BCH 600.01: Cell Organization and Mechanisms

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G 600 Cell Organization and Mechanisms. Offered every other spring. Prereq., BCH 480 or consent of instr. Same as BMED 600. Primary literature exploration of the regulation of structure, function, and dynamics of eukaryotic cells. Topics include membranes, cytoskeleton, transcription, translation, signal transduction, cell motility, cell proliferation, and programmed cell death.

Overview

Cell Biology is vast and dense and encompasses biochemistry, biophysics, molecular biology, microscopy, genetics, physiology, bioinformatics, and developmental biology. We will explore the topics listed below by reading reviews and papers from the primary literature. Papers will be chosen, where possible, that are at the interface between two fields, so a large amount of background reading will be necessary to understand the paper and put it in context. The main learning goals are 1) to learn about a number of topics in cell biology; 2) understand a number of laboratory techniques, their purpose, and how to interpret and evaluate data derived from them; and 3) to gain the confidence and skills to attack any scientific paper even if it is in an unfamiliar area; in other words to learn how to learn new things. Alberts, et al., Molecular Biology of the Cell, (Garland Science; 7th edition) is recommended as excellent textbook that frames the background as we explore the primary literature. (The 4th ed. is available online at http://www.ncbi.nlm.nih.gov/books/NBK21054/. Lodish et al., Molecular Cell Biology, 7th ed. may be substituted if you have already purchased this book. Lecture figures will come from Alberts, et al. and reviews.)

Format

We recognize that students (and human beings in general) have diverse learning styles, personal styles, ethnicity, gender, nationality, and experience. Science is about learning new things, and communicating these things to other people, regardless of this diversity among people.

Presentations will be made by the instructor and graduate students. Instructor will optionally introduce a topic with a lecture, and a student presentation of a paper with data will follow in the next session. The weekly assignment is to read the primary paper(s) and review article(s) for the topic, and prepare to ask at least one question during class.

We intend a relaxed atmosphere where we all ask questions, and no questions are dumb questions. All students will be required to read all papers and ask questions of the presenter. It is expected that the student presenting the paper will be well informed on the topic, which will require extra work. While errors and misunderstandings are forgivable, we expect you to make an effort to understand the paper being presented, especially if you are the one presenting it!

When tackling any research paper in an unfamiliar area, the best way to start is by reading one or more textbooks (use the index and table of contents) and reviews, looking up unknown concepts mentioned in the paper’s introduction (often reviews are cited there too). Then look at the data in the figures. If you don’t understand the methods, look them up. Then read the results and discussion, and decide whether the author’s interpretation of the data is the same or different than yours.
Writing assignments will be a one page summary of the primary paper due the day of the paper presentation, which includes a question to be asked during class, followed by a revision plus a one-half page new hypothesis, question, and experiment that arises from the presented paper.

Presentations

The student's presentation should set the stage for the paper being presented with a brief introduction that draws on recent reviews or textbook figures. Keep in mind the following questions when presenting a paper. What is the hypothesis? What is the key question being addressed by the experiments? What are the key experiments that address the question? Do you believe their interpretation, and did they do the proper controls? Many of the methods used to study cell biology and biochemistry are evolving, and far from perfect, so it is important to look with a critical eye at the data, the methods used to obtain the data, and how the data are interpreted.

Students’ presentation papers will be assigned in advance to allow time for preparation. Graduate students will be assigned one paper from the list below to present to the rest of the class. Before the student presentation to the class, the student will prepare a draft presentation and go over it with the instructor (Mark). The presenter should make sure that the all students understand the background, motivation, hypothesis, question, experimental techniques, data from key experiments, and conclusions in the paper. The expectations for the students in the audience are to ask questions - no questions are dumb questions - to make sure the presentation is clear; and ensure that you understand laboratory techniques used for the key experiments the paper. The presentation to the class should describe key experimental technique(s) and how to interpret the data when presenting the data.

Written questions from all students (except presenting students) will be required for student presentations, and students will be expected to ask those questions (and other questions) during class. There is no such thing as a dumb question!

Writing Assignments

Paper summaries. For all students except for the presenters: one for each paper from the primary literature. Due on the day of the paper presentation as a pdf file uploaded to moodle before the presentation. Put your name and assignment name in the header, and name your file: “YourNameAssignmentName.pdf.” One page maximum, 11 point font minimum. In your own words (do not cut and paste from the paper), in a cohesive summary paragraph, write one-two sentence(s) to answer each question:

1. What is the research topic/question and why is it important/interesting? Include at least one statement of hypothesis, as in, “The authors hypothesize that cortactin binds to a protein at the plasma membrane.”
2. What method/approaches are used? When describing experiments, motivate them as a question. For example, “The investigators asked whether cortactin and protein X were co-localized at the plasma membrane using two experimental approaches…”
3. What are the main results of the paper? (This may take three-four sentences, but should not include experimental details.)
4. What are the conclusions from the experiments, and the significance?
5. What would you like to know more about/understand better? Write down at least one question that you plan to ask the presenter.

The typical timing is expected to be: summaries are due before student presentations on Fridays; revisions due the following Wednesday.

Using AI tools. The student conduct code has recently bee revised to include this definition.

• Plagiarism: Representing words, ideas, data, or materials of another person as one’s own, the student’s own previous work as if it were the student’s own original work, or content derived directly from a generative artificial intelligence tool as if it were the student’s own original work.

This means that you should clearly identify any text in your writing assignments that was generated using generative AI.
Nevertheless, AI has rapidly become a tool that we should not ignore. There are several free services and now we can sign into Microsoft Copilot using our UM ID email.address@umt.edu. So, let's try an experiment. Write version 1 of the paper summary without using any generative AI assistant. Then test it in the following way.

