

MCH 402/502 - Principles of Medicinal Chemistry II

University at Buffalo

Spring Semester 2018

<i>Instructor</i>	<i>Location</i>	<i>Time</i>	<i>Days</i>
Dr. Qing Lin 679 NSC 645-4254 E-mail: qinglin@buffalo.edu Office hours: 1:00 PM – 2:00 PM, Tue/Thu, or by appointment.	Talbert 103	11:00 AM-12:20 PM	Tue/Thu

Optional Textbook/Reference:

R. B. Silverman & M. W. Holladay, "The Organic Chemistry of Drug Design and Drug Action, 3rd Edition," Academic Press, 2014.

Online Journal References:

- *Journal of the American Chemical Society* (<http://pubs.acs.org/journals/jacsat/index.html>)
- *Angewandte Chemie-International Edition* (<http://www3.interscience.wiley.com/cgi-bin/jhome/26737?CRETRY=1&SRETRY=0>)
- *Journal of Medicinal Chemistry* (<http://pubs.acs.org/journals/jmcmr>)
- *ACS Medicinal Chemistry Letter* (<http://pubs.acs.org/journal/amclct>)

These Journals are available through UB Libraries electronic resources. *It is expected that each graduate student and senior undergraduate student in a chemistry department should read the chemistry literature. These journals, and others that may be suggested during the semester, will serve as a supplement to the class. Each new issue should be perused by each student to become acclimated to the medicinal chemistry literature.*

Student Learning Outcomes:

Upon completion of this course:

- 1) Students will have an understanding of the covalent and non-covalent interactions between the drug targets (proteins and nucleic acids) and the small-molecule drugs.
- 2) Students will develop an understanding of the fragment-based drug design, the strategies in detecting and characterizing weakly binding ligands, and some successful examples.
- 3) Students will have a general understanding of the representative antibacterial, antiviral, and anticancer drugs and their respective mechanisms of action. Critical thinking skills will allow students to dissect the various drug resistance mechanisms for different drug classes.
- 4) Students will develop a general understanding of drug metabolism and critical thinking skills in evaluating chemical strategies for modifying drug metabolisms, including the use of prodrug approach.
- 5) Students will have an understanding of the structural features of the protein-protein interaction interfaces and the successful strategies inhibiting the protein-protein interactions.

Assessment Tools:

The various elements of this course are used cumulatively and students are expected to progress from initial recognition of the various concepts to synthesis of these concepts and solve problems using the acquired critical thinking skills.

- 1) The quizzes and mid-term examination will assess students' understanding of all the materials covered in the lectures.
- 2) The presentations by students will assess students' ability to synthesize the learned concepts and apply them to critical reading of current medicinal chemistry literature.
- 3) The final examination will be comprehensive and will examine students' knowledge of the medicinal chemistry principles and critical thinking skills in proposing solutions/hypotheses to problems in current medicinal chemistry literature.

Outline for MCH 402/502

- 1. Protein-Ligand Interactions**
 - 1.1 Molecular forces
 - 1.2 Binding energetics
- 2. Fragment-Based Drug Discovery**
 - 2.1 Overview
 - 2.2 Case studies
- 3. Strategies for Optimizing ADME**
 - 3.1 Chemical modifications
 - 3.2 Prodrug
- 4. Targeting Protein-Protein Interactions**
 - 4.1 Overview
 - 4.2 Case studies
- 5. Antibacterial Drugs**
 - 5.1 Major drug classes
 - 5.2 Drug resistance
- 6. Antiviral Drugs**
 - 6.1 Description of viruses
 - 6.2 Major drug classes
 - 6.3 Drug resistance
- 7. Anticancer Drugs**
 - 7.1 Major cancer drug targets
 - 7.2 MOA of anticancer drugs
 - 7.3 Drug resistance
- 8. Class Presentation**

About the Course:

Lecture:

Students should be properly registered and are expected to attend all lectures. Students should read relevant sections of the Silverman book and the assigned literature articles in advance of the lectures to familiarize themselves with the material. Students are responsible for the assigned materials and all the materials presented in class whether they attend or not. Course grades will be determined by two examinations (a midterm and a final) and one presentation of a journal article selected by the student with approval from Dr. Lin.

