

CHEM 462, ADVANCED TOPICS IN BIOCHEMISTRY, SPRING 2023

Instructor: Prof. Ellinor Haglund

Contact Office: Bilger 208

Email: ellinorh@hawaii.edu

Office Hours: While I won't have set office hours for this course, I am generally available from 1 – 4 pm on Monday – Friday. Look for me in my office, or if you prefer, email me for a specific appointment time.

Classroom: Bilger 341C

Hours: Tuesdays and Thursdays at 9:00-10.15 AM

Course Goals: This class will provide an in-depth knowledge for a better understanding of advanced biochemistry, from the central dogma to protein folding and gene editing utilizing CRISPR techniques and molecular cloning important in drug discovery and human health. The course trains the ability to formulate and test hypotheses, computer-based methods such as for example basic bioinformatics tools. In addition to lectures and practical exercises, the course includes projects, discussions and a scientific writing and aims at improving the students' ability to formulate and test scientific hypotheses.

Academic Integrity: Don't cheat. Cheating in any form on an assignment or exam will, at a minimum, result in a zero grade on that assignment/exam and the filing of an Academic Dishonesty Report Form describing the incident with the Vice President of Student Affairs. I will adhere to the university policy on academic honesty found online at:

http://www.studentaffairs.manoa.hawaii.edu/policies/conduct_code/

What is cheating? For homework assignments, I encourage you to help each other and use your resources: the book, google, and more! You can share photocopies of your work, but do not copy and share screenshots of webpages. For exams, you will receive directions on what your materials you can and cannot use. You are expected to do your own work to learn the material. You cannot use other people for exams.

GOALS

Up until this point, you have learned many of the basic pathways and concepts that are relevant to the cellular metabolism of all species. These include the utilization of carbohydrates and fatty acids for energy, the storage of energy in carbohydrates and fatty acids, the metabolism of amino acids, the structure and role of proteins, the biosynthesis of lipids and biological membranes, and some very basic aspects of the coordination of these activities. Depending on the other courses you have taken, you may have learned some aspects of genetics and the storage of protein sequence information in the DNA sequence of every organism and the central dogma.

The first goal of this course is to cover advanced topics not covered in a traditional Biochemistry course, including:

1. The Central Dogma: The structure, chemistry, and function of nucleic acids. DNA Replication and DNA Repair. Maintaining the fidelity of the DNA sequence and passing this sequence on to future generations is central to sustained life. DNA Transcription and the many uses of RNA. DNA

sequence is converted to RNA, which codes for various proteins, but can also have many other purposes within the cell. RNA Translation and Protein Synthesis. Ribosomes are huge RNA-based enzymes that are capable of reading the RNA sequence and generating proteins with very specific amino acid sequences. Regulation of Gene Expression. Gene expression can be regulated at many different levels and by many different methods, including direct control through protein binding to DNA or RNA, and indirect control (epigenetics) through chemical modification of nucleic acids or proteins bound to DNA. There are also examples of gene regulation at the RNA level.

2. Eukaryotic gene editing, CRISPR/Cas9. Is a technology with the ability to change an organism's DNA *in vivo*, i.e., a type of genetic engineering in which DNA is inserted, deleted, modified or replaced in the genome of living organisms.

3. The life of a protein from synthesis and protein folding to protein degradation. Protein activity is regulated by several factors such as the rate of protein synthesis and proteasomal degradation, allosteric transitions, and chemical modifications called post-translational modifications. Most proteins need to fold into their active 3-dimensional structure to be able to perform its biological function. The process of how proteins fold is essential for life. The mechanism how proteins search through the conformational space to find its stable contacts to reach the lowest energy state is an interesting biological question that remains elusive.

4. Bioinformatics and how to use bioinformatics tools like BLAST, ClustalW2, and Sequence Logo Plot. Bioinformatics is an interdisciplinary field that develops methods and software tools for understanding biological data. Common uses of bioinformatics include the identification of candidate genes and single nucleotide polymorphisms. Often, such identification is made with the aim of better understanding the genetic basis of disease, unique adaptations, desirable properties, or differences between populations.

5. Regulation of Enzyme Function. Enzyme activity can be regulated directly, either through binding of various biomolecules or proteins, or through chemical modification, especially phosphorylation of specific amino acid side chains.

