

Fall 2021
Dr. Christal Sohl

CHEM 765: Molecular Mechanisms of Disease

Mon/Wed

5:00-6:15pm

GMCS 307

We'll explore how cancer and HIV develop, are treated, and achieve therapeutic resistance through the lens of biochemistry, biophysics, and cell and molecular biology. We'll investigate the path of drug development from design through FDA approval while probing the science, business, and ethics of drug discovery and drug companies.

Required course materials

Canvas, access to a computer or laptop and internet, and the free protein structure viewing platform, Pymol (<https://www.pymol.org/>) are required.

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About Dr. Sohl

I'm really interested in learning how enzymes work – and how they run amok upon acquisition of a disease-causing mutation. My lab, which is made up of inquisitive, kind, and hard-working undergraduate, graduate student, and postdoctoral scientists, works on the kinetic, structural, and cellular consequences of mutant forms of human metabolic enzymes and polymerases. One of my favorite parts of my job as a professor is facilitating learning and discovery, both in the lab and in the classroom. I am grateful I get to learn from the unique and diverse perspectives and expertise of my student colleagues!

When I'm not teaching or in the lab, I enjoy hiking and traveling with my partner, Hans, early-morning workouts, reading, and pretending that having backyard barn owls that barf up digested creatures all over the yard is almost as fun as having a dog.

When you need to contact me, use the messaging system in Canvas (preferred), email me at csohl@sdsu.edu, or arrange a time to meet me in my office in CSL 328 for help hours. I look forward to working with you this semester!



Sohl Lab group photo, Summer 2021

*It is hard to look at
the tumor and not
come away with the
feeling that one has
encountered a
powerful monster in
its infancy –
Siddartha
Mukherjee, Emperor
of All Maladies*

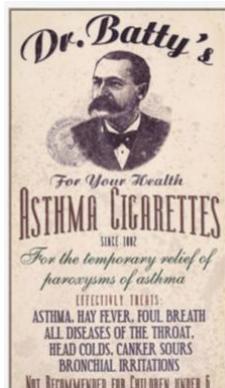
Fast Facts on Course Structure and Features

- **This is a mostly flipped class**
A lot of lecture content is delivered online, and we will discuss, debate, design, practice, and explore during class.
- **We cover many disciplines, so there will be something for everyone**
Students interested in chemistry, biochemistry, biology, pharmacology, business, finance, law, or ethics in the context of human disease will find a topic of interest. Expertise in all/most of these topics is not at all expected.
- **I am committed to creating a supportive, safe, and multiculturally affirming environment for everyone**
Everyone in this room belongs and has important perspectives, experiences, and expertise from which we all can benefit. We cover a lot of charged topics, and it is critical that we have a safe environment that everyone can respectfully contribute their thoughts and questions.
- **Please contact me immediately if you foresee or are experiencing challenges that threaten your success in this class**
You and I are on the same team – we both want you to be successful in this class and in your educational career. Let's work on solutions to keep you on track.
- **To be on campus and in class, you must be following SDSU's COVID policy to be eligible to be on campus.**
No exceptions – these policies are to keep everyone safe.

Course Student Learning Outcomes (SLOs)

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|--|--|
|  1. Think critically and argue/defend a point. |  6. Design hypothesis-driven experiments. |
|  2. Evaluate primary scientific literature. |  7. Assess and present research findings and challenges. |
|  3. Determine the effects of altered protein function in disease. |  8. Discuss and relay scientific information to wider audiences. |
|  4. Apply research tools to solve scientific problems. |  9. Prepare for a biotech career or investing. |
|  5. Explain the basic features and challenges of drug design. |  10. Connect scientific concepts to your life and the world around you. |

<https://www.fda.gov/about-fda/virtual-exhibits-fda-history/80-years-federal-food-drug-and-cosmetic-act>



<http://content.time.com/time/covers/0.16641.20010528.00.html>

Assignments Details

 Why? To use new tools to teach your peers about mechanisms of disease!

 Why? To connect content to your life!

 Why? To practice job interview skills!

 Why? To gain the knowledge to participate in class activities & discussion!

 Why? To tackle real-life scientific problems with your student colleagues!

 Why? To practice applying knowledge gained over the semester!

