BCH 610  Biochemistry of Lipids and Membranes: Spring, 2014

CLASS SCHEDULE: Tues. and Thurs. 2:00-3:15 PM is proposed, but a final decision will be discussed at the first class meeting in B231 BBSRB.

INSTRUCTORS:
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PREREQUISITES:  Two semesters of organic chemistry, one semester of physical chemistry, a comprehensive general biochemistry course.

SCOPE AND OBJECTIVE:  This course will cover basic concepts and technologies in membrane and lipid biochemistry. The major objective will be to critically evaluate the current literature on the biophysical properties, molecular architecture, bio-assembly, and various functions of cellular membranes, as well as the mechanisms involved in the translocation of membrane proteins and lipids from the sites of synthesis to their subcellular residence(s). Selected topics on the structure, physical state, biosynthesis, assembly, and function of membrane-associated molecules in transmembrane signaling and other cellular processes will be discussed. The course will be primarily literature-based, using both assigned reviews and original papers. The technical approaches and experimental strategies used in studies that have contributed significantly to advancing the basic understanding of important aspects of membrane biochemistry and membrane biology will be emphasized.

During the course each student will lead a 20 minute discussion of assigned papers (discuss your presentation with an instructor in advance).

During each class, all students are expected read the assignments prior to class and to participate actively in class.

Final grade will be based on:

Two In Class Exams  (25% each)
Class Presentation  (15%)
Class Participation  (5%)
Primary Reviewer’s Report and Presentation  (5%)
Term Paper (in lieu of a final exam)  (25%)

A = 90-100; B = 80-89; C = 70-79; E = 0-69.
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Ground Rules and Objectives for BCH 610 Term Paper (This is not the NIH format. You are requesting funding from the BCH610 Foundation, so follow our instructions.)

The objective of the term paper is to provide a format so you can apply the knowledge you have gained in this course to solve a scientifically interesting problem in membrane biochemistry and cell biology. This experience will help graduate students in the basic sciences develop the skills needed to write an effective grant application. The proposal may be a logical extension of a currently "hot" area of research in membrane biochemistry or a novel, hypothetical problem based on topics covered during this course. Potential topics must be discussed with and approved by one of the course lecturers. The process should take the whole semester. You may not use your own research topic.

**FORMAT:** The paper is to be written as a mini-grant proposal.

**Title:** Provide a clear descriptive title. Do not exceed 56 total characters and spaces.

**Hypothesis:** Clearly state a hypothesis. A hypothesis can be a description or model of how you think a particular biological process can occur. It must be testable.

**Specific Aims:** List a small set of specific aims (2-3) that you will undertake to support your hypothesis (or not). (no more than one page)

**Background and Significance:** Use this section to describe how you derived your hypothesis and to support your experimental approach. State clearly the problem you will try to solve and explain why it is a significant scientific problem. Describe what pertinent information is already known and precisely what gaps in this information will be filled by your proposed research.

**Experimental Design:** For each specific aim give sufficient experimental details to permit the reader to evaluate the possibilities of success and your knowledge of the problem. It is wise to offer alternative experimental approaches to achieve a given Specific Aim, in case your initial plan does not work. Include, in this section, possible experimental outcomes and their interpretations. How will your data support your hypothesis (or not)?

**References:** Complete list of references cited in grant. Please include complete titles.

**Text format:** single line spacing with 2 cm margins (top/bottom and left/right) and 11 point Arial type font. Deviations will not be accepted. Place page numbers at the bottom of the page. Text in Figure Legends should be no smaller than 9 point.

**Page limitations:** Title, Introduction, Hypothesis, and Specific Aims (1 page), Background (4-5 pages), and Experimental Design (4-5 pages): a **maximum of ten pages total** (not including References). Print a separate coversheet with your name and the grant title. Do not include your name in the body of the grant but do include the title on the first page.

**Review Panel Meeting and Report:** Each student will be assigned to be primary reviewer of one grant proposal. The primary reviewer must evaluate the proposal and determine its scientific soundness and feasibility based on the current knowledge of the field. The reviewer will be required to write a one page critique of the proposal including a one paragraph summary of the work proposed and a description of the grant’s strengths and weaknesses. The primary reviewer will also be responsible for orally presenting (in 10 min) the grant to the review panel on April 22 or 24.

