

BIOL/BCHM 495 Biological & Structural Aspects of Drug Design and Action

Spring, 2016
MWF 9:30 to 10:20 am
Biochemistry Building Room 105

Course Coordinator

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Office Hours:
MW: 7:30am - 9:00am
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TBD
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Course Description

This course will provide a general overview of the modern day drug discovery pipeline process and an in-depth look at the basic biology, structure, and mechanisms-of-action behind currently marketed therapeutics. The course will start with a historical account of the discovery of natural product drugs such as aspirin and penicillin and will then venture into the modern day era of the drug discovery pipeline with an emphasis on the general principles of target selection, assay development, high-throughput screening and structure-based drug design. We will explore different classes of antibiotics, antiviral, and anti-cancer drugs and their interactions with molecular targets. The majority of the course will be on small molecule drugs with some examples of modern biologics-based drugs near the end of the semester. Students will learn the fundamental properties of protein structure, enzyme kinetics and mechanisms, and will then learn how to apply these principles to drug interactions and design.

Prerequisites

BIOL 23100 or 23000 and CHM 25600 or 26605 or MCMP 20500. **Note:** A course in Biochemistry such as BCHM 36100, 46200 or CHM 53300, and/or a course in Structural Biology such as BIOL 39500 (Macromolecules), BIOL 44207 or BCHM 46300 is helpful but not required.

Course Goals

From the biological/pharmacological aspects* of drug action, students should be able to:

1. discuss the site and mechanism-of-action of a drug
2. discuss the relationship between the pharmacologic mechanism and the therapeutic use of a drug
3. discuss the scientific basis for the therapeutic use of a drug

From the chemical/structural aspects* of drug action, students should be able to:

1. predict, verbally or in writing, the biological response, if any, from a given chemical structure
2. discuss the relationship between the structural features of a compound and the physicochemical properties that might influence biological response or the design of new agents
3. predict, verbally or in writing, the biochemical mechanism-of-action of a biologically active substrate or compound from its chemical structure
4. discuss the relationship between the chemical structure of a biologically active compound and the receptor or active binding site, using enzyme or receptor models
5. predict, verbally or in writing, the biological response resulting from the chemical alteration or biochemical pathways
6. discuss the relationship between *in vitro* reaction mechanisms and the structural features that alter the *in vivo* biotransformation of a drug

From the therapeutic aspects* of drug action, students should be able to:

1. describe the pathophysiologic processes associated with a particular disease state, and how they might be affected by drug therapy

*NOTE: structures, compounds, drugs, & disease state therapeutics refer to those discussed within this course or as part of a homework assignment or course project.

Required Texts

For the Spring 2016 semester, there are no required textbooks to purchase. Every attempt will be made to provide students with reading material electronically, in print form, or on reserve in a library.

Lecture Notes and Other Paper Handouts

Due to the tuition freezes at Purdue and the necessary budget cuts to implement these freezes, the Departments have put a ban on distribution of any printed material with the exception of the Course Syllabus, Quizzes and Exams. Students are responsible for bringing notes (printed or electronic) to class for annotation during lecture. Lecture notes and material will be uploaded to Black Board ~1 day prior to the lecture.

General Course Policies

1. Students are required to attend class and actively participate in each scheduled lecture, group activity, quiz or examination at the time specified.
2. The Course Instructor and Teaching Assistant(s) will inform you of their office hours. Questions concerning lecture content should be discussed directly with the given lecturer during classroom time or at a mutually agreed upon time. All other questions, including any questions concerning grading, should be discussed with the Course Instructor.
3. All examinations and quizzes are closed notes, closed book and closed smart phone. For quizzes and exams that require calculations, a standard scientific calculator that is unable to connect to the internet (no WiFi, no 3G or 4G connections etc) are to be used.
4. All requests for corrections to an exam, quiz, homework or project score should be made to the Course Instructor within **5 class days** after your exam, quiz, homework or project score has been returned to you. You will have 5 class days after the start of the summer term for requests for corrections in the final examination score. It is your responsibility to notify the course instructor of any grading error. No correction of any error in addition or subtraction will be made after the final grade has been submitted.
5. **Make-up examinations will be given only for an excused absence.** Any student who misses an exam must notify the Office of the Dean of Students of his/her absence prior to the scheduled examination to obtain an excused absence from the instructor/course coordinator. Failure to comply with this policy will result in a score of a zero for the missed examination. **The course instructor will set the day and time of the make-up examination.**
6. **Make-up Quizzes, Homework or Team Projects.** You will not be allowed to make-up quizzes or homework assignments if you miss them or fail to hand them in at the specified or scheduled class date and time. If you are unable to attend class to hand in a homework assignment, you must arrange to have the homework assignment delivered to the Course Instructor or Teaching assistant **before** the scheduled due date and time. One lowest, or missing, quiz or homework score will be dropped from the final calculation of each student's final grade. Make-up times, dates, etc on Team Projects will not be allowed. Missed presentations or late submission of written proposals or projects will receive a grade of zero.
7. **Academic Dishonesty**, as defined in the Purdue University "Academic Integrity: A Guide for Students" <https://www.purdue.edu/odos/academic-integrity/> will not be tolerated. Students caught cheating will, at a minimum, receive a zero or letter grade of F for the assignment. The student may also receive a grade of an F for the course. Additionally, the circumstances surrounding the event will be reported to appropriate administrative officials for further action https://www.purdue.edu/odos/osrr/resources/documents/responding_to_academic_dishonesty.html
8. The course instructor reserves the right to make alterations in the course schedule at any time for new course material, snow days etc.

