Instructor:
Dr. Christal Sohl, Ph.D.
Department of Chemistry and Biochemistry
Office: CSL 328
Email: csohl@sdsu.edu

Course time: Mon/Wed, 5:00-6:15 pm via zoom. Online synchronous attendance is mandatory since the course has significant emphasis on discussion, groupwork, and active learning.

Office hours:
E-mail me to make an appointment.

Textbooks:
No textbooks are required for this course. Instead, mandatory reading is in the form of scientific literature provided in PDF format through blackboard.

Other course materials:
We will be using Canvas. You also need to download the free software Pymol on your computer or tablet. Please let me know ASAP if you do not have access to a computer/laptop.

Course details:
This class is capped at 20 students. This is a graduate-level course, but advanced Chemistry and Biology major undergraduates may enroll provided they meet the prerequisites and are comfortable reading primary scientific literature. Having had research experience is also beneficial. In order to enroll in 600-700 level graduate level courses, an undergraduate senior must have completed a minimum of 90 units, with a GPA of 3.0 or better in their last 60 units.

Prerequisites – General Biochemistry CHEM 560 or CHEM 365, and CHEM 232 and 432 (or equivalent at previous institutions).

Course description – Students will probe the implications of altered enzymes from the catalytic and structural perspective to the physiological manifestations in the patient to understand the molecular mechanisms of cancer and HIV. We will study how diseases are therapeutically targeted and the mechanisms of drug resistance, explore the process of drug development from design to FDA approval, understand basic principles of pharmacology and kinetics, and navigate the science/business/ethics/promise of drug companies and therapeutics. Students will have extensive opportunity to explore the mechanistic features of disease, highlighting research techniques discussed in this class and in their own labs. Finally, students will research local biotech companies of interest to them through the lens of preparing for a job interview and/or considering financial investment. This course emphasizes active learning, critical discussion, hands-on tutorials, student-led learning, oral presentations, and career development/job preparation. Students interested in biotechnology, biochemistry, pharmacology, medicinal chemistry, pharmacology, enzymology, cancer biology, structural biology, drug regulatory processes, patent law, and/or bioethics will enjoy this course.

Learning objectives:
1) To think critically and argue/defend a point.
2) To critically read and evaluate primary scientific literature.
3) To examine the functional effects altered protein folding and/or activity can have and interpret the downstream consequences.
4) To use research tools like cBioPortal (http://www.cbioportal.org/), PDB
Sohl, CHEM 765

To explain the basic features and challenges of drug design.

To design hypothesis-driven experiments to address questions in their own research.

To evaluate and orally present current research findings and challenges.

To have the tools to evaluate the biological functions at work in health and disease.

To help society in evaluating and disseminating accurate scientific information, and explore ethical issues in medicine and drug design.

To pose and answer important questions needed to prepare for a career or investing in biotech.

Resources available to students - The lectures and scientific articles are the primary resources for this course. Slides used in lectures will be posted in Canvas after that day’s class. Make an appointment with me to ask questions about material you find confusing.

Participation – This includes active participation in in-class discussions, evaluating peers on their oral presentations, asking questions during lecture and student presentations, and attendance.

Assignments – More details will be provided in class. Assignment 1 is due by the end of the day (11:59 pm) via email (csohl@sdsu.edu) or via Canvas by the assigned deadline. I will take the assignment up to four days late, but I will take off 10 percentage points each day it is late. I will not accept assignments after four days, no exceptions. Slides for presentations submitted to me will be penalized by 10 percentage points for each day it is late. I will not accept your slides after two days, no exceptions.

Take home assignment: “Assessing FDA-approved drugs through the lens of a medicinal chemist”: You will select one active-site-binding, small molecule drug approved by the FDA in the previous year that has both typical “drug-like” features, and features that would fail Lipinski’s Rule of 5. Based on the molecular target and natural substrate, you will hypothesize how the drug interacts with the target. Undergraduates and graduate students will turn in this assignment.

Literature reading assignments: Of the assigned papers, graduate students will select THREE to perform a review. I strongly encourage you to read all the assigned papers. Please submit via Canvas a typed version of the form provided by the end of the day (11:59 pm) one day after the paper was assigned. This is to help you to distill complicated concepts down to a few key points. I will not accept literature reviews late – you instead simply need to pick a different paper. Undergraduate students taking this course will select ONE of the assigned papers to perform a literature review. One additional literature review can be submitted worth up to 1.5 percentage points.

Presentation #1: “Mechanisms of oncoproteins and tumor suppressors in cancer.” You will use Pubmed, cBioPortal, PDB, and Pymol to explore an assigned oncogene or tumor suppressor implicated in cancer. You will describe the molecular and physiological mechanisms of the protein and describe attempts to target it. You will teach the class about the structural and functional features of the protein, drug-like features of therapeutic interventions, challenges and consequences in targeting attempts, and any mechanisms of resistance to therapy. Your presentation slides are due on a specific date to me regardless of presentation order so that everyone will have the same deadline and cannot alter their talk after hearing others’ presentations. Undergraduate and graduate students will give a presentation.

