



University of Wisconsin-Madison

Course Subject, Number and Title

Pharmacology, 781, Molecular and Cellular Principles in Pharmacology

Credits

4

Canvas Course URL

Course Designations and Attributes

General Education

Grad 50% - Counts toward 50% graduate coursework requirement

Tuesdays and Thursdays, 1:30 p.m. – 3:30 p.m., Room 7001B WIMR

Instructional Mode:

All face-to-face

Specify how Credit Hours are met by the Course

This class meets for a total of 4 class period hours [1:30-3:30 Tuesdays and Thursdays] each week over the spring semester and carries the expectation that students will work on course learning activities (reading, writing, problem sets, studying, etc) for about 4 hours out of classroom for every class period. The syllabus includes additional information about meeting times and expectations for student work.

INSTRUCTORS AND TEACHING ASSISTANTS

Instructor Title and Name

Anjon Audhya, Professor

Instructor Availability

By appointment – email Prof. Audhya to schedule a meeting.

Instructor Email/Preferred Contact

audhya@wisc.edu

OFFICIAL COURSE DESCRIPTION

Course Description

Provides an in-depth introduction to the molecular and cellular principles of pharmacology. Emphasis is on the mechanisms of drug and small molecule action in cells, with a particular focus on downstream signaling pathways, second messenger systems, protein kinase cascades, and the regulation of gene transcription.

Requisites

Graduate or professional standing

LEARNING OUTCOMES**Course Learning Outcomes**

Upon successful completion of this course, both undergraduates and graduate students should be able to:

1. Recognize the fundamental principles of drug actions at their target sites (e.g. receptors, enzymes, etc)
2. Understand the various mechanisms by which drugs can mediate their pharmacological effect
3. Describe how drugs mimic or modify physiological function, including the various actions and clinical uses
4. Describe the major classes of therapeutic drugs that affect the primary systems within the body
5. Choose a relevant experimental system to test experimental hypotheses (e.g. in vitro or in vivo; animal species, etc)
6. Design experiments which are properly controlled and which use appropriate statistical methods of data analysis

GRADING

1. Evaluation will be based on:

- 1) class participation (50%), including participation in the discussion of assigned literature each week (300 points possible)
- 2) 50% on producing a cogent NIH F31-style research proposal that focuses on the mechanism of drug action. The course director will read and provide a critique and assign a score out of 300 points. Instruction on writing the grant proposal will be provided during the first few weeks of the course. Additionally, each discussion session will be focused on providing students with an approach to understanding the mechanism of action of a particular drug or small molecule. Based on the methodologies presented, students should be able to assemble a grant proposal to study the mechanism of action of a drug of their choice. A final draft of the proposal will be due during week 15 of the course. The proposal will be graded based on: 1) background provided on the drug selected (literature review; 150 points) and 2) approaches described and whether they would enable a feasible assessment of the mechanism of drug action (150 points).

2. Since a large portion of the grade depends on class participation, evaluation will be conducted under the following guidelines (each instructor will provide a score for participation during each class):

- 300 points: This student was present for every class, always completes assigned readings, and comes to class prepared to think carefully, making connections between readings and across topics. He or she is willing to take the lead in discussion periodically, posing interesting questions or taking risks by answering tough questions. He or she avoids dominating discussion, instead participating mindfully in discussion with other students, considering their ideas and responding thoughtfully and respectfully. He or she helps to create a sense of a shared conversation in the group as a whole. This student shows passion for the work of the class and is committed fully to our work while in the classroom.
- 260 points: This student does most of what a 300 pt. student does, but may be slightly deficient in one area – for instance, he or she may be a conscientious reader and thinker

who tends not to listen to other students or otherwise dominates conversation instead of engaging in productive deliberation. Or, he or she may have been late to class a few times, or may have missed a reading or two which limited contributions to discussions on occasion.

220 points: This student participates often, but not consistently. He or she may attend every class and do all the readings but avoids taking the lead in discussion, instead only responding to questions or adding periodically to others' ideas. This student may participate well, but may have missed a class and failed to submit the makeup assignment.