Policy on Student Conduct

Purdue University has a formal description of the “Purdue University Student Conduct Code” that can be found on the Office of the Dean of Students website in the section of Office of Student Rights and Responsibilities.

Students are responsible for observing the policies, rules, and regulations of Purdue University. These, in general, state the expectation that Purdue students will at all time conduct themselves as responsible citizens. Failure to show respect for duly established laws or University regulations will be handled by the Office of Student Rights and Responsibilities in conformance with the various policies and regulations.

Additional details can be found at the website which is:

http://www.purdue.edu/studentregulations/student_conduct/regulations.html

Students in Biological & Structural Aspects of Drug Design and Action are expected to behave in a civil fashion toward instructors, staff, and their fellow students. Sometimes we fail to realize that our behavior disrupts or offends others. It is important to be sensitive to the goals and feelings of your instructors and classmates.

Please attend to the business of the class while in the classroom. It is rude to talk with a friend, read a newspaper, or engage in non-class activities during class. Help to build a good classroom environment by being a supportive listener and making relevant contributions to the topics being discussed. Please make every attempt to arrive in the classroom and be prepared for lecture and/or recitation at the proper time. Walking in after the bell has sounded and the lecture and/or recitation have begun disrupts the other students and the faculty. Please be courteous at all times.

Policy on Diversity and Nondiscrimination

In accordance to Purdue’s [Nondiscrimination Policy Statement](#), BIOL/BCHM 495 Students, Teaching Assistants and Instructors will be committed “*to maintaining a community which recognizes and values the inherent worth and dignity of every person; fosters tolerance, sensitivity, understanding, and mutual respect among its members; and encourages each individual to strive to reach his or her own potential*”. In addition, in pursuit of our goal of academic excellence in BIOL/BCHM495, Students, Teaching Assistants and Instructors will seek to develop and nurture diversity. Purdue University believes that diversity among its many members strengthens the institution, stimulates creativity, promotes the exchange of ideas, and enriches campus life and BIOL/BCHM495 will be a reflection of those values. For more information, please see http://www.purdue.edu/purdue/ea_eou_statement.html.

Purdue University prohibits discrimination against any member of the University community on the basis of race, religion, color, sex, age, national origin or ancestry, genetic information, marital status, parental status, sexual orientation, gender identity and expression, disability, or status as a veteran. The University will conduct its programs, services and activities consistent with applicable federal, state and local laws, regulations and orders and in conformance with the procedures and limitations as set forth in Purdue’s Equal Opportunity,

Equal Access and Affirmative Action policy which provides specific contractual rights and remedies. Additionally, the University promotes the full realization of equal employment opportunity for women, minorities, persons with disabilities and veterans through its affirmative action program.

Anti-Harassment Policy -- Strictly following and interpreting existing University Policy: *Purdue University is committed to maintaining an environment that recognizes the inherent worth and dignity of every person; fosters tolerance, sensitivity, understanding and mutual respect; and encourages its members to strive to reach their potential. The most effective way to work toward preventing Harassment is through education that emphasizes respect for every individual.*

Students with Disabilities

Purdue University is required to respond to the needs of the students with disabilities as outlined in both the Rehabilitation Act of 1973 and the Americans with Disabilities Act of 1990 through the provision of auxiliary aids and services that allow a student with a disability to fully access and participate in the programs, services, and activities at Purdue University.

If you have a disability that requires special academic accommodation, please make an appointment to speak with me within the first three (3) weeks of the semester in order to discuss any adjustments. It is important that we talk about this at the beginning of the semester. It is the student's responsibility to notify the Disability Resource Center <http://www.purdue.edu/studentsuccess/specialized/drc/> of an impairment/condition that may require accommodations and/or classroom modifications.

Students with disabilities can find more information on available resources at the Disability Resource Center (DRC) website.

