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BMED 615.01: Molecular Pharmacology

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Molecular Pharmacology (BMED 615)

Spring 2022 (3 credits)
Tuesday/Wednesday/Thursday 2:00-2:50 pm
Location: Skaggs 174

Coordinator:	Travis Hughes	Office: SB 391	Phone: 406-243-2750
Instructors:	Kasper Hansen	Office: ISB 216	Phone: 406-243-4820
	Richard Bridges	Office:	Phone: 406-243-4972
	Dave Holley	Office: SB 482	Phone: 406-243-5194

Course Description: This course is an introduction to molecular pharmacology. In general, a theme or concept will be presented over three lecture/conference hours, one hour will involve lecture/discussion on the theme followed by one hour of discussing a paper or review directly relevant to this theme, and then hands on problem solving related to the theme. The topics covered are outlined in the course schedule below.

Course Goals: The goals of the course are to give students a basic understanding of 1) what types of drug targets that are typically explored using molecular pharmacology approaches 2) how drugs induce physiologically relevant effects that can be measured using pharmacological assays, and 3) conceptual models and assays that are used to quantify these effects.

Recommended Prerequisites: Advanced coursework in biochemistry and cell biology.

Recommended Textbooks:
A Pharmacology Primer, 5th Edition
Techniques for More Effective and Strategic Drug Discovery
Authors: Terry Kenakin
eBook ISBN: 9780128139585 Paperback ISBN: 9780128139578

Free: Chapter 3 of **Goodman and Gilman's Manual of Pharmacology and Therapeutics, 2e**
Randa Hilal-Dandan, Laurence L. Brunton
https://accesspharmacy.mhmedical.com/book.aspx?bookid=1810

These books will be supplemented with articles from the primary literature. Materials will be posted on Moodle. Moodle is our learning management system (LMS) prescribed by the University. Moodle is our conduit for posting course announcements, information, lecture notes, grades, etc. Moodle will also be used by the instructors for communicating with students through bulletins and email. ***All correspondence will be through your official UM email account, so be sure to check this account regularly***. Students should be familiar and competent with Moodle. There are Moodle tutorials etc. available on the UM Online web site https://moodle.umt.edu/ or contact IT for further assistance.

Course Evaluation:
Classroom attendance is mandatory. Students are responsible for all material covered in class. Assigned textbook readings are meant to assist the student in their comprehension of course materials.

1. The student's grade will be based on two examinations and class participation:
    a. The midterm examination (150 points) will consist of two separate evaluations: 1) An in-class exam (1 hour, 75 points) that includes questions related to general molecular pharmacology knowledge. 2) A take-home exam (1 week, 75 points) of problems to be solved and data to be analyzed.
    b. The final examination (100 points) will be one hour long and include general molecular pharmacology knowledge.
    c. The midterm and final examinations will be comprehensive, covering all the material presented in the course to that point.

d. Students will be evaluated based on class participation and in class questions (worth a total of 50 pts) according to the following criteria:
    i. Attendance is mandatory and repeated absence without valid reasons diminish class participation points.
    ii. Students will receive a positive evaluation for participation in classroom discussions and asking questions in class.
    iii. Students are expected to read the material provided by the instructor.
    iv. Student are expected to complete evaluations for all the professors who provide instruction.

Course grades will be determined as follows: A 90-100%, B+ 87-89%, B 83-86%, B- 80-82%, C+ 77-79%, C 73-76%, C- 70-72%, D 63-66%, D- 60-62%, <60% F.#

Exam Policies: No exams will be given early. Only under extraordinary circumstances will an exception from the exam schedule be permitted and then only with the approval of the course coordinator. Please contact Dr. Hughes to request an exception. When such an exception is approved, a makeup exam that may be in either written or oral format must be taken within one week of the original exam date. It is the responsibility of the student to ensure that a makeup exam is scheduled.

Cheating on exams may be grounds for expulsion from the program. Bathroom breaks will not be allowed during exams. Please do not ask. Use of cell phones or other electronic devices during exams is prohibited.

Students are allowed to appeal exam questions or grading to the course coordinator. Appeals must be written, attached to the original exam and submitted to the course coordinator within **one week** from the time the exam is returned.

Students with disabilities have the responsibility to contact the course coordinator at least three days before the exam to make accommodations.

