, make proper evaluations related to drug design and development, and communicate with professionals in the pharmaceutical community.

After an introduction to the critical issues in drug design and development, students will work on specific topics that are important in drug discovery. In this semester, we will focus on a series of case studies and research on idiosyncratic (individual-dependent) adverse drug reactions. The students are expected to identify critical needs for idiosyncratic toxicology assays, identify drugs that are withdrawn from the market due to idiosyncratic toxicity, explore existing assay platforms for predicting *in vivo* toxicity, explain the principles of the existing assays and analytical instrument used, propose new/improved methods to better predict idiosyncratic adverse drug reactions *in vivo*. The students are also expected to participate heavily in class discussions, present their work to the class, and critically evaluate peer's work with regard to its significance, innovation, and approach for problem identification and solving. Class attendance and a capability of reading and understanding relevant research articles are required.

Course Materials:

1. Drugs: From discovery to approval by Rick Ng, Wiley-Blackwell, 2 edition (2008)
2. Real world drug discovery: A chemist's guide to biotech and pharmaceutical research by Robert M. Rydzewski, Elsevier Science, 1 edition (2008)
3. Drug discovery and development: Technology in transition by Raymond G Hill, Churchill Livingstone, 2 edition (2012)
4. Literature – review and research articles

These books are only suggestions and there is no need to purchase them. The material covered in the course will be drawn from these books and other sources, and lecture notes will be provided to students.

Grading Policy:

- Class attendance/participation: 10%
- Quiz: 10%
- Mid-term and final exam: 40% total
- Student project: 30%
- Homework: 10%

Topical Outline:

1. Drug discovery business to date
2. Drug discovery business to come
3. Target identification and validation
4. High-throughput screening and hit generation
   A. Small molecule drugs
   B. Large molecule drugs
5. Lead compound optimization
   A. Properties of drugable compounds
   B. Pharmacodynamics and pharmacokinetics (PD/PK) properties
   C. Toxicity-related properties
6. Preclinical studies with animal models
   A. Pharmacodynamics (PD)
   B. Pharmacokinetics (PK)
   C. Toxicology
   D. *In vitro* assays, *in silico* methods, and animal tests
   E. Drug formulations and delivery systems
7. Clinical trials
8. Regulatory authorities
9. Regulatory applications
10. Good manufacturing practice (GMP): Regulatory requirements and drug manufacturing
11. **Student project**: **Idiosyncratic adverse drug responses**
    A. Introduction
    ✓ Identify critical needs/problems for idiosyncratic toxicology measurements
    ✓ Provide the epidemiology of idiosyncratic adverse drug responses with supporting *in vivo* evidences
    ✓ Introduce mechanisms of idiosyncratic adverse drug responses
    ✓ Provide names of drugs that are withdrawn from the market due to the specific mechanisms of idiosyncratic toxicity
    B. Experimental approaches for idiosyncratic adverse drug responses
    ✓ Describe experimental approaches (including animal models, *in vitro* assays, and computational methods) developed to predict idiosyncratic adverse drug responses
    ✓ Explain basic principles of experimental approaches mentioned
    ✓ Describe what analytical instrument is being used for measurements
    ✓ Discuss advantages and limitations of experimental approaches
    C. Conclusions
    ✓ Draw proper conclusions
    D. References
    ✓ Provide relevant literatures
    E. Future direction (bonus points if submitted)
    ✓ Propose new/improved methods to better predict idiosyncratic adverse drug responses

*The topics are subject to change.