Presentation #1: “Mechanisms of oncoproteins and tumor suppressors in cancer.” You will use research tools that you will learn and practice with in class to explore a tumor-driving protein. You will describe the molecular and physiological mechanisms of the protein and attempts to target it, and teach the class about the structural and functional features of the protein, features of therapeutic interventions, the challenges and consequences in drug targeting efforts, and any mechanisms of resistance to therapy. More details are on canvas. SLO #1, 2, 3, 7, 8. **Due Sept. 21 at 11:59 pm.**

Reflections: Twice during this class you will be asked to reflect on ways in which what you've been learning applies to your own lives, interests, hobbies, etc. It has been shown that assignments that give you the freedom to put material within your own greater purpose and relevance boost motivation and interest. More details are on canvas. SLO #10. **Due Oct 18 and Nov. 22 at 11:59 pm.**

Presentation #2: “Biotech startup due diligence: preparing for a job/investing in industry.” You will research a local biotech start-up company of interest to you, reporting on their science, history, financials, and more. You'll practice framing your skills as an asset to the company, prepare questions you'd ask as a potential job interviewee, and advise the class whether we should invest in the company. More details are on canvas. SLO #1, 2, 4, 5, 7, 8, 9, 10. **Due Nov. 21 at 11:59 pm.**

Online embedded lecture quizzes: You'll view lectures prior to class and take the embedded quiz as many times as you like (only the highest score is retained) within the allotted time window. More details are on canvas. SLO #1, 3, 5, 10. **Due by the dates listed in the calendar below.**

Groupwork: You will have the opportunity to apply the ideas and content presented in class in small teams. Please make sure you come prepared for groupwork – this may include required watching online lectures, reading assignments, etc. More details are on canvas. SLO #1, 2, 3, 4, 5, 6, 7, 8, 9, 10. **Due by the end of the class period as listed in the calendar below.**

Take home assignment: “Assessing FDA-approved drugs”: You will select one active-site-binding small molecule drug recently approved by the FDA to practice the evaluative studies that scientists perform during drug discovery and development. More details are on canvas. SLO #1, 2, 3, 4, 5, 6, 7, 8. **Due Dec. 8 at 11:59 pm.**

Grading and Points Information

Take home assignment: 200 points total

Presentation #1: 150 points total (125 points from professor evaluation of individual, 25 points from audience evaluation (average)).

Presentation #2: 150 points total (125 points from professor evaluation of individual, 25 points from audience evaluation (average)).

Groupwork: 140 points total (20 points per assignment, lowest score dropped).

Online embedded lecture quizzes: 50 (5 points per lecture).

Reflection #1: 25 points total

Reflection #2: 25 points total

Total points: 740

A = $\geq 92.5\%$
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%

The following tentative schedule provides the topics, readings, and important dates.
Dates/content subject to change, look for Canvas announcements describing any changes!

Date	Topic	Suggested reading to check out	Assignments, due dates
Part 1: Mechanisms of cancer, and strategies to combat it			
8/23	Discussion #1: Brief cancer history, hallmarks of cancer	Hanahan <i>Cell</i> 2011, Malta <i>Cell</i> 2018, Pleasance <i>Nature</i> 2010	
8/25	Discussion #2 -- Cancer development	Nandi <i>J Biol Chem</i> 2020, Xu <i>Mol Cell</i> 1999	Draw for tumor drivers
Deadline of 8/29 to watch Online Lecture #1: <i>In vitro</i> tools to study cancer -- biochemistry and biophysics			
8/30	Groupwork 1: study a tumor driver using biochemical/biophysical methods		Bring your laptop
Deadline of 8/31 to watch Online Lecture #2 -- <i>In vitro</i> tools to study cancer – cellular methods			
9/1	Groupwork 2: study a tumor driver using cellular methods	Drebin <i>Nature</i> 1984, Tateishi <i>Canc Cell</i> 2015, Douglass <i>Sci Immunol</i> 2021, Hsiue <i>Science</i> 2021	Bring your laptop
9/6: No class, Happy Labor Day!			
Deadline of 9/7 to watch Online Lecture #3 -- Methods of fighting cancer			
9/8	Discussion #3: Kinases -- structure, function, druggability; x-ray crystallography	Paez <i>Science</i> 2004, Middleton <i>Nature</i> 2020, Müller <i>Nat Chem Bio</i> 2015	
9/13	Discussion #4: Using Pymol		Bring your laptop with pymol loaded
9/15	Discussion #5: TCGA/cbioportal, Elevator pitches, additional pymol ?s		Bring your laptop with pymol loaded
9/20	Discussion #6: Kinase inhibition and resistance		Bring your laptop
Deadline of 9/21 to email your slides to Dr. Sohl by 11:59 pm. You will be randomly assigned a presentation order			
9/22	In-class presentations		
9/27	In-class presentations		
9/29	In-class presentations		
10/4	In-class presentations		
10/6	In-class presentations		
Part 2: Drug design, development, and clinical trials through the lens of HIV			
Deadline of 10/10 to watch Online Lecture #4 -- PK/PD, ADME basics			
10/11	Groupwork 3: HIV infection and design-a-drug challenge	Vitaku <i>J Med Chem</i> 2014, Murcko <i>J Med Chem</i> 2018	Bring your laptop with pymol loaded
Deadline of 10/12 to watch Online Lecture #5 -- Kinetics and inhibition			
10/13	Groupwork 4: Designing inhibitor binding experiments	Pollard <i>Mol Biol Cell</i> 2013	Bring your laptop
Deadline of 10/17 to watch Online Lecture #6 – Transient-state kinetics			
10/18	Discussion #7: Practicing with Transient-state kinetics		Reflection #1 due 10/18 by 11:59 pm