180 points: This student may be a frequent but superficial discussion participant. The student may let shyness keep him or her from participating as fully as he or she should. At times the student may seem not to have done the readings, though he or she usually comes prepared.

140 points: This student is intermittently prepared for class (e.g., participates well but has missed two classes without submitting a makeup assignment). He or she may have flashes of brilliance, but rarely participates beyond the occasional superficial comment.

100 points: This student very rarely participates, and only in superficial ways.

<100 points: This student has missed three classes without submitting a makeup assignment and/or attends most classes but never participates.

***Each instructor will be provided a handout with pictures of all students in the class and whether they are undergraduate or graduate students. This will enable the instructors to keep track of student participation. Scores and brief comments regarding participation of each student will be submitted to the course director within 24 hours after the discussion session. The course director will convey scores/comments to each student, so they can learn their strengths and weakness. As is necessary, the course director will also include suggestions for improvement.

3. Letter grades of A, AB, B, BC, C, D and F will be assigned based on the cumulative points earned in the course (out of a maximum of 600 points each semester) – the grading scale is identical for undergraduate and graduate students. A: 100 - 90%, AB: 89 – 83%, B: 82 – 76%, BC: 75 – 69%, C: 68 – 62%, D: 61 – 55%, F: below 55%

Note: Based on the broad topics covered in this course, experts in each area have been recruited to teach. Although this entails bringing in a large number of lecturers to the course, the experience of each instructor is critical to clearly illustrate the mechanisms of drug action in the various areas of Pharmacology. The course director has discussed this issue with all instructors involved, and a similar format will be used for all meetings (50-60 minutes of lecture, followed by 50-60 minutes of discussion of relevant literature). Although teaching styles will vary, the importance of having experts lead each topic outweighs continuity of having only a few lecturers that lack expertise in one or more areas to be covered.

REQUIRED TEXTBOOK, SOFTWARE & OTHER COURSE MATERIALS

- There are no required textbooks or software. However, each instructor will assign readings from primary literature that are relevant to the topic to be discussed. For

examples, see representative list of readings below. All readings will be made available to students on-line (using a shared 'Box' folder). Presentations given by professors will also be shared via 'Box'.

Representative list of readings

Renault L, Guibert B, Cherfils J. 2003. Structural snapshots of the mechanism and inhibition of a guanine nucleotide exchange factor. *Nature*. 426(6966):525-530.

Vasquez RJ, Howell B, Yvon AM, Wadsworth P, Cassimeris L. 1997. Nanomolar concentrations of nocodazole alter microtubule dynamic instability in vivo and in vitro. *Mol Biol Cell*. 8(6):973–985.

Maximiano S, Magalhães P, Guerreiro MP, Morgado M. 2016. Trastuzumab in the Treatment of Breast Cancer. *BioDrugs*. 30(2):75-86.

EXAMS, QUIZZES, PAPERS & OTHER MAJOR GRADED WORK

- There are no quizzes, but a final NIH-style grant proposal must be submitted and evaluated. As described earlier, instructions on grant writing will be included as part of this course, and feedback will also be provided on preliminary drafts submitted by students.

HOMEWORK & OTHER ASSIGNMENTS

The major out of class homework will be reading primary literature assigned by each professor. Students must be prepared to discuss the manuscripts assigned in detail and participate extensively in classroom discussions.

OTHER COURSE INFORMATION

- None.

RULES, RIGHTS & RESPONSIBILITIES

- See the Guide's to [Rules, Rights and Responsibilities](#)

ACADEMIC INTEGRITY

By enrolling in this course, each student assumes the responsibilities of an active participant in UW-Madison's community of scholars in which everyone's academic work and behavior are held to the highest academic integrity standards. Academic misconduct compromises the integrity of the university. Cheating, fabrication, plagiarism, unauthorized collaboration, and helping others commit these acts are examples of academic misconduct, which can result in disciplinary action. This includes but is not limited to failure on the assignment/course, disciplinary probation, or suspension. Substantial or repeated cases of misconduct will be forwarded to the Office of Student Conduct & Community Standards for additional review. For more information, refer to studentconduct.wiscweb.wisc.edu/academic-integrity/.