Policy on Class Attendance

BIOL/BCHM 495 will follow the guidelines on attendance provided by Purdue University; <http://www.purdue.edu/advocacy/students/absences.html>. Students are expected to be present for every meeting of the class. **Only the Course Instructor can excuse a student from classes or course responsibilities.** In the event of an illness, accident, or emergency, when circumstances permit, students should make direct contact with the Course Instructor, preferably before a class or an exam takes place. If the instructor cannot be reached in person or by telephone, the student should leave a message in the instructor's department mailbox or with the instructor's administrative assistant.

When a student is unable to make direct contact with the instructor and is unable to leave word with the instructor's department because of circumstances beyond the student's control, the student or the student's representative should contact the Office of the Dean of Students if the reported absence is expected to be for an extended period of time (normally **more than five days**). A member of the Dean of Students staff will notify the student's instructor(s) of the circumstances. Only the instructor may excuse class absences. The student should be aware that this intervention does not change, in any way, the outcome of the instructor's decision regarding the student's academic work and performance in any given course. The student must make personal contact with the instructor(s) as soon as it is

possible to do so. The student may discuss the circumstances of the absence with a member of the Office of the Dean of Students for advice on how to proceed.

If a student will be absent for **more than five days**, has not been able to reach the instructor in person or by telephone, or through leaving notification of the student's circumstances with the instructor's secretary, the student or the student's representative should notify the Office of the Dean of Students, at **765-494-1747** as soon as possible after becoming aware that the absence is necessary. Be advised, the student, or the student's representative may be asked by the instructor(s) to provide documentation from an authorized professional or agency which supports an explanation for the student's absence.

As an incentive, students who attend ~90% of the lectures will be invited to Professor Mesecar's house for an end of the semester party. This party will likely take place the weekend before finals, usually Sunday evening. Daily attendance sheets will be distributed at each lecture.

Arrive to Class On-Time

You are expected to arrive to class on time. Exams will start promptly at 9:30 am and quizzes are often given right at 9:30 am also. You will NOT be given any extra time if you are late. No exceptions. Homework is often collected at the beginning of class also. If you are not there to turn in your homework when collected it will be considered late and will not be counted. It is not my problem that another professor goes over time with his/her lecture before BIOL/BCHM 495, if you are slow walking to class because you have to talk to someone on a cell phone between classes, or if parking is inconvenient. You need to find a way. If you have a documented handicap or have sustained a temporary injury (ruptured Achilles-happened to me one year, broken leg etc) that is documented by a health care professional then appropriate accommodations will be made.

For the past 5 years, there has been a direct correlation between the number of lectures missed by a student and their point total (and final grade) for the semester. That is, the more you miss you class, the more points you tend to miss on quizzes and exams. This trend has been consistent each of the past 4 years I have taught this class. I expect this 5th year to be no different.

Policy on Taping or Recording of Lectures in BIOL/BCHM495:

In general, you are not allowed to record any of the lectures via any electronic format (voice or video recorders, cell phones etc. The lectures will be recorded for you by the Course Instructor and edited if necessary. These recordings will be posted on Blackboard within 1 week of the lecture. However, if necessary, the procedure for taping/recording lectures in BIOL/BCHM 495 is as follows:

A student can only record a class for personal use if they do all of the following:

1. Obtain written consent (see Consent Form below) of the faculty member lecturing BEFORE the student tapes the lecture (this protects the student from having somebody say later that they didn't give permission); the consent needs to be signed by the student and indicate that it is only for personal use and it won't be posted on the internet; a copy of the form should be kept by the student and given to the faculty member.
2. Use the recorded material solely for their own use; lecture cannot be duplicated and given to other class members.
3. Recorded material cannot be posted on the internet or disseminated in any way.

BIOL/BCHM 495 LECTURE RECORDING CONSENT FORM

I _____ permit _____
 (PRINT LECTURER'S NAME) (PRINT STUDENT'S NAME)

to record lecture material from BIOL/BCHM 495.

I understand that:

§ recordings will be used solely for personal note-taking purposes without being duplicated and/or distributed to other individuals;

§ recordings will not be posted on the internet or unlawfully distributed in any other public forum.

Lecturer's signature _____ Date _____

Student's signature _____ Date _____

Policy on Distribution of Course Material in BIOL/BCHM495:

You are not allowed to distribute any course material given to you in class, out of class, or via email or Blackboard etc. to any other entity.

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BIOL/BCHM 495 COURSE MATERIAL DISTRIBUTION AGREEMENT

I, _____ fully understand that I am NOT to:
(PRINT STUDENT'S NAME)

distribute, post, upload to the internet, or email any of the course material provided to me by my instructor in class, out of class, via email or BlackBoard. I understand that this material is provided to me for use in BIOL/BCHM 495 and that it is not to be made publically available unless I obtain written permission by my course instructor, Professor Andrew Mesecar, and Purdue University. I understand that all material provided to me is property of Purdue University and that it is subject to certain Copyright laws.