6. Hormones and Control of Mammalian Signaling Pathways. In organisms that have multiple organs and tissues, the function of these tissues must be coordinated to benefit the organism. The primary method of control is through the release, binding, and exerted action of various types of hormones and neurotransmitters. Living organisms constantly receive and interpret signals from our environment in the form of light, heat, odors, touch or sound. The cells also receive signals from other cells to keep cells alive and functioning as well as to stimulate important events such as cell division and differentiation. Signals are most often chemicals that can be found in the extracellular fluid around cells:

- ✓ **Endocrine signaling** by hormones
- ✓ **Paracrine signaling** from nearby cells
- ✓ **Autocrine signaling** secreted by the same cell

7. Cutting edge research and development of a scientific mindset. The class will be taught like a research group covering several cutting-edge research topics to prepare the students for a future in biochemical research.

The second goal of this course is to introduce you to how scientists advance the field of biochemistry through incremental improvements in our knowledge of very specific topics. We don't just wake up one day with a fully formed understanding of how things work. Based on prior studies and theories, we acquire knowledge and experience to formulate various hypotheses, decide which ones are worth testing, and devise various types of experiments that can hopefully

unambiguously prove or disprove a hypothesis. In this class you will acquire knowledge from the lectures, the book and from research articles summarized into the final research project writing a review style manuscript.

I will treat this class as a “research group” and we will study three research topics to begin to look at how scientists:

- approach a problem
- learn an appropriate amount of background information to understand the relevant issues
- ask questions about how the system works and formulate hypotheses and aims
- design experiments with appropriate controls to test the hypotheses
- present cutting edge research topics from peer review publications

In the final month of the course, you will pick an area of research you find most interesting, study the literature to arrive at some understanding of the current state of knowledge, and prepare a written research manuscript that will organize your hypotheses and previous published knowledge in the field. This will be written in the style mini-review article.

TEXTBOOK

LEHNINGER: PRINCIPLES OF BIOCHEMISTRY, 8TH EDITION

Authors: Daniel L. Nelson and Michael M. Cox, Publisher: W.H. Freeman & Co., New York, NY
We are using this textbook because it was already used for BIOL 402. Much of the information content is excellent, but the images are not particularly interesting. We will jump around and cover roughly 9 chapters in this book.

I will also occasionally be sending out PDFs of papers and copies of pages from other textbooks and online journals. Important: Please read the reading assignments before class, I will assume that you have.

This class requires consistent internet access, a computer with a web camera, and a scientific calculator. There will be assignments where you will need pen and paper.

LECTURES & DISCUSSIONS

- The class will be divided into 4 Modules. The class will be taught by Dr. Ellinor Haglund (the main instructor) and one guest lecturer, Dr Jesse Owens.
- Most lectures will be based on the textbook or peer reviewed scientific articles.
- Lectures will be very informal. I want this to be more like a group meeting where we come to a collective understanding of how the experimental system works.
- We will also have instructor and student-led discussions of journal articles.

HOMEWORK, QUIZZES & EXAMS

- Reading assignments will be given prior to each lecture.
- There will be short pop quizzes throughout the class. Typically, the quiz will be short answer questions that will take ~15-20 min.
- There will be 3 exams throughout the semester and a final writing assignment.

WRITING ASSIGNMENTS

Students must adequately complete all writing assignments to pass the course with a D grade or better. Students who do not complete all writing assignments will get a D- or an F.

- Students will prepare a research manuscript written as a review article based upon an independent research idea. This idea can be based on journal articles or the work of a specific scientist but should be a new idea or concept that extends the current published work.
- Draft versions of each component of the manuscript will be turned in or uploaded to Laulima with specific due dates.
- Feedback on content and writing style will be provided through peer reviewing.
- Project summary (abstract) and specific aims – email feedback from the instructor
- Intro and Background – peer review from another student
- Summary and Future directions– in-class writing workshops studying successful publications in Trends in Biochemical Science (TiBS).
- The final version of the manuscript will be due in class on the last day of the semester.

PRESENTING ASSIGNMENTS

Present a research paper covering different mammalian signaling pathways involved in cell signaling. The presentation will be done in groups covering the six signal transduction pathways. Each presentation should cover the main pathways and cell responses, the receptor-ligand structures (if known or predicted by AlphaFold), and ligand-receptor interactions. Their individual role in human health and possibility to be used as drug targets.

TENTATIVE GRADING BREAKDOWN

Exams: There will be three Midterm Exams. Make-up exams will *NOT* be given. Exams will be in person on the assigned day and time on the course calendar. Only excused medical absences will allow students to take an exam at a later date. Contact me ASAP if you miss an exam, otherwise, no credit will be given. Any medical emergency must be documented by a hand-written doctor's note by a local doctor with a physical address and phone number on the heading of the note. Accommodations for conflicting work schedules, vacation plans, or any other non-emergency situations will not be made. Make-up exams or early exams are at the discretion of the professor, regardless of the excuse.