Professionalism and Student Conduct:
All students must act professionally and practice academic honesty. Academic misconduct is subject to academic penalty by the course instructors and/or disciplinary sanction by the University.

Students with Disabilities:
Students with disabilities may request reasonable accommodations by contacting the course coordinator. The University of Montana assures equal access to instruction through collaboration between students with disabilities, instructors, and Disability Services for Students (DSS). “Reasonable” means the University permits no fundamental alterations of academic standards or retroactive modifications. For more information, please consult http://www.umt.edu/disability.

Student Evaluations: Students have the right to evaluate each professor’s instruction. Evaluations are conducted online using Moodle. Students should take the faculty evaluations seriously and be professional.

Course Schedule:

Week	*Date*	*Instructor*	*Literature*	*Topic*
1	1/18	Hansen	Goodman and Gilman Chapter 3	**Metabotropic and ionotropic membrane receptor targets**
	1/19			Paper: Berg & Clarke (2018). Int J Neuropsychopharmacol 21, 962-977.
	1/20			Workshop: Intro to GraphPad Prism for data analysis and modeling
2	1/25	Hughes		**Intracellular receptor targets (IP3, nuclear and sigma receptors)**
	1/26			Paper: A comprehensive map of molecular drug targets *Nature Reviews Drug Discovery* 2017 16:19-34 http://dx.doi.org/10.1038/nrd.2016.230
	1/27			Workshop: Using GraphPad Prism for data analysis and modeling part II
3	2/1	Bridges		**Enzyme and transporter targets**
	2/2			Paper: TBD
	2/3			Workshop: TBD
4	2/8	Hansen	Kenakin 2014 Chapters 1-3	**Drug-receptor theory I**
	2/9			Paper: Kenakin T (2016). Br J Clin Pharmacol 81, 41-51.
	2/10			Workshop: Quantification of agonist activity
5	2/15	Hansen	Kenakin 2014 Chapters 1-3	**Drug-receptor theory II**
	2/16			Paper: Auberson et al (2002). Bioorg Med Chem Lett 12, 1099-1102.
	2/17			Workshop: Quantification of antagonist activity
6	2/22	Bridges		**Drug actions at enzymes and transporters**
	2/23			Paper: TBD
	2/24			Workshop: TBD
7	3/1	Holley		**Computational modeling of molecular interactions**
	3/2			Paper: NA
	3/3			Workshop: NA
8	3/8	Hughes		**Molecular ligand-protein interactions**
	3/9			Paper: Wingler and Suomiviori co-published papers (Science)
	3/10			Workshop: Analysis of ligand-protein interactions using crystals and other structural data
9	3/15	**EXAM 1**		**Take home and in-class exam.**
	3/16			
	3/17			
10	3/22	**Spring Break**		
	3/23			
	3/24			
11	3/29	Hughes		**An atomistic and statistical mechanical view of binding**
	3/30			Paper: How Does a Drug Molecule Find Its Target Binding Site? and How and when does an anticancer drug leave its binding site?
	3/31			Workshop: TBD
12	4/5	Hughes		**Allosteric modulation I**
	4/6			Paper: Biochemistry 43, 16056–16066 (2004).
	4/7			Workshop: Determining the dissociation constant through direct measurement
13	4/12	Hughes		**Allosteric modulation II**
	4/13			Paper:
	4/14			Workshop: Calculating dissociation constant through tracer displacement
14	4/19	Hughes		**Biased agonism**
	4/20			Paper: Biased signaling: from simple switches to allosteric microprocessors Nature Reviews Drug Discovery 2018 17:243-260 http://dx.doi.org/10.1038/nrd.2017.229
	4/21			Workshop: Quantifying ligand bias
15	4/26	Hansen	Colquhoun (1998) Kenakin 2014 Chapter 4	**The binding-gating (or binding-effect) problem**
	4/27			Paper: Colquhoun (1998). Br J Pharmacol 125, 924-947.
	4/28			Workshop: Modeling of the binding-effect problem
16	5/3	Hansen	Christopoulos (1998)	**To log or not to log: How to report binding affinities or potencies**
	5/4			Paper: Christopoulos (1998). Trends Pharmacol Sci 19, 351-357.
	5/5			Workshop: Modeling of normal versus lognormal distributions
Finals week	TBD	**FINAL EXAM**		In-class exam (date to be decided)