10/20	Discussion #8 -- SAR, features of a successful drug		Bring your laptop
Deadline of 10/24 to watch Online Lecture #7 – Drug regulation and approval			
10/25	Groupwork 5: Using transient-state kinetics to study polymerases	Villalba <i>J Biol Chem</i> 2020, Kellinger <i>PNAS</i> 2010	Bring your laptop with pymol loaded
Deadline of 10/26 to watch Online Lecture #8 -- Ethical minefield of drug pricing			
10/27	Groupwork 6: 1980s-you designs your 1980s AIDS drug trial		Bring your laptop
11/1	Groupwork 6 Debate: share your trial design	Xu <i>N Engl J Med</i> 2019	Bring your laptop
Part 3: Business and ethics of science			
Deadline of 11/2 to watch Online Lecture #9 -- Researching a drug company"			
11/3	Groupwork 7: Effective pitches -- elevator and investment	Kneller <i>Nat Rev Drug Discov</i> 2010, Scannell <i>Nat Rev Drug Disc</i> 2012	Bring your laptop Select startup company for presentation #2 here
11/8	Discussion #9: The story of Vioxx	Ross <i>JAMA</i> 2008	Check your group assignment on Canvas for the BRCA trial, and begin required reading
11/10	Discussion #10: The story of BiDil	Reverby <i>J Law Med Ethics</i> 2008	
Deadline of 11/14 to watch online Lecture #10 – Patents and BRCA , and finish required reading for Patent trial!			
11/15	Groupwork 8: Patent law case study: BRCA		Bring your laptop You must have read the assigned reading before class!
11/17	Groupwork 8 Debate: Present your case!		Bring your laptop
Deadline of 11/21 to email your slides to Dr. Sohl by 11:59 pm. Students will be presenting in reverse order from presentation 1			
11/22	In-class presentations		Reflection #2 due 11/22 by 11:59 pm
11/24: No class, Happy Thanksgiving!			
11/29	In-class presentations		
12/1	In-class presentations		
12/6	In-class presentations		
12/8	In-class presentations		Take-home assignment due 12/8 by 11:59 pm



<https://news.wjct.org/post/mystery-solved-how-hiv-came-us>

Effort and persistence in this course matters, and it is through these things, not innate ability, that define our ability to grow and learn. I look forward to joining you in your journey of learning!

Diversity and Inclusion Commitment

Equality/Equity Statement

I am firmly committed to diversity, creating and maintaining an inclusive community, and equality and equity in all areas of campus life, including specifically members of minoritized and historically excluded communities. In this class I will work to promote an anti-discriminatory environment where everyone feels safe and welcome. I recognize that discrimination can be direct or indirect and take place at both institutional and personal levels. I believe that such discrimination is unacceptable and I am committed to providing equality of opportunity for all by eliminating any and all discrimination, harassment, bullying, or victimization. The success of this policy relies on the support and understanding of everyone in this class. We all have a responsibility not to be offensive to each other, and to explicitly call out and stop harassment or discrimination of any kind.

Safe Zone Statement

I am part of the Safe Zone Ally community network of trained SDSU faculty/staff/students who are available to listen and support you in a safe and confidential manner. As a Safe Zone Ally, I can help you connect with resources on campus to address concerns you may face that interfere with your academic and social success on campus as it relates to issues surrounding sexual orientation/gender identity. My goal is to help you be successful and to maintain a safe and equitable campus.

Undocumented & Mixed Status Inclusivity Statement

I and SDSU in general value diversity and are committed to creating and maintaining an inclusive community, which includes members of the Undocumented and Mixed Immigration status community. I will work towards promoting an anti-discriminatory environment, which may be direct or indirect that take place in the class, at the institution and on a personal level. I will treat your disclosure with the utmost confidentiality permitted and value your trust. I will work with you on a one-to-one basis should you encounter barriers to your academic and developmental success.

