Course Syllabus - TRBIO 450

Course Number:	TRBIO 450
Course Name:	Drug Discovery and Development
Quarter:	WI
Year:	2017
Start Date:	01/05/2017
End Date:	03/24/2017
Credits:	3.0
Last Date To Add This Course:	01/13/2017
Last Date To Drop This Course:	01/13/2017
Last Date To Change Grading Option:	01/13/2017
Minimum Class Size:	1

Meeting Days and Times

Day	Start	End	Location	Description
T	12:15 pm	1:45 pm	CA Campus	Large Conference Room
T	3:15 pm	4:45 pm	FL Campus	A116
TH	12:15 pm	1:45 pm	CA Campus	Large Conference Room
TH	3:15 pm	4:45 pm	FL Campus	A116

Course Managers

Role	Last Name	First Name	Department	Mail Code	Phone	Email	Organization Name (non-TSRI personnel)
Course Director	McDonald	Patricia	Department of Molecular Therapeutics	2A2	(561) 228-2222	mcdonaph@scripps.edu	
Course Director	Duckett	Derek	Department of Molecular Therapeutics	2A2	(561) 228-2224	ducketdr@scripps.edu	
Admin	Clark	Pamela	Department of Molecular Therapeutics	2A2	(561) 228-2029	paclark@scripps.edu	
TA	Nieto Gutierrez	Ainhoa	Department of Molecular Therapeutics	2A1	(561) 228-2856	anieto@scripps.edu	
TA	Vaughan	Megan	TSRI Graduate Program	TPC-19	(858) 784-8469	mevaugha@scripps.edu	

Course Description

The course reviews the processes through which potential new therapeutics are identified. This includes the description of the roles played by a wide range of scientific disciplines, including biology, chemistry, in vitro/in vivo pharmacology, drug metabolism, pharmacokinetics, and ADME/Tox in the early drug discovery process. The complexity of ddiscovering drugs that may be a commercial success, or a public health success, involves a complex interaction between investors, industry, academia, patent laws, regulatory exclusivity, marketing and the need to balance secrecy with communication will be reviewed. A historical perspective is considered by reviewing classical pharmacology/phenotypic and drug discovery or the idea that the effect of a drug in the human body is mediated by specific interactions of the drug molecule with biological macromolecules. Landmark drugs will be discussed.

Concepts in pharmacology will be reviewed including:
• Forward Pharmacology /Target Base Drug Discovery (TDD),
• Reverse Pharmacology; agents that have a history of therapeutic activity are used as a starting point for drug discovery
• Dose Response Relationships

Modern drug discovery concepts will be reviewed including:
• Target ID
• Target Validation
• Assay Development
• Screening
• Hit to Lead (H2L)
• Lead Identification
• Lead Optimization
• Candidate Selection
• Pre-clinical
• Clinical

The multidisciplinary approach of drug discovery and development will be reviewed including the role of:
• Biologist
• Pharmacologist
• Medicinal Chemist
• DMPK
• ADME/Tox
• Safety Assessment

Screening and Design will be covered including:
• Natural Products
• Small molecule
• Biologics (antibodies/peptides)
• HTS
• Virtual screening

Background Preparation (Prerequisites)

Exposure to one or more of the following courses is helpful, but not required.
• Molecular and Cellular Biology Boot Camp
• Molecular Biology
• Cell Biology
• Basics of Chemistry
• Medicinal Chemistry
• Drugs of Today

Texts and Journal References

Type	Title	Author	Date	ISBN/ISSN
Required	Required reading will be generated by selecting current journal articles that exemplify the subject matter of each lecture			
Useful To Consult	A Pharmacology Primer, 4th Edition: Techniques for More Effective and Strategic Drug Discovery	Terry Kenakin	2014	978-0124076631

Course Learning Outcomes

By the end of this course, students will be able to:
1. Demonstrate knowledge of the process through which potential new therapeutics are identified
2. Demonstrate an understanding of landmark drug discoveries
3. Demonstrate an understanding of pharmacology concepts including: forward pharmacology or target base drug discovery; reverse pharmacology; and dose response relationships
4. Demonstrate knowledge of modern drug discovery techniques and methodologies
5. Demonstrate understanding of the complex multidisciplinary approach required to develop drugs
6. Understand and identify approaches to screening and design
7. Present advanced knowledge in order to demonstrate understanding of drug discovery and development

Course Requirements and Assignments

1. Midterm: Synoptic Case Study assessment, this takes the form of an essay that encompasses aspects of the taught elements of the course, and is based on identification of a novel drug target, evaluation of its biological significance and its possible role in pathophysiology of diseases.
2. Final Exam

