CHM 6306 – Special Topics in Biological Chemistry
"Structural and Biophysical Methods for Studying Cell Surface Receptor Proteins"

Spring 2020

Instructor

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Lectures

T 3 – 3:50 PM, Th 1:55 – 3:50 PM, JHH 323 (3rd floor conference room)

Office Hours

Wed 3 – 4, and by appointment; I am also generally available via email

Required Textbooks

No required textbooks.

Recommended Reading

Recommended readings will be announced in CANVAS and posted prior to the corresponding lecture by the instructor. Additionally, "A Pharmacology Primer: Techniques for More Effective and Strategic Drug Discovery" by Terry Kenakin, 4th edition and "The Membranes of Cells" by Philip L. Yeagle are texts that will be utilized throughout the course.

Course Description

This course presents an overview to modern biophysical and structural biology techniques employed in the study of membrane proteins, with special emphasis on integrative techniques used to study human G protein-coupled receptors (GPCRs). GPCRs are integral membrane protein cell surface receptors found in the plasma membranes of Eukaryotic organisms. Background information will be provided on cell signaling generally and the biochemical and biophysical tools used to investigate cell surface receptors. This will serve as a foundation for students to critically evaluate and present current relevant literature. Broadly, topics include: structural biology (i.e., x-ray crystallography, cryo-EM, and nuclear magnetic resonance), pharmacology, biological membranes and their properties, protein engineering, and applicable biophysical methods (e.g. fluorescence-based techniques, ligand binding techniques, etc).

Course Objectives

Major goals for completing this course are for students to be able to critically evaluate current topical scientific literature and to clearly communicate their own independent scientific ideas in writing and through oral and written presentations. Additional goals are for students to develop a broad understanding of different biophysical methods and their relative strengths, and how information from different biophysical and structural techniques can be integrated and compared with correlative functional assays to provide a comprehensive view of protein structure-function relationships.

Grading

Grades will be determined from the following criteria:

25% Class participation
30% In-class presentations
30% Written topical review paper
15% Final Presentations

The following is the grading scale for this class:

A 90% - 100%
B 80% - 89 %
C 70% - 79 %
D 60% - 69 %
F 50% - 59 %

Cell Phones

Please put all cell phones and other digital devices on “silent mode” during all class periods and avoid use during class.

Class Attendance and Make-Up Policy

Class attendance and participation is expected. Late final project proposal papers will not be accepted.

Students Requiring Accommodations

Students with disabilities requesting accommodations should first register with the Disability Resource Center (352-392-8565, www.dso.ufl.edu/drc/) by providing appropriate documentation. Once registered, students will receive an accommodation letter which must be presented to the instructor when requesting accommodation. Students with disabilities should follow this procedure as early as possible in the semester.

Course Evaluations

Students are expected to provide feedback on the quality of instruction in this course by completing online evaluations at https://evaluations.ufl.edu. Evaluations are typically open during the last two or three weeks of the semester, but students will be given specific times when they are open. Summary results of these assessments are available to students at https://evaluations.ufl.edu/results/

Materials and Supplies Fees

There are no additional fees for this course.

University Honor Policy

This class will operate under the policies of the student honor code, which can be found at: http://www.registrar.ufl.edu/catalog/policies/students.html. The students and instructor are honor-bound to comply with the Honors Pledge: *We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honesty and integrity.*

More specific to this course is the expectation that any submitted written assignments are in your own language. This means that submission of verbatim or nearly-verbatim text taken from other sources and repurposed for your own assignments without proper acknowledgement of the original citation will be considered a violation of the honor code and treated as such.

Counseling and Wellness Center

Contact information for the Counseling and Wellness Center:
http://www.counseling.ufl.edu/cwc/Default.aspx, 392-1575; and the University Police Department: 392-1111 or 9-1-1 for emergencies.