Student's signature _____ Date _____

Grading

Tentative Plan Course Point Distribution:

First 1-Hour Examination: Covers X lectures @ 10 to 15 pts each	~130
Second 1-Hour Examination: Covers Y lectures @ 10 to 15 pts each	~140
Third 1-Hour Exam: Covers Z lectures @ 10 to 15 pts each	~130
Final Examination Cumulative (<i>may be optional- will depend on course performance</i>)	200
Announced and Pop Quizzes: 3 to 5 @ 10 to 15 pts each = 30 to 90 pts	30 to 90 pts
Homework 3 to 5 @ 10 to 15 pts each = 30 to 75 pts	30 to 75 pts
Student Team Projects and Presentations: Written Proposal (50), Presentation (100), Team Member Evaluation (25) Peer-Evaluation (25)	200
Lowest Quiz or Homework Score Dropped	-10 or -15
Total Points for this Course:	850 - 950

Examinations:

There will be at least three (3) examinations and one (1) two-hour cumulative final examination. Regular exams will be given during our scheduled class hour. This gives us flexibility in scheduling the day of the exam and it eliminates evening scheduling conflicts. Therefore, all students will be able to take the examinations without excuses.

Type of Examination Questions:

In general, problem-solving questions requiring short, concise answers that may involve chemical structures, models for drug-receptor/enzyme interactions and therapeutic applications will be given. In addition, matching and/or multiple-choice questions will also be used. In general, about 10 to 15 points will be assigned per lecture to arrive at the amount of points assigned to each exam.

Quizzes (Scheduled and Pop):

We will have a few scheduled or unscheduled "Pop" quizzes throughout the semester. The final number is not set at this point and will depend on class progress.

Homework

We will have at least 3 homework problem sets during the semester, but more may be given depending on the academic needs of students.

Team Proposal Project

We are going to have a team project where each team of 3 to 4 students will select a potential drug target and then “sell” their idea to develop this target to a scientific board of a fictitious pharmaceutical company. The enzyme or receptor target will not yet have a marketed therapeutic developed, but will have enough BIOL/BCHMogy and lead discovery performed to enable its further development. It will be the goal of each project team to convince the company that their target is the best one to move forward in the development pipeline. Only 1 or 2 of these targets, depending on the class size, will be selected to move forward. A written proposal and presentation will be required. Individual team member assessments will be performed by each team member, and presentations will be peer-reviewed. More details will follow.

Grading System:

A minimum of 60% of the total points is required to guarantee that you will receive a passing grade of a D. All students achieving 90% or above of the total points will receive an A for the course. Grades of B and C will be assigned by the instructor/course coordinator for students receiving above 80% and 70% respectively. Plus (+) and minus (-) may also be assigned to grades based on final percentages. The final cut-off for each grade will be determined based on the overall performance of the class.

Academic Dishonesty

Academic Dishonesty will not be tolerated. BIOL/BCHM495 will adopt and abide by the rules and policies of Purdue University for Academic Dishonesty

Purdue prohibits "dishonesty in connection with any University activity. Cheating, plagiarism, or knowingly furnishing false information to the University are examples of dishonesty." [Part 5, Section III-B-2-a, University Regulations] Furthermore, the University Senate has stipulated that "the commitment of acts of cheating, lying, and deceit in any of their diverse forms (such as the use of substitutes for taking examinations, the use of illegal cribs, plagiarism, and copying during examinations) is dishonest and must not be tolerated. Moreover, knowingly to aid and abet, directly or indirectly, other parties in committing dishonest acts is in itself dishonest." [University Senate Document 72-18, December 15, 1972]

Please read a “Guide for Students” on Academic Integrity which can be found at the following website

http://www.purdue.edu/cie/teachingtips/academic_integrity/index.html.

Plagiarism

There are few intellectual offenses more serious than plagiarism in academic and professional contexts. The Purdue Online Writing Lab (OWL) resource offers advice on how to avoid plagiarism in your work. See

<https://owl.english.purdue.edu/owl/resource/589/02/>.

The iThenticate Plagiarism Detection Software resource <http://www.ithenticate.com/> and SafeAssign function in Blackboard will be used for plagiarism detection.

Emergencies

In the event of a major campus emergency, course requirements, deadlines and grading percentages are subject to changes that may be necessitated by a revised semester calendar or other circumstances beyond the instructor's control. Relevant changes to this course will be posted onto the course website or can be obtained by contacting the instructors or TAs via email or phone. You are expected to read your @purdue.edu email on a frequent basis.