Preferred Name & Gender Pronouns

My preferred gender pronouns are she/her/hers. Class rosters are provided to me with only your legal name, and I will gladly honor your request to address you by an alternate name and/or gender pronoun. Please let me know at the beginning of the semester so I may make the necessary changes to my records.

Mental Health and Wellness

I see and interact with you as bright, creative, and hard-working students in my class. However, I know that sometimes life's circumstances can be intense, and as a result, you may have a hard time prioritizing coursework due to mental health, economic stability, or other challenges. You're not alone -- we all experience periods at some point in our lives where circumstances demand too much of our mental resources. It is really tempting to disengage during these times, and not let anyone know you need help -- but please resist this temptation! It takes courage to reach out for help, and I and others on campus are here to help -- and we want to. This is because we know how much potential you have, and we want to empower you to ensure you can achieve anything you want! I've included a list of resources on Canvas if you find you're grappling with things beyond the classroom (if it's course content...just ask me for help during class or request help hours!) You can also reach out to me, and I will help you connect to services you need. To prepare myself to better guide you to resources, I have trained to be an Adult Mental Health First Aid (MHFA) and Economic Crisis Response Team (ECRT) advocate. I'd be happy and honored to help -- I've done so for students in the past, and know I will for years to come.



“All sorts of things can happen when you’re open to new ideas and playing around with things.” –

**Stephanie Kwolek,
chemist**

Additional Course Details

Prerequisites

This is a graduate-level course, but STEM undergraduates may enroll provided they meet the prerequisites and are at least somewhat comfortable reading primary scientific literature. Undergraduates must have completed General Biochemistry CHEM 560 or CHEM 365, and CHEM 232 and 432 (or equivalent at previous institutions) with \geq B- grade. Having had research experience is also beneficial. In general, 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. Talk to me after class during the first week for details or advice.

Attendance and absences

Class attendance is mandatory as this is a “flipped” class with a lot of class discussion, debate, and activities. That being said, we are still in the grip of a worldwide pandemic, and we are depending on each other to make safe decisions regarding our own health and the health of our fellow colleagues. If you have a medical or other emergency that prevents you from completing any assignments on time, contact me at csohl@sdsu.edu ASAP so we can figure out your strategy for success in this class. If it is a known/planned absence, contact me at least one week before the missed day. If it was unexpected/emergency, contact me within 1 week of the missed deadline/class period. If you miss a groupwork day, you will be able to complete the assignment on your own if it is turned in within one week of the deadline. Turning in late assignments in general results in a loss of points. If you have a conflict for one of the individual presentation days, let me know ASAP so that I can try to accommodate you. There are no make-ups for presentations, but in the case of quarantining or other issues, zoom is always a possibility. In sum, when you have an upcoming or recent absence, email me ASAP so we can find a solution – I can’t help if I don’t know, and if too much time passes, solutions may be limited.

Religious Observances

By the end of the first week of classes, students should notify me of any planned absences for religious observances. We will work together to reasonably accommodate students who have notified in advance of absences for religious observances.



<https://www.npr.org/sections/health-shots/2019/02/09/689924838/how-to-demand-a-medical-breakthrough-lessons-from-the-aids-fight>

Students with disabilities

The University and I are committed to providing reasonable academic accommodation to students deemed eligible. This includes COVID-related accommodations.

If you require accommodation, contact the Student Ability Success Center (SASC, http://go.sdsu.edu/student_affairs/sds/). Unfortunately, I cannot provide any accommodations without prior consent of SASC.

Statement on Cheating and Plagiarism

The University and I adhere to a strict [policy regarding cheating and plagiarism](http://studentaffairs.sdsu.edu/srr/conduct1.html) (<http://studentaffairs.sdsu.edu/srr/conduct1.html>). If you cheat, you likely will receive an F for the course, and you will be referred to the University for disciplinary measures. For this class, cheating can include plagiarizing/copying answers from others or from online or other resources for assignments. Instead, work individually unless it is specified groupwork, and make sure your assignment represents your own thoughts and ideas, albeit with guidance from what you’ve learned in the literature or in class. Your writing must be in your own words. If you have questions on plagiarism, consult the [policy](http://www.sa.sdsu.edu/srr/conduct1.html) (<http://www.sa.sdsu.edu/srr/conduct1.html>). If you feel overwhelmed, make an appointment with me. Appreciate how cheating can derail and even ruin your bright future!