CHEM 3075
Introduction to Drug Discovery
York University – Department of Chemistry

Lectures: F, 14:30 (180 min), LSB 103

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               Office hours: appointments can be made by email.

Calendar description: This course introduces students to the fundamental chemistry, structural biology, and pharmacological aspects of the medicinal chemistry of modern drug development, from identifying molecular targets and selecting a lead compound, to commercialization of the final drug.

Course objectives:
1. Understand how drugs are processed in the body and how molecular characteristics impact the success of pharmaceutical drugs.
2. Discuss and describe molecular interactions that form the basis of drug-receptor interactions and how to enhance such interactions to make more effective therapeutics.
3. Understand and predict how drugs are metabolized as the molecular level, including functional groups that are metabolic liabilities and those that are toxic.
4. Understand the process for virtual drug screening and be able to perform a simple low-level molecular docking of a known drug and predict how changes to its structure impact its binding
5. Discuss and describe modern strategies to identify chemical compounds from large chemical libraries that may serve as a source for new drugs.

Lecture format:
Standard lecture format: 180 minutes

Zoom Lectures:
There will be no scheduled Zoom lectures, unless otherwise specified due to unforeseen circumstances.

Textbooks:
There will be no specific textbook for this course. All testable material will be derived from the lectures. Course notes that are posted on the course website will be supplemented during the lecture. There will be no recordings of lectures posted. Links to relevant literature will be provided. Any basic medicinal chemistry textbook will provide sufficient background, as necessary. Below is a link to a free textbook (accessible to YorkU students):

Richard Silverman, *The Organic Chemistry of Drug Design and Drug Action*, 3rd Ed., Academic Press:
https://www.sciencedirect.com/book/9780123820303/the-organic-chemistry-of-drug-design-and-drug-action

Marking Scheme
Online quizzes: 20% (5% each, throughout the term)
Midterm: 30% (25 October 2024)
Assignment: 15%
Final Exam: 35%

Grading: A letter grade for the course will be assigned based on the final percentage grade
(A+=90-100, A=80-89, B+=75-79, B=70-74, C+=65-69, C=60-64, D+=55-59, D=50-54,
E=40-49, F=0-39).

Assignment
1 page, single-spaced (not including figures) report on the optimization of an inhibitor.
Details: Students will receive a protein and reported inhibitor to optimise using virtual docking. All required technical aspects of virtual docking will be taught during class to equip students with the skill set to complete the project. Students will dock the reported inhibitor in the protein active site, and report the free energy of binding, non-covalent interactions, and provide an image of the docked pose. Then, through rationale design, students will attempt to optimise the non-covalent interactions to improve the virtual docking scores (we'll work through an example in class). Students will need to describe the rationale for their design/optimisation, the outcome of the docking (free energy and non-covalent interactions achieved), and an image of the inhibitor docked in the active site. Students will describe the following attributes of their molecule: MW, cLogD(ph7) or cLogP, HBD, and HBA. Students will also need to describe possible metabolic liabilities of their molecule, including one reasonable metabolite. *Full information will be provided in class.*

Academic Honesty
York students are required to maintain the highest levels of academic honesty and they are subject to the Senate Policy on Academic Honesty:
https://www.yorku.ca/secretariat/policies/policies/academic-honesty-senate-policy-on/
The Policy affirms the responsibility of faculty members to foster acceptable standards of academic conduct and of the student to abide by such standards.

There is also an academic integrity website with comprehensive information about academic honesty and how to find resources at York to improve students' research and writing skills, and cope with university life. Students are expected to review the materials on the Academic Integrity website: https://spark.library.yorku.ca/academic-integrity-what-is-academic-integrity

<center>**Lecture modules and important dates**</center>

Note this is a tentative schedule.

Date	Module	Assessment
06-Sep	Introduction	
13-Sep	Characteristics of successful leads	
20-Sep	Drug-receptor interactions	QUIZ ONE
27-Sep	Approaches to optimize drug-receptor interactions	
04-Oct	no class	

11-Oct	Drug Metabolism	QUIZ TWO
18-Oct	READING WEEK	
25-Oct	MIDTERM	MIDTERM
01-Nov	Virtual screening	
08-Nov	Hit generation methods	QUIZ THREE
15-Nov	Fragment-based lead generation	
22-Nov	Improving drug selectivity	
29-Nov	DNA-encoded libraries	QUIZ FOUR & Assignment due

Final exam policy
The final exam schedule will not be known until mid-October. However, all students are expected to be available for the **complete** final exam period and no travel or other arrangements should be made to start before the end of the exam period. This is to allow for weather emergencies and other reasons for rescheduling. A conflict with previously made travel arrangements is **not** an acceptable reason for missed final exams.