Active Shooter(s) and Shelter in Place

Purdue University has issued guidelines for Active Shooters. See the following site; https://www.purdue.edu/epps/emergency_preparedness/flipchart/activeshooter.html
Our BCHM 105 classroom is capable of being locked. Please familiarize yourselves with how to lock the door.

Purdue Emergency Notification

I encourage all of my students to subscribe to our emergency notification service. Please go to the following website and subscribe.
http://www.purdue.edu/newsroom/health_safety/mail.html

I do allow my students to keep their cell phones on vibrate during class so they can get these messages.

Academic Calendar - Spring Semester 2016

<https://www.purdue.edu/registrar/calendars/currentAcademic.html>

January

Monday	11	CLASSES BEGIN
Monday	18	Martin Luther King Jr. Day (No Classes)
Tuesday	19	Last day for registration without a late fee
Monday	25	Last day to cancel a course assignment without it appearing on record

February

Monday	8	<i>Last day to withdraw a course with a grade of W or to add/modify a course with instructor and advisor signature</i>
Monday	22	Last day for grade correction for Fall 2015 semester.

March

Monday	7	Second Eight-Week Courses Begin
Monday	11	<i>Last day to Withdraw from a Course with a W or WF grade</i>
Monday	11	Last day to Add/Modify a course with Instructor, Advisor and Department Head signature.
Mon.-Sat.	14-19	SPRING VACATION

April

Saturday	30	CLASSES END
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May

Mon-Sat	2-7	FINAL EXAMS
Saturday	7	SEMESTER ENDS
Saturday	7	Deadline for pending incomplete grades to become failing grades
Tuesday	10	Grades Due
Friday	13	Commencement (1 st Division)
Saturday	14	Commencement (2 nd Division)
		Commencement (3 rd Division)
Sunday	15	Commencement (4 th Division)
		Commencement (5 th Division)

BIOL/BCHM 495 Tentative Class Schedule (Weeks 1 thru 4)

Wk	Lecture	Day	Date	Topic
1	1	Mon	Jan 11	Brief Overview of Syllabus and Course History and Overview of Drug Discovery
	2	Wed	Jan 13	History and Overview of Drug Discovery
	3	Fri	Jan 15	History and Overview of Drug Discovery
2	MLK	Mon	Jan 18	Martin Luther King Holiday (no class)
	4	Wed	Jan 20	History and Overview of Drug Discovery
	5	Fri	Jan 22	Protein Structure – Structure of Water, Amino Acid Side Chain Properties, Bonding Forces
3	6	Mon	Jan 25	Protein Structure & Molecular Interactions - Basic Forces and Bonding, pKa's and acid-base chemistry.
	7	Wed	Jan 27	Protein Structure – Peptide Bonds and Primary Structure, Secondary Structures & Motifs
	8	Fri	Jan 29	Protein Structure – Tertiary & Quaternary Structures
4	9	Mon	Feb 1	Forces that stabilize Proteins and Their Interactions with Drug Molecules Introduction to Antibiotics Principles and Biology of Antibiotic Target Selection
	10	Wed	Feb 3	Antibiotics - Penicillins
	11	Fri	Feb 5	Antibiotics – Penicillins Beta-Lactamase mechanism and Inhibitors

BIOL/BCHM 495 Tentative Class Schedule (Weeks 5 thru 8)

Wk	Lecture	Day	Date	Topic
5	12	Mon	Feb 8	Enzymes Kinetics – zero and first order reactions Single Substrate Reactions Michelis-Menten Equation Briggs-Haldane Equation Meaning of Km and Vmax (Last day to withdraw from a course without a grade, to add a course, or change to pass/not-pass option)
EXAM 1		Wed	Feb 10	Covers Material to Lecture 11
	13	Fri	Feb 12	Meaning of Vmax/Km and relation to MIC of antibiotics Bi-substrate Reactions (Sequential and Ping-Pong)
6	14	Mon	Feb 15	Inhibitor Interactions with Enzymes Competitive, non-competitive, uncompetitive Meaning of Ki values Meaning of IC50 Values
	15	Wed	Feb 17	Chemical Modification of Enzymes by Covalent Inhibitors
	16	Fri	Feb 19	Antibiotics – Beta Lactamases and their Mechanisms of Inhibition and Resistance
7	17	Mon	Feb 22	Antibiotics – Sulfonamide Drugs and Their Targets
	18	Wed	Feb 24	Antibiotics – Susceptibility Testing and Trimethoprim
	19	Fri	Feb 26	Antibiotics – Targeting the Ribosome
8	20	Mon	Feb 29	Antibiotics – Targeting DNA Gyrase
		Wed	Mar 2	Antivirals - The Flu Virus and Neuraminidase
	21	Fri	Mar 4	Antivirals -Neuraminidase Mechanism and Inhibitors Give Team Assignments