Presentation:

Each student is required to give a presentation on current publications of their choosing that is focused on medicinal chemistry. *Each talk will be 25 min with 5 min for questions, assigned dates for these presentations will be provided later on Blackboard.*

This article will be a recent medicinal chemistry publication (i.e. within the last 3 years) focused on one of the topics covered in this course, such as an enzyme inhibitor drug discovery effort, a drug metabolism study, prodrugs, anticancer drugs, etc. The article **MUST** be approved by Prof. Lin at least 1 week prior to the presentation and the presentation slides should be emailed to Prof. Lin by noon the day before the presentation. Presentations will be 20 min with 5 min for questions. *All articles and associated student presentations are subject to being on the exams and will be posted on UB learns.*

Grading:

Midterm Exam	30%
Quizzes and Assignments	10%
Comprehensive Final Exam	40%
Presentation	20%

Student Presentation Grading Criteria:

- Selection of paper (interesting to class, important to medicinal chemistry)
- Depth of knowledge of paper
- Presentation clarity, slide quality, proper use of presentation time
- Ability to clearly answer questions

Make-up Policy:

Students who are unavoidably absent from an exam must notify Dr. Lin in advance. For all absences, students must be prepared to document the reason for the absence if requested to do so (See incompletes for more detail). Since the final exam will be comprehensive, students who miss the midterm exam with a valid excuse will have their grade determined by the total points from their final exam and their presentation, re-scaled accordingly to accommodate the missed midterm exam. ***If you are unable to make the date in which your class presentation was scheduled you must find another student to switch with.***

Incompletes:

Students who present a valid written excuse for failure to take the Final Examination within 48 hours of that exam will be given a grade of I (incomplete) if they had a passing grade without counting the potential final exam points. The default grade for an incomplete will be computed with the final examination counting 0 points. Students with failing grades (before counting the final exam) are not eligible for incompletes and will be assigned a grade of F if they do not take the Final Examination. Incompletes must be removed by examination within 15 months, by taking a make-up exam at a time to be announced.

Students requesting an incomplete are hereby reminded that University regulations prohibit a second registration in a course for which they currently have an I-grade and that all I-grades must be removed before graduation. Students who stop attending, as judged by their absence from the Mid-Term and the Final Examination, without officially resigning, will be assigned the grade of F and their lack of attendance will be reported to the Office of Financial Aid at the end of the semester.

Academic Integrity:

The University community depends upon shared academic standards. Academic dishonesty in any form represents a fundamental impairment of these standards. If, after consultation with the student, an instructor believes the student has committed an act of academic dishonesty, the instructor has the authority to impose sanctions in keeping with this principle. The MINIMUM sanctions to be imposed are as follows:

First infraction: The maximum point value for a test will be subtracted from the student's point total. A subsequent infraction will result in a minimum penalty of 20 total points.

Students should consult the Academic Regulations and Procedures section of the Undergraduate Academic Integrity Policy or the Graduate Academic Integrity Policy for a more detailed discussion of possible harsher sanctions and the appeals process.

Academic dishonesty includes, but is not limited to, the following:

1. The possession of crib sheets or unauthorized notes at an examination or quiz, whether or not they are used. (Calculator memory banks, calculator cases or other articles are subject to inspection by the proctors.)
2. Copying from another person's examination paper or quiz, or deliberately allowing another person to copy from you.
3. Changing any of the answers on an examination paper or quiz, and then requesting that the paper be re-graded for additional credit.

Accessibility Resources:

Students with disabilities may require accommodations to ensure full participation in a class. A student requesting such accommodation at any time during the term should be referred to [Accessibility Resources Office](#) where an assessment can be completed and appropriate accommodations determined. Students with such documented accommodations should be instructed accordingly.

Miscellaneous:

Exam papers that students wish to have re-graded must be turned in within one week after the paper has been received by the student. The nature of the problem must be specified on an attached sheet. Papers containing "white-out" corrections will not be re-graded. The entire exam is subject to re-grading and the new grade reported.

Course Website:

The course website is now available on Blackboard. You may access your course by navigating to:

<https://ublearns.buffalo.edu>

Each student's username will be his or her UBIT name.

Letter Grade:

The final course grade (A – F, including +/-) will be determined solely on the basis of total points accumulated. While final grades will be assigned on a curve, students receiving 85% of all possible points are assured of an "A", students receiving 75% are assured of a "B", students receiving 60% are assured of a "C", and students receiving 50% are assured of a "D". Students

missing a midterm examination, without a valid excuse, will receive a grade of “0” for that examination. There will be no makeup anytime for unexcused absences. Students may receive an excused absence by providing a valid, written excuse within 48 h of the examination.

NOTE: During examinations, students may not use cell phones/smart phones and cell phones/smart phones must be kept out of sight and turned off. Violation of these rules will result in a grade of “0” for the examination.