Homework: Homework will be assigned weekly. You are responsible for checking deadlines and completing your homework on time. No late Homework accepted.

GRADING

- ✓ **Module 1 (Exam 1):** Focus on previous knowledge about the central dogma, i.e., from DNA-to-proteins the first week of the semester (The exam will be curved at a B average): Total of 10%
- ✓ **Module 2 (including Exam 2), by Dr Jesse Owens:** Total of 20%
- ✓ **Module 3, Home Exam (Exam 3) and Cell Signaling Presentation:** Total of 20% + 10% respectively for the mini-review and group presentation covering the different cell signaling pathways, Tot of 30%

- ✓ **Module 4, Mini-Review (Final Project):** There will be NO final exam. The final version of the manuscript will serve as your final project and will be due on the last day of class: Total of 30%
- ✓ **Quizzes and Homework:** Total of 10%

Approximate grading scale: Letter grades will be determined based on your percentage and are up to the discretion of the professor. Grades will be rounded to the nearest 0.1%. For example, 89.69% rounds to 89%, which is a B+.

A+ 98 – 100	B+ 87 – 89	C+ 77 – 79	D 50 – 69	F < 49%
A 94 – 97	B 84 – 86	C 74 – 76		
A- 90 – 93	B- 80 – 83	C- 70 – 73		

STUDENT LEARNING OUTCOME

- Students will understand the chemical principles that underlie DNA replication and transcription, and RNA translation and protein synthesis.
- Students will understand the interplay between methods for regulating networks of biochemical reactions, including genetic regulation, hormones and signal transduction, and protein activation and inhibition.
- Students will understand how biochemical reactions can be described at an atomic level, including how enzyme catalysts and cofactors can accelerate difficult reactions.
- Students will use literature search processes to gain knowledge of recent advances in biochemistry, develop a hypothesis-driven research proposal, summarized as a review article.
- Students will develop a scientific mindset and prepare them for real life experiences from protein biochemistry, human health, and drug discovery

ATTENDANCE AND PARTICIPATION

Attendance at class sessions is expected.

LATE POLICY

Deadlines will not be extended. Do not waste your time asking me for extension (except with valid medical and civic reasons). No-make up exam will be given. For missed exams, a medical note, police report, or obituary notice is required.

KOKUA

Students with conditions that may require test accommodations are encouraged to contact me privately and contact the KOKUA Program (the Office for Students with Disabilities). KOKUA can be reached at (808) 956-7511 or (808) 956-7612 (voice/text) in Room 013 of the Queen Lili'uokalani Center for Student Services. If you are a student with a disability, please contact KOKUA to make arrangements to provide you with the best learning environment possible. I will be happy to work with you and KOKUA to address your access needs.

OTHER POLICIES

A tentative topic and schedule are listed in the Schedule (sent separately). Topics may be modified throughout the semester. Announcements will be sent by email and through Laulima.

ACADEMIC MISCONDUCT

UH Manoa Student Conduct Code Executive Policy 7.208. IV.B.1a “Acts of dishonesty, including but not limited to the following: Cheating, plagiarism, or other forms of academic dishonesty. Cheating is an act of academic dishonesty and includes, but is not limited to: (1) use of any unauthorized assistance in taking quizzes, tests, or examinations; (2) use of sources beyond those authorized by the instructor in writing papers, preparing reports, solving problems, or carrying out other assignments; (3) the acquisition, without permission, of tests or other academic material belonging to a member of the UH faculty, staff or student body; and (4) engaging in any behavior specifically prohibited by a faculty member in the course syllabus or class discussion.

Plagiarism is also an act of academic dishonesty and includes, but is not limited to, the use, by paraphrase or direct quotation, of the published or unpublished work of another person without full and clear acknowledgement. It also includes the unacknowledged use of materials prepared by another person or agency engaged in the selling of term papers or other academic materials.”

Plagiarism penalty: First offense, students will be asked to re-write the report without the offending material and will be given lower credit(s) if they do so. Subsequent offense: student will receive zero credit and the matter will be referred to the Department Chair and Dean for further action.

Likewise, cheating on an exam will be dealt with severely. A student will receive no credit for the entire exam, and the offense will be reported to the Department Chair and Dean for further action.