BIOL/BCHM 495 Tentative Class Schedule (Weeks 9 thru 12)

Wk	Lecture	Day	Date	Topic
9	22	Mon	Mar 7	Antivirals - HIV and HIV Protease
	23	Wed	Mar 9	Antivirals- HIV Protease Mechanism and Inhibitors
	24	Fri	Mar 11	Antivirals- Finish HIV Protease (Last day to withdraw from a course with a passing W or failing WF grade)
10				Spring Break March 14 – March 19
11	25	Mon	Mar 21	Team Exercise – PharmaX Project Overview, Team Formation and General Discussion.
	EXAM 2	Wed	Mar 23	Covers Material to Lecture 24
	26	Fri	Mar 25	Antivirals - SARS Virus and SARS Proteases
12	27	Mon	Mar 28	Antivirals - SARS Virus and SARS Papain-like Protease Inhibitors Team Drug Target Choices Due
	28	Wed	Mar 30	Anticancer Drugs- Overview of Cancer as a disease and the three stages of carcinogenesis and metastasis
	29	Fri	Apr 1	Anticancer Drugs - Thymidylate Synthetase mechanism and design of anti-cancer drugs

BIOL/BCHM 495 Tentative Class Schedule (Weeks 12 thru 16)

Wk		Day	Date	Topic
13	30	Mon	Apr 4	Anticancer Drugs - Dihydrofolate Reductase mechanism and inhibition by methotrexate
	31	Wed	Apr 6	Anticancer Drugs - Topoisomerase Inhibitors
	32	Fri	Apr 8	Anticancer Drugs -Protein Kinases in Cancer Mechanism of Gleevec and BCR-ABL
14	33	Mon	Apr 11	Anti-inflammatory Drugs Inflammation, Rheumatoid Arthritis and DMARDS
	34	Wed	Apr 13	Anti-inflammatory Drugs Mechanism of Cox1 and Cox 2 and Non-Steroidal Anti-inflammatory Drugs (NSAIDS)
	35	Fri	Apr 15	Anti-inflammatory Drugs Biological Drugs – Humira, Embrel, Orencia etc.
15	36	Mon	Apr 18	Anti-inflammatory Drugs Biological Drugs - Continued
	37	Wed	Apr 20	TBD, Student Team Presentations, or Exam 3
	EXAM 3	Fri	Apr 22	Covers Material to Lecture 36 or 37
16		Mon	Apr 25	Student Team Presentations A & B Team PowerPoint Presentations Due (Jump Drives for ALL groups due by 9:00 am to Prof. Mesecar)
		Wed	Apr 27	Student Team Presentations C & D Team Project Written Reports Due Team Member Evaluations Due (by Noon to Professor Mesecar)
		Fri	Apr 29	Student Team Presentations Results and Final Discussion
16		Fri	May 2-7	Final Exam Week
17		Fri-Sun	May 13-16	Commencements

This syllabus is subject to change at anytime. Should changes be made, all students will be contacted in-class and/or through the course website.

BIOL/BCHM 495
Biological & Structural Aspects of Drug Design and Action
Spring 2016

PharmaX Team Project Proposal (Draft)

PharmaX is a large pharmaceutical company that has average annual gross sales of \$10 billion dollars. One of its major drugs, *Lipimin*®, which had a total annual sale of \$7 billion in 2012, is going off patent next year, 2014. Currently, there are no new drug molecules in the pipeline of *PharmaX* that will be approved by the FDA in time to replace their current leading drug that is set to expire. It is estimated that the generic version of *Lipimin*®, will capture a market share of \$3 billion in the first year of sales thereby reducing *PharmaX*'s total annual sales by approximately 30%. Fortunately, *PharmaX* does have a rich set of drug development projects ongoing in its portfolio that could produce a new drug within 2 years after the patent expires. In an effort to accelerate the development of a new drug from the project portfolio of *PharmaX*, the scientific advisory board and board of directors has decided to focus resources on only 1 of its 4 ongoing projects. To decide on which project to move forward in an accelerated product development pipeline, the scientific board has asked each of the 4 project teams to draft a 10 to 15 page project proposal/description that describes the merits of their project and why they should receive continued but elevated funding for drug development. They have also asked each project team to give a 20 minute presentation on the scientific merits and the potential impact of their project to *PharmaX*'s bottom line. From these presentations and written proposals, the scientific advisory board will make a recommendation to the board of directors as to which project(s) to invest in by providing additional resources to those projects. The unsuccessful project teams will be terminated to help capture a portion of the anticipated revenue loss 30% or \$3 billion per year.