Other Information

Expectations and Logistics

It takes over 10 years and $1billion to develop a new medicine. This course will explore the concepts behind the drug discovery process and will describe some of the key concepts involved in early stage drug discovery drawing on examples from current pharmaceuticals. The course will start with a brief historical overview of drug discovery, with early examples such as beta blockers. We will then explore the process of selecting a disease and a biological target. Discussion on how advances in biology have transformed our thinking about drug targets. There will then be a general consideration of the different classes of drug targets, with a particular focus on G protein coupled-receptors (GPCRs) and Kinases. We will also explore the different classes of drugs designed to interact with these drug targets and explain the mechanisms of their biological activity. We will discuss the properties required of a drug and show how chemists discover the starting points for drug development, highlighting the importance of protein biochemistry, structural biology and synthetic organic chemistry.
Modern drug discovery utilises a screening cascade consisting of a range of assays designed to probe whether a given compound meets different aspects of the drug profile. We will explore these different assays; the distinction between a research tool compound and a molecule that can be developed into a drug will be explained. This will introduce topics such as toxicity, metabolism, and clearance. One of the major ways to initiate a drug discovery project is to carry out a screen of small molecules against the drug target. This process often referred to as HTS, will be outlined. The strengths and weaknesses of this approach will be explored briefly. The concepts of chemical space and molecular diversity will be outlined. An interdisciplinary review of biophysical methods being used in modern drug discovery highlighting key experimental approaches including nuclear magnetic resonance (NMR) spectroscopy, X-ray crystallography, Mass spectrometry, as well as computer modeling, with emphasis on their applications to ligand- and structure-based drug design.
Behavioral pharmacology in drug discovery will be reviewed. This course will prepare students to understand the advantages, shortcomings and pitfalls of the use of live, behaving animals in drug discovery. The material covered will include an analysis of ethical issues in animal research.
There will then be an outline description of the later stages of the drug discovery process, Intellectual property, Regulatory bodies etc. What is involved in clinical trials? How long do they take?
The final lecture will explore the current challenges and changes to the drug discovery industry and make some predictions of how things are likely to develop in the coming years.

Attendance Statement

Students are expected to attend all classes. Students who are unable to attend class must seek permission for an excused absence from the course director or teaching assistant. Unapproved absences or late attendance for three or more classes may result in a lower grade or an “incomplete” for the course. If a student has to miss a class, he or she should arrange to get notes from a fellow student and is strongly encouraged to meet with the teaching assistant to obtain the missed material. Missed extra-credit quizzes will not be available for re-taking.

Scientific and Professional Ethics

The work you do in this course must be your own. Feel free to build on, react to, criticize, and analyze the ideas of others but, when you do, make it known whose ideas you are working with. You must explicitly acknowledge when your work builds on someone else's ideas, including ideas of classmates, professors, and authors you read. If you ever have questions about drawing the line between others' work and your own, ask the course professor who will give you clear guidance. Exams must be completed independently. Any collaboration on answers to exams, unless expressly permitted, may result in an automatic failing grade and possible expulsion from the Graduate Program.

Course Grading Statement

The midterm and final each constitute 25% of the final grade. 40% of the grade is presentations and 10% is participation

Letter Grade Descriptions

Letter Grade	Grade Point	Description	Learning Outcome
A	4.00	Outstanding achievement. Student performance demonstrates full command of the course subject matter and evinces a high level of originality and/or creativity that far surpasses course expectations.	
A-	3.67	Excellent achievement. Student performance demonstrates thorough knowledge of the course subject matter and exceeds course expectations by completing all requirements in a superior manner.	
B+	3.33	Very good work. Student performance demonstrates above-average comprehension of the course subject matter and exceeds course expectations on all tasks as defined in the course syllabus. There is notable insight and originality.	
B	3.00	Satisfactory work. Student performance meets designated course expectations and demonstrates understanding of the course subject matter at an acceptable level.	
B-	2.67	Marginal work. Student performance demonstrates incomplete understanding of course subject matter. There is limited perception and originality.	
C+	2.33	Unsatisfactory work. Student performance demonstrates incomplete and inadequate understanding of course subject matter. There is severely limited or no perception or originality. Course will not count toward degree.	
C	2.00	Unsatisfactory work. Student performance demonstrates incomplete and inadequate understanding of course subject matter. There is severely limited or no perception or originality. Course will not count toward degree.	
P	0.00	Satisfactory work. Student performance demonstrated complete and adequate understanding of course subject matter. Course will count toward degree.	
F	0.00	Unacceptable work/Failure. Student performance is unacceptably low level of knowledge and understanding of course subject matter. Course will not count toward degree. Student may continue in program only with permission of the Dean.	
I	0.00	Incomplete is assigned when work is of passing quality but is incomplete for a pre-approved reason. Once an incomplete grade is assigned, it remains on student's permanent record until a grade is awarded.	
W	0.00	Withdrew from the course with Dean's permission beyond the second week of the term.	