ACCOMMODATIONS FOR STUDENTS WITH DISABILITIES

McBurney Disability Resource Center syllabus statement: The University of Wisconsin-Madison supports the right of all enrolled students to a full and equal educational opportunity. The Americans with Disabilities Act (ADA), Wisconsin State Statute (36.12), and UW-Madison policy (Faculty Document 1071) require that students with disabilities be reasonably accommodated in instruction and campus life. Reasonable accommodations for students with disabilities is a shared faculty and student responsibility. Students are expected to inform faculty [me] of their need for instructional accommodations by the end of the third week of the semester, or as soon as possible after a disability has been incurred or recognized. Faculty [I], will work either directly with the student [you] or in coordination with the McBurney Center to identify and provide reasonable instructional accommodations. Disability information, including instructional accommodations as part of a student's educational record, is confidential and protected under FERPA. <http://mcburney.wisc.edu/facstaffother/faculty/syllabus.php>

DIVERSITY & INCLUSION

Institutional statement on diversity: Diversity is a source of strength, creativity, and innovation for UW-Madison. We value the contributions of each person and respect the profound ways their identity, culture, background, experience, status, abilities, and opinion enrich the university community. We commit ourselves to the pursuit of excellence in teaching, research, outreach, and diversity as inextricably linked goals.

The University of Wisconsin-Madison fulfills its public mission by creating a welcoming and inclusive community for people from every background – people who as students, faculty, and staff serve Wisconsin and the world. <https://diversity.wisc.edu/>

MOLECULAR AND CELLULAR PRINCIPLES IN PHARMACOLOGY (Course #724-781)

Tuesdays and Thursdays –SPRING 2020

Time: 2 hours per class (1:30PM-3:30PM), Location: WIMR 7001B

WK	DATE/	TOPICS	INSTRUCTORS	SECTION
1	January 21	Pharmacology of β 3AR in brown adipose tissue Discussion (literature paper) Drugs: B3-adrenergic receptor agonists mirabegron and CL-316243 for weight loss	Simcox Simcox and students	Metabolic Pharmacology
1	January 23	Instruction on grant writing Discussion	Audhya Audhya and students	Miscellaneous Pharmacology
2	January 28	Pharmacology of the Immune System Discussion (literature paper) Drugs: Steroids, NSAIDs, anti-IL1, anti-TNF, and anti-IL6	Huttenlocher Huttenlocher and students	Neuro Pharmacology
2	January 30	Pharmacology of Neurotoxins Discussion (literature paper) Drugs: Botulinum neurotoxins A-G (and beyond), tetanus toxin	Chapman Chapman and students	Neuro Pharmacology
3	February 4	CSF1R inhibitors and the effects on microglia Discussion (literature paper) Drugs: Perxidartinib, BLZ-945	Collier Collier and students	Neuro Pharmacology
3	February 6	Pharmacology of Parkinson's Disease Discussion (literature paper) Drugs: L-dopa, Carbidopa, Entacapone, Selegiline, alpha-synuclein	Johnson Johnson and students	Neuro Pharmacology
4	February 11	PI3 Kinase in neurodevelopment and disorders Discussion (literature paper) Drugs: PI3 Kinase/AKT/MDM2 in neurodevelopment and disorders	Zhao Zhao and students	Neuro Pharmacology
4	February 13	Pharmacology of Pain and Reward Drugs: Opioids	Wenthur Wenthur and students	Neuro/Immuno Pharmacology
5	February 18	Mass Spectrometry in Neuropharmacology Discussion (literature paper) Mass spec technologies for low-level endogenous neuropeptide discovery, sequencing, quantitation and spatial distribution	Li Li and students	Neuro/Immuno Pharmacology
5	February 20	Pharmacology of Pluripotency Discussion (literature paper) Drugs/chemicals: Ascorbic Acid, MEK and GSK inhibitors, and DotI methyltransferase inhibitor	Sridharan Sridharan and students	Miscellaneous Pharmacology
6	February 25	Pharmacology of Cardiac Regeneration Discussion (literature paper) Drugs/Targets: Cell cycle activators, Hippo signaling inhibition	Mahmoud Mahmoud and students	Cardio Pharmacology
6	February 27	Pharmacology of Heart Development and Disease Discussion (literature paper) Drugs: Neuregulin1, Trastuzumab, and ErbB receptors in heart development and disease	Lee Lee and students	Cardio Pharmacology
7	March 3	Pharmacology of HCN Channels Drugs/chemicals: Ivabradin, other therapeutical applications and pathological significance	Glukhov Glukhov and students	Cardio Pharmacology
7	March 5	Pharmacology of Cardiovascular Disease Discussion (literature paper) Drugs: β-adrenergic – propranolol, metoprolol, albuterol	Kamp Kamp and students	Cardio Pharmacology