**Deadlines:** Not meeting these deadlines will result in a loss of 5 points from the final grade.

Jan. 30 Last date to choose a topic. You must hand in a short summary of the topic (<1 page).

Feb. 27 Have a **Hypothesis** and set of **Specific Aims** approved by the instructor familiar with the topic you have chosen. A draft of this section (1 page) must be handed in.

Apr. 3 Grant must be submitted to the review panel, by email as a PDF file before 5:00PM.

Apr. 22, 24 Review Panel Meetings

May 7 before 5:00 PM a Paper Copy of Final Grant is Due
2014 Student Presentations:  This should be a ~20 minute presentation of the key points of the papers listed below. (You do not need to show all of the figures.) Discuss the presentation with the relevant instructor at least one week prior to the assigned date so that your presentation can be coordinated with the rest of the class time.

Jan. 28  vd Kooi  Physical Properties of Biological Membranes

Jan. 30  Rush  Structure and Isolation of Membranes

Feb. 6  Waechter  Flippases & Topology of Membrane Lipid Biosynthesis

Feb. 27  Dickson  Sphingolipid Signaling 2

Mar. 11  Dutch  Other Viral Membrane Fusion Systems

Mar. 27  Galperin  Endomembrane Systems 2

Apr. 8  vd Westy  Regulation of Cholesterol Biosynthesis II

Apr. 29  Whiteheart  SNARE Hypothesis
2014 Class Reading List: Most of the assigned papers are now online. However, there are a few that are not. Those can be “borrowed” from the lecturer. We recommend (strongly encourage!!) that you download the papers and read as many as you can prior to the class session. Get a ring-binder to keep them in.

Jan. 21 Vander Kooi Physical Properties of Lipids and Membranes


Jan. 23 Vander Kooi Physical Properties of Membrane Proteins


Jan. 28 Vander Kooi Physical Properties of Biological Membranes


Jan. 30 Rush Structure and Isolation of Membranes


Fleischer, S., and Packer, L., eds. (1974) "Biomembranes." *Methods in Enzymology* Vol. XXXI (For use as a good general reference for the isolation of subcellular fractions from mammalian and prokaryotic cells, read sections as appropriate for your use.).


**Feb. 4 Rush**

**Extraction and Separation of Lipids: Applications**

Higgins, J. A. (1987) "Separation and Analysis of Membrane Lipid Components." Chapter 4, pp. 103-137 in *Biological Membranes: a practical approach* (ed. J. B. C. Findlay and W. H. Evans) IRL Press. (Handout. Read through section 1.3 in detail, be familiar with the specific examples in the remainder of the chapter; the chapter contains some very useful examples of the application of classic techniques of lipid extraction, separation and analysis to study membrane lipids).


**Feb. 6 Waechter**

**Flipases and Topology of Membrane Lipid Biosynthesis**


**Feb. 11 Waechter**

**Lipid-Mediated Protein N-Glycosylation in the ER**


Feb. 18  Rush  Quality Control in the ER


Feb. 20  Whiteheart  Translocation of Proteins into the ER


Mar. 6 Dutch Influenza Viral Membrane Fusion


Mar. 11 Dutch Other Viral Membrane Fusion Systems


Mar. 13 Galperin Endomembrane Systems 1

Clathrin-dependent, -independent endocytosis, recycling, endocytic machinery for cell motility and adhesion


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Mar. 25 Galperin Endomembrane Systems 2

Mechanisms of receptor endocytosis and signaling: adaptor molecules and ubiquitination/endocytic machinery in receptor endocytosis: RTKs (EGF, TGFβ), GPCR + β-arrestins) and NOTCH signaling).


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Mar. 27 Galperin Endomembrane Systems 2

Post-endocytic receptor trafficking: sustained signaling in endosomes (EGFR and TrkA), signaling attenuation, ESCORT complex, late endosomes and exosomes


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**Apr. 1 Whiteheart The Golgi Complex**


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**Apr. 3/8 Westy Regulation of Cholesterol Biosynthesis I/II**


Apr. 10 Westy Cholesterol Trafficking in Cells


Apr. 17 Whiteheart Transport Vesicle Production


Field MC, Sali A, Rout MP. (2011) “Evolution: On a bender--BARs, ESCRTs, COPs, and finally getting your coat.” J Cell Biol. 193, 963-72. (Review)


Arp. 29/May 1 Whiteheart SNARE Hypothesis / Regulation