Presentation #2: “Biotech startup due diligence: preparing for a job/investing in industry.” You will research extensively one local (San Diego area) biotech start-up company of interest to you, reporting on their history/origin story, science, financing, and management/culture/compensation. You will also formulate three interview questions you’d ask as a potential interviewee, and advise the class whether we should invest in the company if/when it is publicly traded. Your presentation slides are due on a specific date to me regardless of presentation order so that everyone will have the same deadline and cannot alter their talk after hearing others’ presentations. Undergraduate and graduate students will give a presentation.
Grading –
Take home assignment: “Assessing FDA-approved drugs through the lens of a medicinal chemist”: 150 points

Literature reviews: 25 points per review (3 for grad students, 1 for undergraduate students)
Presentation #1: 100 points (75 points from professor evaluation of individual, 25 points from audience evaluation (average))
Presentation #2: 100 points (75 points from professor evaluation of individual, 25 points from audience evaluation (average))
Class participation: 100 points (participating in class discussion, judging and asking questions after student presentations). A percentage of effort-to-date will be shown on blackboard to prevent end-of-year surprises and encourage improvement.
Total points: 525 for graduate students/475 for undergraduate students

Grading scale – The course is not intended to be curved.
A = ≥ 92.5%
A- = 89.5-92.4%
B+ = 87.5-89.4%
B = 82.5-87.4%
B- = 79.5-82.4%
C+ = 77.5-79.4%
C = 72.5-77.4%
C- = 69.5-72.4%
D+ = 67.5-69.4%
D = 62.5-67.4%
D- = 59.5-62.4%
F < 59.4%

Expectations - I expect you to:
1) Attend lectures and actively participate in learning.
2) Help provide a positive and safe space for learning. This includes showing respect to your peers and me by not using cell phones, laptops, or other technology, or disrupting others by websurfing.
3) Make an appointment with me if you are needing help in the course.

Attendance and absences – Class attendance is mandatory. If you have a medical or other emergency that prevents you from completing an assignment on time, I need a note from your physician to allow you to turn in an assignment late. Otherwise you will lose points as described. If you have a conflict that requires you to present your individual presentation on a particular day, let me know as soon as possible to accommodate you. There are no make-ups for presentations.

Students with differing abilities - The University is committed to providing reasonable academic accommodation to students for those who have been deemed eligible. If you require accommodation, contact the Student Disability Services Office (or visit http://go.sdsu.edu/student_affairs/sds/) at (619) 594-6473. The instructor cannot provide any accommodations without prior consent of Student Disability Services.

Religious Observances - By the end of the first week of classes, students should notify me of any planned absences for religious observances. The student and I will work together to reasonably accommodate students who have notified in advance of absences for religious observances.

Statement on Cheating and Plagiarism – Basically, don’t cheat, no exceptions! The University adheres to a strict policy regarding cheating and plagiarism (http://studentaffairs.sdsu.edu/srr/conduct1.html). If you cheat, you will receive an F for the course, and you will be referred to the University for disciplinary measures. If you have questions on plagiarism, consult the policy (http://www.sa.sdsu.edu/srr/conduct1.html). If you feel overwhelmed, make an appointment with the professor. Appreciate how cheating can ruin your bright future.
**Syllabus is Subject to Change** - This syllabus and schedule are subject to change. If you are absent from class, it is your responsibility to check on announcements made while absent.

*The following schedule provides the topics, required readings, and important dates.*