Guidelines for Target Selection

1. Each project team needs to choose a disease area of focus, e.g anti-infectives, anticancer, anti-inflammatory, cardiovascular, neurological etc.
2. Each project team needs to choose a specific target enzyme or receptor to develop. This enzyme or receptor target MUST have an X-ray or NMR structure available (PDB file must be available) and there can be NO marketed (FDA Approved) therapeutic for this target. It is ok, however, if there are small molecule drugs in *Phase 1* or *Phase 2* clinical trials for your target. This may help give validation of the target and will provide important details.
3. *PharmaX* is only interested in developing small molecule drugs, i.e non-biological based drugs, so monoclonal antibodies or engineered proteins are not acceptable.
4. In class, we have discussed a number of factors to consider with target selection including potential market, target biology and validation, and available information on the structure and mechanism of the target. You need to utilize all of this information in selected the best target for development.

Written Proposal Guidelines (15 Pages Maximum) 50 Total Points.

1. The written proposal should be typed using single spaces and Arial 11 or 12 point font. Margins should be 1 inch all around.
2. Figures are allowed but must be accompanied by a Figure Legend (10 to 11 point font) underneath the figure. Figures should be utilized effectively in the proposal by describing them in the text of the proposal. Do not put figures in the proposal that are superfluous.
3. The proposal should contain the following elements:
 - a. **Title Page: Title of Project and Names of Team Members**
 - b. **Abstract/Summary Page (Limit of 1/2 to 1 Page)**-Sell your project in this one page summary based on the most important elements to convince the scientific review board as to why your project is "hot".
 - c. **Proposal Body (Limit of 15 pages)**. Give the details of your target of interest and provide the details of the basis for why your team thinks this is the best target to move forward. Some of the elements to be considered for the proposal body could include the following;
 - i. Target disease area and target biology background
 - ii. Number of people affected in the US and worldwide
 - iii. Chronic versus short term therapy
 - iv. Market Potential for Sales
 - v. Market -share with other products
 - vi. Target biology unique or already validated by others
 - vii. Target biology validation and methods of validation (siRNA, known small molecule inhibitors etc)
 - viii. Off target effects, eg. Kinase inhibitors
 - ix. Target Structures available and Mechanism-of-Action
 - x. Essentiality of target protein in cell and context of essentiality e.g conditionally essential in the disease state only
 - xi. Other isoforms or isozymes of the target e.g. Cox 1 and Cox 2
 - xii. Known inhibitors of the target and strengths of interactions
 - xiii. New scaffolds for inhibitors of targets and how they were discovered
 - xiv. Examples of structure-based drug design against target
 - xv. Any clinical trials already in progress

**Project Proposal Presentation Guidelines (20 minutes + 5 minutes for Questions)
100 Points Total**

1. Each project team will give a PowerPoint Presentation describing their project and why it should move on for advanced drug development. The presentation should include the most important elements from the written proposal necessary to persuade the scientific advisory team. Often times the presentation is what carries the most weight in terms of persuading individuals of the merits of their project versus just a written proposal/description.
2. Each presentation will be given no more than 20 minutes. At the end of 20 minutes, the presenters will be cut off (mid-sentence if necessary) for the question answer period. We only have 50 minutes for the class so we have to stick to the timeline.
3. Presentations should be constructed using Microsoft PowerPoint.

4. Presentations should be given by 1 to four of the team member(s). The number of team members participating in the presentation and the length of their part of the presentation is up to each team.
5. Each team member should be able to answer any question asked. However, you can assign a person(s) to answer questions after the presentation.
6. 20 Points of the 100 points will be given based upon peer review (other project teams) of your presentation.

Team Member Evaluation (50 Points)

1. If you feel that a team member(s) have not done their part in helping the team prepare the written proposal or the presentation, you will be able to state this on the team member evaluation sheets.

BIOL/BCHM 495 PharmaX Team Project Proposal Deadlines (Tentative) 2016

Tentative Target Selection

Friday, March 28th

Each team needs to provide me with a list of their TOP 3 Target Enzymes and/or Receptors that they are interested in pursuing. Please rank order your choices with the Top Choice being number 1. The earlier you select your target, the earlier I can approve it. We cannot have duplicate targets so approval and assignment of targets will be on a first come, first serve basis. This means that you really need to research each of your potential targets and meet to discuss your priorities before Spring Break to get a good start. One target that is off the list is Beta-secretase (BACE 1 and 2) also known as Memapsin 2 and Memapsin 1. I will approve the targets on a rolling basis but all must be approved by Monday, March 30th.

PowerPoint Presentations

April 20th, 22nd or 25th by 9:00 am

One of your team members needs to bring a Jump Drive with your final presentation to me in my office in Hockmeyer by 9 am on Friday. All 4 presentations will be loaded onto the computers (PC or Mac laptop). Presentation order will be random and will occur by selection on the day of class. All team members should be present for all presentations. You cannot change your PowerPoint presentation after you turn it in. It is what it is.