Tentative Lecture Schedule

Weeks	Dates	Topics	Review Article Dates
1 – 2	Jan 7 – Jan 14	Introduction to pharmacology, receptor theory, overview of cell surface receptors	
2	Jan 16 – 21	Molecular biology of GPCRs and signaling, introduction to GPCR topology	
3	Jan 23 – 30	GPCR structural biology (part 1): x-ray crystallography and protein engineering	**Jan 24: Prospectus Due**
4	Feb 4 – 11	GPCR structural biology (part 2): x-ray crystallography & cryo-EM	**Feb 10: Reference List Due**
5	Feb 13 – 20	Conformational Dynamics of Membrane Proteins Part 1: NMR in xolution	**Feb 17: Outline Due**
6	Feb 25 – 28	Conformational Dynamics of GPCRs Part 2: NMR in solution and in solids	
7	March 3 – 5	Spring Break	**March 2: Figures & Figure Legends Draft Due**
8	March 10 – 12	Conformational Dynamics of GPCRs Part 3: fluorescence techniques	
9	March 17 – 19	The structures, chemical, and physical properties of biological membranes	**March 16: Draft 1 Due**
10	March 24 – 26	GPCRs, membrane proteins, and methods for studying lipid-protein interactions	**Instructor Comments Returned**
11	March 31 – April 2	GPCRs & biological membranes continued	**April 6: Peer Reviewer Comments Due**
12	April 7 – 9	Advanced topics 1: polypharmacology, biased signaling, structure-based drug design	
13	April 14 - 16	Advanced topics 2: optogenetics, designer drug-receptor systems	**Presentations During Final Week of Class**
14	April 21	Final Presentations; Last day of class April 21	**April 25: Final Papers Due**

Description of Class Assignments

1. Current Opinions Review Article

A primary activity of the course will be writing a short review article on a topic in the area of "GPCR Structural Biology" in the style and format of Current Opinions in Structural Biology.

You may find the instructions to authors here:
https://www.elsevier.com/journals/current-opinion-in-structural-biology/0959-440X/guide-for-authors

This activity will take place over the entire course and involve several individual assignments as described, below. Specific due dates are included in the syllabus.

A. Prospectus. Write a short paragraph describing your proposed topic. In your paragraph include a broad description of the topic, specific sub-topics you wish to explore, Describe the significance of the topic to science and why the topic would be of interest to a broad audience. This will serve as your abstract in the first draft of your paper.

- Pick an area you would like to know in more depth.
- You may select a topic covered in class but using literature that is complementary to papers covered in class.
- Ideally look for an area that has been reviewed, but not very recently, and provide a comprehensive update.

B. Key literature list. Create a list of the top 15 or more review articles and papers that you are likely to cover in your review article. You need not have read the articles in detail yet, but they should cover the most recent articles in the area (i.e. no papers older than 2007)

- Start by searching for your topic using pubmed (https://www.ncbi.nlm.nih.gov/pubmed/); for example search "GPCR drugs and cancer" and scan the publications in the last 2 years.
- Try variations on your topic phrase and use the "See reviews" and "See similar" options under the Similar Articles section
- Create a folder and download PDFs papers you think you may cover, cast a broad net, then go back and iteratively refine the collection of PDFs until key trends or areas emerge.

C. Outline. Write an outline that covers the background and recent advances in your topic area. The outline does not need to be detailed, but must cover your entire article and include an attempt to organize section headings and topic sentences for each paragraph. You may use the following format as an example:

TITLE

1. Abstract
2. Background
    a. Topic sentence
        i. Fact
        ii. Detail
        iii. Summary sentence
2. Section heading
    a. Topic sentence
        i. Fact
        ii. Point
        iii. Transition sentence
    b. Topic sentence
        i. Fact
        ii. Point,
        iii. Concluding sentence

- This is the hardest part of the process and will take the most time, plan accordingly.
- You may need to research more of the literature or expand your literature list as you develop your outline.
- Try reading the abstract of each article and scanning the text, take notes on each paper either electronically or by hand for each of the papers in your literature list.
- Identify key trends or sub-topics from your notes and from those covered in relevant review articles. Use these trends/topics to write your section headings.
- Do not be afraid of iterative revision in developing your outline. Start with a broad perspective rough draft and add detail as you become more familiar with the individual papers in your literature list. However, you will probably need to revisit your overall organization more than once during this process.

D. Figures. Provide a draft of the key figures and text of the figure legends to be included in your review. This will include both adapted figures from the literature you have collected and 1 to 2 original figures that illustrate a major concept or theme from your topic.