<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Reading assignment</th>
<th>Assignments, due dates</th>
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</table>
| 8/24  | #1 Part I: Cancer  
Brief cancer history, hallmarks of cancer |                                  |                                              |
| 8/26  | #2 Part I: Cancer  
Cancer progression    | Hanahan *Cell* 2011              | Oncoproteins assigned for presentation #1   |
| 8/31  | #3 Part I: Cancer  
Cancer metabolism: zoom out |                                  |                                              |
| 9/2   | #4 Part I: Cancer  
Cancer metabolism: zoom in     | Badur *Cell Rep* 2018            |                                              |
| 9/7   | #5 Part I: Cancer  
Methods of fighting cancer       |                                  |                                              |
| 9/9   | #6 Part I: Cancer  
Kinases: structure, function, druggability; x-ray crystallography | Müller *Nat Chem Bio* 2015      |                                              |
| 9/14  | #7 Part I: Cancer  
Tutorial – TCGA/cbioportal, using Pymol |                                  | Bring your laptop to class!                 |
| 9/16  | #8 Part I: Cancer  
Tutorial – using Pymol, cont.                    | Paez *Science* 2004             | Bring your laptop to class!                 |
| 9/21  | #9 Part I: Cancer  
Case studies: Gleevec and erlotinib in kinase inhibition |                                  |                                              |
|       | **9/21: Email your slides to Dr. Sohl by 11:59pm, DO NOT BE LATE; she will randomly assign a presentation order** |                                  |                                              |
| 9/23  | Part II: In-class presentations:  
Oncogenes and tumor suppressors                      |                                  |                                              |
| 9/28  | Part II: In-class presentations:  
Oncogenes and tumor suppressors                      |                                  |                                              |
| 9/30  | Part II: In-class presentations:  
Oncogenes and tumor suppressors                      |                                  |                                              |
| 10/5  | Part II: In-class presentations:  
Oncogenes and tumor suppressors                      |                                  |                                              |
| 10/7  | Part II: In-class presentations:  
Oncogenes and tumor suppressors                      |                                  |                                              |
| 10/12 | Part II: In-class presentations:  
Oncogenes and tumor suppressors                      |                                  |                                              |
| 10/14 | #10 Part III: Drug design and ethics  
PK/PD, ADME basics                                 | Vitaku *J Med Chem* 2014        | Check your group assignment on Canvas for the BRCA trial! |
| 10/19 | #11 Part III: Drug design, HIV, and ethics  
SAR, features of a successful drug                  | Murcko *J Med Chem* 2018       |                                              |
| 10/21 | #12 Part III: Drug design, HIV, and ethics  
Kinetics and inhibition                           | Pollard *Mol Biol Cell* 2013 (problem set not necessary) | Read required reading by class on 10/26 |
| 10/26 | #13 Part III: Drug design, HIV, and ethics  
Patent law case study: BRCA                        | Required reading: your team’s material, all group material | You must have read assigned reading before class! |
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<thead>
<tr>
<th>Date</th>
<th>#</th>
<th>Topic</th>
<th>Reading/Assignment</th>
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</thead>
<tbody>
<tr>
<td>10/28</td>
<td>#14</td>
<td>Part III: Drug design, HIV, and ethics</td>
<td>Patent law case study: BRCA: Present your case!</td>
</tr>
<tr>
<td>11/2</td>
<td>#15</td>
<td>Part III: Drug design, HIV, and ethics</td>
<td>Ethics in clinical trials: the story of Vioxx</td>
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<td>Ross <em>JAMA</em> 2008</td>
<td>Select your startup company for presentation #2</td>
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<tr>
<td>11/4</td>
<td>#16</td>
<td>Part III: Drug design, HIV, and ethics</td>
<td>Kellinger <em>Nat Rev Drug Discov</em> 2010</td>
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<td>Select your startup company for presentation #2</td>
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<tr>
<td>11/9</td>
<td>#17</td>
<td>Part III: Drug design, HIV, and ethics</td>
<td>Kellinger <em>PNAS</em> 2010</td>
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<td>Bring your laptops with pymol loaded!</td>
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<tr>
<td>11/11</td>
<td>#18</td>
<td>Part III: Drug design, HIV and ethics</td>
<td>Treating HIV, drug regulation</td>
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<td>Take-home assignment due by the end of the day!</td>
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<tr>
<td>11/16</td>
<td>#19</td>
<td>Part III: Drug design, HIV, and ethics</td>
<td>Scannell <em>Nat Rev Drug Discov</em> 2012</td>
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<td>Bring your laptops!</td>
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<tr>
<td>11/18</td>
<td>#20</td>
<td>Part III: Drug design, HIV, and ethics</td>
<td>Ethical minefield of drug pricing</td>
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<tr>
<td>11/23</td>
<td>#21</td>
<td>Part III: Drug design, HIV, and ethics</td>
<td>Regulation and this years' FDA approvals</td>
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<td>Xu <em>N Engl J Med</em> 2019</td>
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<tr>
<td>11/25</td>
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<td><strong>No class, Happy Thanksgiving!</strong></td>
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<tr>
<td>11/28</td>
<td></td>
<td><strong>Email your slides to Dr. Sohl by 11:59pm, DO NOT BE LATE; students will be presenting in reverse order from presentation 1</strong></td>
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<tr>
<td>11/30</td>
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<td>Part IV: In-class presentations</td>
<td>Industry due diligence</td>
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<tr>
<td>12/2</td>
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<tr>
<td>12/7</td>
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<td>Part IV: In-class presentations</td>
<td>Industry due diligence</td>
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<tr>
<td>12/9</td>
<td></td>
<td>Part IV: In-class presentations</td>
<td>Industry due diligence</td>
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<tr>
<td>12/11, 3:30-5:30</td>
<td>Final exam day: Part IV: In-class presentations</td>
<td>Industry due diligence</td>
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</table>

*Dates/content subject to change! Be sure to check finals schedule, as these are sometimes altered as well.*