- All courses will be recorded and maintained in the student's permanent academic record; only courses that apply towards the degree will appear on the academic transcript. Non-credit or audited courses will not appear on the transcript.
- 4 core courses taken for a letter grade (pass = A or B for a core course)
- 2 elective courses taken pass/fail (pass = A, B, C for an elective)
- Because students are encouraged to take electives outside their area of expertise, a "C" letter grade is passing.
- Grading will be based on general attendance/participation, student presentations of the classic and contemporary publications, and

Course Schedule

Date	Type	Topic or Lecture Title	Presenter Last Name	Presenter First Name	Presenter Department	Presenter Mail	Presenter Phone	Presenter Email	Organization Name (non-TSRI personnel)
01/05/2017	Lecture	Historical Overview to Drug Discovery	Duckett	Derek	Department of Molecular Therapeutics	2A2	(561) 228-2224	ducketdr@scripps.edu	
01/10/2017	Lecture	Key concepts involved in Early Drug Discovery	McDonald	Patricia	Department of Molecular Therapeutics	2A2	(561) 228-2222	mcdonaph@scripps.edu	
01/12/2017	Lecture	Key Concepts in Pharmacology	Stahl	Edward	Department of Molecular Therapeutics	2A2	(561) 228-2432	estahl@scripps.edu	
01/17/2017	Lecture	Dose Response Relationships	Stahl	Edward	Department of Molecular Therapeutics	2A2	(561) 228-2432	estahl@scripps.edu	
01/26/2017	Lecture	Assay Development	Spicer	Timothy	Department of Molecular Therapeutics	1A1	(561) 228-2150	spicert@scripps.edu	
01/31/2017	Lecture	Compound Library and Screening Set Selection / LeadID / HTS	Scampavia	Louis	Department of Molecular Therapeutics	1A1	(561) 228-2101	scampl@scripps.edu	
02/02/2017	Lecture	Drug Design Principles Generally Applicable to all Medicinal Chemistry Programs	Bannister	Thomas	Department of Chemistry	3A1	(561) 228-2206	tbannist@scripps.edu	
02/07/2017	Lecture	Optimizing Physical Properties of Molecules to Achieve High Quality Clinical Candidates	Bannister	Thomas	Department of Chemistry	3A1	(561) 228-2206	tbannist@scripps.edu	
02/09/2017	Exam	Mid-Term							
02/14/2017	Lecture	Introduction to Drug Metabolism and Pharmacokinetics (DMPK) Part I	Cameron	Michael	Department of Molecular Therapeutics	2A2	(561) 228-2223	cameron@scripps.edu	
02/16/2017	Lecture	Evaluation of ADME/Tox Drug Properties in Drug Development	Cameron	Michael	Department of Molecular Therapeutics	2A2	(561) 228-2223	cameron@scripps.edu	
02/21/2017	Lecture	Biophysical Methods in DD	Kojetin	Douglas	Department of Molecular Therapeutics	2A2	(561) 228-2298	dkojetin@scripps.edu	
02/23/2017	Lecture	Target ID, Validation and Drug Discovery: GLP-1R a Case Study	McDonald	Patricia	Department of Molecular Therapeutics	2A2	(561) 228-2222	mcdonaph@scripps.edu	
02/28/2017	Lecture	Drug Discovery for Nuclear Hormone Receptors	Griffin	Patrick	Department of Molecular Therapeutics	2A2	(561) 228-2200	pgriffin@scripps.edu	

03/02/2017	Lecture	Animal Models of Disease States	McDonald	Patricia	Department of Molecular Therapeutics	2A2	(561) 228-2222	mcdonaph@scripps.edu	
03/07/2017	Lecture	IND Filing: Lab tests and documents	Shah	Rekha			561-972-7583	rstechsoln@gmail.com	Tech-Prob Solutions
			von Nehring	Gordon				Vonnehring@aol.com	R/S Tech-Prob Solutions
03/09/2017	Lecture	IND Filing: Regulatory requirements	Shah	Rekha			561-972-7583	rstechsoln@gmail.com	Tech-Prob Solutions
			von Nehring	Gordon				Vonnehring@aol.com	R/S Tech-Prob Solutions
03/14/2017	Lecture	Animal Models of Disease States	McDonald	Patricia	Department of Molecular Therapeutics	2A2	(561) 228-2222	mcdonaph@scripps.edu	
03/16/2017	Lecture	Disease Selection/Biological Target (Target ID/Target Validation) Specific Examples: Different Classes of Drugs designed to interact with receptors/kinases	Duckett	Derek	Department of Molecular Therapeutics	2A2	(561) 228-2224	ducketdr@scripps.edu	
03/21/2017	Lecture	Current Challenges in Drug Discovery Industry	McDonald	Patricia	Department of Molecular Therapeutics	2A2	(561) 228-2222	mcdonaph@scripps.edu	
03/23/2017	Exam	Final Exam							