E. Draft 1. Expand your outline into a rough draft of your entire article that includes all sections. Try to identify (underlining helps) the topic sentence and conclusion/transition sentence for each and every paragraph. Ideally, these will come from the second level of your outline. Comments will be returned with suggestions on length and coverage as soon as possible after submission (a few days hopefully!)

F. Draft 2. Revise your Draft 1 according to instructor comments and your own revisions based on re-reading your draft and literature list. This draft does not have to be perfect, but must is expected to be much improved. Although it is understood that these are still in draft stage, keep in mind that your Draft 2 will be shared with two classmates for comments, so take care to submit a draft free of typos and incomplete sentences.

G. Reviewer comments. Read and provide feedback and comments on the two Draft 2 articles you are assigned. The goal of this exercise is to help improve the final submitted articles, as well as to develop skills in providing useful and collegial feedback to colleagues on their writing and critiquing their ideas.

- Use the "track changes" feature of MS word, or type your comments and provide as a separate document.
- Be collegial and provide constructive and supportive feedback to your classmates. Be considerate and image that you are talking to them in person when writing your comments.
- If you have strong negative opinions about one of your articles that you believe need to be conveyed, then provide them to the instructor.
- Identify strengths as well as weaknesses and include them in your comments.
- Help your classmates with the clarify of their writing, and try to provide specific examples of alternative text if possible.

G. Final submission. Submit your final version by email after incorporation of comments from reviewers. You may feel free to have other readers provide comments as well.

2. Journal Article Presentations

- Select a paper from the suggested list, or identify one from the current literature with permission of instructor.
- Create a Powerpoint presentation that has a few slides that introduce the topic, one or more slides for each figure, and a conclusion slide that summarizes the main points of the paper.
- Please do not go over time. You do not need to cover every detail in the paper. Identify and focus on the key point or points, or select a specific technique or experimental approach to cover.
- Try to construct a narrative with a beginning, middle and end.
- Consider foreshadowing a key aspect of the main conclusions at the beginning of your presentation, then coming back to them as you proceed through each figure.
- For each figure using the following general framework to organize the discussion
    - o What question are the authors asking in this experiment?
    - o How is the experiment designed to answer this question?
    - o What result is observed and does it answer the question?

    - o Do you believe the interpretation? What limits to the interpretation do you see?
- Animations and advanced graphics are useful, but your oral description of the slides is most important
- Be critical (without being insulting). Consider how you would do things differently, or specific questions you would ask the author.

3. Final Topic presentations.

For the last week of class each student will present an overview of their review article. The goal of this exercise is to convey what you have learned in writing your article to the rest of the class. It is not required, but you may elect to share your final submission of your review articles with the rest of the class. Your presentation does not have to be lengthy, select a particular conceptual or experimental advance that you think the class should know and address is concisely.

- Create a short Powerpoint presentation that includes the figures of your review article and any background or conclusion figures required for clarity.
- Focus on a particular important, surprising or novel insight you gained in writing your article.
- Write a scripted 20 minute presentation (essentially a voiceover for your presentation) that covers the main points for each figure.
- Write a strong concluding statement of sentence that concisely sums up your topic. Feel free to reinforce or reiterate key themes or points addressed in class.

4. Class participation

- Read the papers before class! Increased awareness of the current GPCR structural biology literature is a primary learning objective of the course.
- Do not be frustrated if you do not comprehend every detail in the paper. Select among the things you do not understand a few specific questions that you have or experiments that your do not understand and bring them up in class.
- Do not hesitate to ask very basic questions. It is understood that the experience level of different students will vary widely.
- The expectation is that the understanding of GPCR function and, more generally, structural understanding of receptor-drug interactions, will improve significantly for all students but the starting and ending points for levels of understanding may differ.
- Students with more advanced understanding of molecular biology are expected to help answer basic questions by less experienced students.
- Do not be discouraged if at first you are confused by the level of detail or pace of the course. This is a crash course in modern membrane protein structural biology and related topics, which is intended to convey some fundamental concepts and inform you on the most up to date topics in structural biology.