8	March 10	Pharmacological Control of Hematopoiesis Discussion (literature paper) Drugs/targets: c-Kit, Flt3, Bcl2, GATA-2	Bresnick Bresnick and students	Cardio Pharmacology
8	March 12	Anti-mitotic agents in Cancer Pharmacology Discussion (literature paper) Drugs: Taxanes, vinca alkaloids	Weaver Weaver and students	Cancer Pharmacology
2020 SPRING BREAK				
9	March 24	Pharmacology of Ubiquitin Ligase and Targeted Protein Degradation Discussion (literature paper) Drugs: Thalidomide, dBET1	Tang Tang and students	Cancer Pharmacology
9	March 26	Pharmacology of Diabetes Discussion (literature paper) Drugs: Recombinant insulin(s), sulfonylureas, and stable GLP-1 analogs/DPP4 inhibitors	Kimple Kimple and students	Metabolic Pharmacology
10	March 31st	Pharmacology of Epigenetics Discussion (literature paper) Drugs: DNMT inhibitors (Azacytidine) and histone deacetylase inhibitors	Svaren Svaren and students	Cancer Pharmacology
10	April 2	Jon will work with the students on finalizing grant proposals	Workshop	Miscellaneous Pharmacology
11	April 7	Precision medicine in Cancer Therapy Discussion (literature paper) Drugs: Trastuzumab, crizotinib, and PARPi	Burkard Burkard and students	Cancer Pharmacology
11	April 9	Mass Spectrometry in Pharmacology – Discussion (literature paper) Mass Spec for characterization of antibody-drug conjugates	Ge Ge and students	Miscellaneous Pharmacology
12	April 14	Pharmacology of Aging Discussion (literature paper) Drugs: Rapamycin, Metformin, Resveratrol, Farnesyltransferase inhibitors (treatment for Progeria), Senolytics like navitoclax or Hsp90 inhibitors	Moore Moore and students	Miscellaneous Pharmacology
12	April 16	Pharmacology of NF-kappaB signaling Discussion (literature paper) Drugs: Proteasome inhibitors - Bortezomib, ixazomib, carfilzomib	Miyamoto Miyamoto and students	Miscellaneous Pharmacology
13	April 21	Pharmacology of HIV and other viruses Discussion (literature paper) Drugs: antiviral nucleoside analogs (acyclovir, AZT), HIV protease and integrase inhibitors, flu antivirals (adamantadine, oseltamivir/Tamiflu), HCV antiviral cure drugs (ribavirin, telaprevir, interferon)	Sherer Sherer and students	Miscellaneous Pharmacology
13	April 23	Pharmacology of Natural Products Discussion (literature paper) Using chemical genomics to understand the mechanism of action of natural products	Bugni Bugni and students	Miscellaneous Pharmacology
14	April 28	Pharmacology of DNA Repair and Chemosensitization Discussion (literature paper) Drugs: cyclophosphamide, methotrexate, cisplatin, doxorubicin, and etoposide	Tibbetts Tibbetts and students	Miscellaneous Pharmacology
14	April 30	Pharmacology of sex steroid hormones in brain development, function, and disease Discussion (literature paper) Drugs: sex steroid hormones in brain development, function, and disease	Werling Werling and Students	Miscellaneous Pharmacology
May 6 FINAL RESEARCH PROPOSAL DUE				