UHM TITLE IX SYLLABUS INFORMATION

The University of Hawaii is committed to providing a learning, working and living environment that promotes personal integrity, civility, and mutual respect and is free of all forms of sex discrimination and gender-based violence, including sexual assault, sexual harassment, gender-based harassment, domestic violence, dating violence, and stalking. If you or someone you know experiences any of these, UHM has staff and resources on campus to support and assist you. Staff also can direct you to resources in the community. Here are some of your options:

If you wish to remain **ANONYMOUS**, speak with someone **CONFIDENTIALLY**, or would like to receive information and support in a **CONFIDENTIAL** setting, contact:

Office of Gender Equity

The Office of Gender Equity offers direct services to victims and survivors of sexual harassment and sexual assault. Services offered include crisis screening and assessment, case referral, safety planning and risk assessment.

Paxon Chang (available Tuesdays, Wednesdays, and Fridays)

Telephone: (808) 956-9499

Email: geneq@hawaii.edu

Queen Lili‘uokalani Center for Student Services 210 2600 Campus Road
Honolulu, HI 96822

Website: <https://blog.hawaii.edu/genderequity/>

UH Confidential Advocacy

The UH Confidential Advocates provide confidential advocacy services and case management to victims* of sex discrimination and gender-based violence (including sexual harassment, gender-based harassment, dating and domestic violence, stalking, sexual exploitation, and sexual assault) who are involved in the University system on Oahu.

Natalia Villegas

Telephone: (808) 341-4952 Email: nataliat@hawaii.edu

Pop in/Walk in Services:

Join Zoom Meeting: <https://hawaii.zoom.us/my/hccmanoaadvocate>

Mondays: 1PM – 3:30 PM

Tuesdays: 9:30 AM – 12 PM

Wednesdays 9:00AM – 11:00AM

Thursdays 4:30PM – 6:30PM **Student Parents At Mānoa (SPAM)**

Student Parents At Mānoa (SPAM) seeks to increase the visibility of and resources for student parents at UH Mānoa as they pursue education while parenting. SPAM staff provide advocacy, support, and referrals for pregnant and parenting students to help them succeed in their educational goals.

Teresa Bill

2600 Campus Road

Queen Lili‘uokalani Center for Student Services 211 Honolulu, HI 96822

(808) 956-8059

gotkids@hawaii.edu

<http://manoa.hawaii.edu/studentparents/>

Counseling and Student Development Center (CSDC)

The Counseling and Student Development Center (CSDC) offers support to UHM students, staff, and faculty to assist with personal, academic, and career concerns. All services are confidential, and most are free of charge for Mānoa students. They also offer free consultation to faculty and staff on personal and student-related issues as well. CSDC office hours are from 8:00 a.m. to 4:30 p.m., Monday through Friday. They also offer immediate walk-in appointments for urgent or emergency/crisis services during their regular daily hours.

Queen Lili‘uokalani Center for Student Services 312 2600 Campus Road

Honolulu, HI 96822

(808) 956-7927

uhmcsdc@hawaii.edu

www.manoa.hawaii.edu/counseling

University Health Services Mānoa (UHSM)

The University Health Services Mānoa (UHSM) is staffed by physicians, nurse clinicians, nurses, and other support staff, and offers a wide range of medical services and programs to UH Mānoa students, with many of the services also available to UH Mānoa faculty and staff and students from other UH campuses. Services include general medical care on a walk-in basis; women’s health, sports medicine, psychiatry, and dermatology clinics by appointment; pharmacy and clinical laboratory; and student training, employment and volunteer opportunities.

1710 East West Road
Honolulu, Hawaii 96822
Honolulu, HI 96822
(808) 956- 8965
www.hawaii.edu/shs/

or

If you wish to remain ANONYMOUS, speak with someone CONFIDENTIALLY, or would like to receive information and support in a CONFIDENTIAL setting, contact the confidential resources available here: <http://www.manoa.hawaii.edu/titleix/resources.html#confidential>

If you wish to REPORT an incident of sex discrimination or gender-based violence including sexual assault, sexual harassment, gender-based harassment, domestic violence, dating violence or stalking as well as receive information and support, contact:

Dee Uwono
Director and Title IX Coordinator
Hawai'i Hall 124
2500 Campus Road
Honolulu, HI 96822
(808) 956-2299
t9uhm@hawaii.edu

As a member of the University faculty, I am required to immediately report any incident of sex discrimination or gender-based violence to the campus Title IX Coordinator. Although the Title IX Coordinator and I cannot guarantee confidentiality, you will still have options about how your case will be handled. My goal is to make sure you are aware of the range of options available to you and have access to the resources and support you need. For more information regarding sex discrimination and gender-based violence, the University's Title IX resources and the University's Policy, EP 1.204, go to: <http://www.manoa.hawaii.edu/titleix/>