Written Project Proposal Descriptions

Wednesday, April 27th by noon

Bring the proposals to me at class time or to my office in Hockmeyer by noon. I want both a Word Document and a PDF file. I will be running an iThenticate plagiarism check on each written report before I read them. If the server scores and analysis indicates the document or parts of the document have been plagiarized, it will be returned to you without evaluation and your score will be zero.

Team Member Evaluation Sheets

Wednesday, April 27 ^{purduepu} by noon

Bring the evaluations to me at class time or to my office in Hockmeyer by noon 12:00. Alternatively you can email a PDF file to me by noon (12:00pm)

BIOL/BCHM 495 STUDENT TEAM EVALUATION FORMS

Name of Evaluator _____

Team Number _____

With regards to your personal contribution to the group project, to what extent do you agree with the following statements? Highlight the appropriate number on the scale from "Agree" (5) to "Disagree." (1)

- | | | | | | |
|---|---|---|---|---|---|
| 1. My attitude contributed positively to the group project. | 5 | 4 | 3 | 2 | 1 |
| 2. I showed up for meetings on time and prepared. | 5 | 4 | 3 | 2 | 1 |
| 3. I helped the group make important project decisions. | 5 | 4 | 3 | 2 | 1 |
| 4. I completed my share of the work in a competent and timely manner. | 5 | 4 | 3 | 2 | 1 |

Additional comments:

Team Member's Name _____

With regard to this team member, to what extent do you agree with the following statements? Highlight the appropriate number on the scale from "Agree" (5) to "Disagree." (1)

- | | | | | | |
|--|---|---|---|---|---|
| 1. His/her attitude contributed positively to the group project. | 5 | 4 | 3 | 2 | 1 |
| 2. He/she showed up for meetings on time and prepared. | 5 | 4 | 3 | 2 | 1 |
| 3. He/she helped the group make important project decisions. | 5 | 4 | 3 | 2 | 1 |
| 4. He/she completed his/her work in a competent & timely manner. | 5 | 4 | 3 | 2 | 1 |
| 5. I would want this person on my team again. | 5 | 4 | 3 | 2 | 1 |

Additional comments:

Team Member's Name _____

With regard to this team member, to what extent do you agree with the following statements? Highlight the appropriate number on the scale from "Agree" (5) to "Disagree." (1)

- | | | | | | |
|--|---|---|---|---|---|
| 1. His/her attitude contributed positively to the group project. | 5 | 4 | 3 | 2 | 1 |
| 2. He/she showed up for meetings on time and prepared. | 5 | 4 | 3 | 2 | 1 |
| 3. He/she helped the group make important project decisions. | 5 | 4 | 3 | 2 | 1 |
| 4. He/she completed his/her work in a competent & timely manner. | 5 | 4 | 3 | 2 | 1 |
| 5. I would want this person on my team again. | 5 | 4 | 3 | 2 | 1 |

Additional comments:

Team Member's Name _____

With regard to this team member, to what extent do you agree with the following statements?

Highlight the appropriate number on the scale from "Agree" (5) to "Disagree." (1)

- | | | | | | |
|--|---|---|---|---|---|
| 1. His/her attitude contributed positively to the group project. | 5 | 4 | 3 | 2 | 1 |
| 2. He/she showed up for meetings on time and prepared. | 5 | 4 | 3 | 2 | 1 |
| 3. He/she helped the group make important project decisions. | 5 | 4 | 3 | 2 | 1 |
| 4. He/she completed his/her work in a competent & timely manner. | 5 | 4 | 3 | 2 | 1 |
| 5. I would want this person on my team again. | 5 | 4 | 3 | 2 | 1 |

Additional comments:

Team Member's Name _____

With regard to this team member, to what extent do you agree with the following statements?

Highlight the appropriate number on the scale from "Agree" (5) to "Disagree." (1)

- | | | | | | |
|--|---|---|---|---|---|
| 1. His/her attitude contributed positively to the group project. | 5 | 4 | 3 | 2 | 1 |
| 2. He/she showed up for meetings on time and prepared. | 5 | 4 | 3 | 2 | 1 |
| 3. He/she helped the group make important project decisions. | 5 | 4 | 3 | 2 | 1 |
| 4. He/she completed his/her work in a competent & timely manner. | 5 | 4 | 3 | 2 | 1 |
| 5. I would want this person on my team again. | 5 | 4 | 3 | 2 | 1 |

Additional comments:

EVALUATOR NAME _____ DATE _____

Comments:

Additional Summary Comments may be provided on the back of this form