**Revisions:** The intent for the rewrite is 1) to clear up your thinking and writing after we discuss the paper in class and 2) to come up with a new hypothesis, question, and experiment in the topic. 

1) After the presentation, construct a series of prompts to a generative AI of your choice based on criteria in the text above (hypothesis, methods, results, conclusions, question). Compare your first version to the AI’s version. Using your improved understanding derived from discussing the paper in class, rate your summary and the AI’s summary for accuracy. Then revise your summary according to your (hopefully) better understanding of the paper after the presentation and address any requested revisions or clarifications. Do not copy the AI’s sentences exactly (even if you like them).

2) In the revision, use an additional one-half page maximum to identify a hypothesis and question that emerges from the paper that represents a next step towards understanding the biological mechanism under study. What technique(s) would you use to answer the question with an experiment? Keep this brief, but think about it carefully. Use the review article(s) to help frame the hypothesis and question. Think of this as a rough draft of an idea for a proposal. If you would like to use generative AI for this, go ahead, but please clearly identify any AI-generated sentences and ideas, and show the prompts you used as references or footnotes. (This practice should be used for any writing assignment in this class, and likely beyond. We are learning as we go!)

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**Bioinformatics assignment**

1. See [http://www.ncbi.nlm.nih.gov/guide/](http://www.ncbi.nlm.nih.gov/guide/) and [http://www.genenames.org/](http://www.genenames.org/). Pick a gene, preferably a gene from the paper you will be presenting (you may find this exercise useful as background information for your presentation), and find its HUGO gene name, nucleic acid and protein sequence, and domain structure. If there is a structure for the protein, find the structure. Use [http://stitch.embl.de](http://stitch.embl.de) to ask if any drugs bind to the protein; [http://www.hprd.org](http://www.hprd.org) and [http://www.phosphosite.org](http://www.phosphosite.org) to find the domain structure and post-translational modifications of the protein.

2. Use two different Protein-Protein Interaction (PPI) resources [see PSICQUIC (http://www.ebi.ac.uk/Tools/webservices/psicquic/view/main.xhtml); I recommend GeneMANIA (genemania.org) and String (string-db.org)] to retrieve interacting partners based only on physical interactions, pathways (knowledge), genetic interactions, and predictions from interactions known to occur in other species or due to the domain structure (not text-mining, homology, or co-expression; check the edges to be sure what is shown). (If there are no known interacting partners, pick another gene.) Use PubMed (https://www.ncbi.nlm.nih.gov/pubmed) to find evidence (published papers) showing that your gene and one of the interacting partners retrieved by PPI resources actually interact with each other.

3. Report the gene name, synonyms, gene structure, protein domain structure, 3D structure (if available; if not, try AlphaFold.com), modifications, network graphs, and one or two references for interactions. Optional: use Cytoscape (http://www.cytoscape.org) to graph the networks, otherwise copying and pasting diagrams and graphs from the websites is sufficient. Write a short paragraph summarizing the results and conclusions. Save the report as a pdf file and email it to the instructor.

Each student must pick their own gene and submit their own report. Due by the 5th week of class (February 23 or sooner).
Science is useful proposal

Imagine that a new Scientific Special Forces Creative Reserve (SSFCR) was established by the Rational Approach to Government Act (RAGA). The RAGA was passed by unanimous vote by both houses of Congress and signed into law by President Stacy Abrams. Its budget is equal to the Apollo program at its height, 5% of GDP. All graduate students in scientific fields are paid a generous stipend if they join the SSFCR, and 99% of graduate students (including you) enrolled within six months of passage of RAGA.

Your proposal should be based on a hypothesis and question that emerged from one of the papers, or something related. We'll work in groups or pairs to focus initial ideas. The format of the proposal is as follows.

A 5 minute “elevator pitch” oral presentation. Imagine you find yourself in an elevator with a Senator and have five minutes to pitch your idea.
A 100-word summary in language understandable to politicians and the lay public.
A one-page Specific Aims document that may include figures (single spaced, 11 point Arial or Helvetica font; 0.5 inch margins all around). The hypothesis must be clearly stated. One to three Aims will outline key experiments to test the hypothesis.
References to support the proposal, separate from the Specific Aims page.

The level of funding (graded A-C) will be determined by the effort put into coming up with a scientifically valid, technically achievable, well-written, and well-researched proposal.

Assessment

The course grade will be assigned based on oral presentations, written assignments, and one exam in which interpretation of data will be emphasized. For the exam, the instructor will identify key figures to focus on from papers that have been presented. Expect broad questions about the motivation for the experiments (e.g., “What signaling pathway is under investigation?”), and specific questions about the data (e.g., “Which lane in Figure 4 shows that cortactin is bound to a plasma membrane protein?”).

Point values:
Bioinformatics assignment: 20 points.
Paper review summaries: 10 points each (split between first drafts and revisions). One lowest score will be dropped.
Exam: 100 points.
Presentation: 100 points each.
Proposal and elevator pitch: 100 points

The Provost’s Official Fine Print

All students must practice academic honesty. Academic misconduct is subject to an academic penalty by the course instructor and/or a disciplinary sanction by the University.

All students need to be familiar with the Student Conduct Code. The Code is available for review online here. Treat each other with respect!

COVID-19 - From the Provost’s Office:

If you feel sick and/or are exhibiting COVID symptoms, please don’t come to class and contact the Curry Health Center at (406) 243-4330.

If you are required to isolate or quarantine, you will receive support in the class to ensure continued academic progress. We will provide zoom access if necessary.

UM (and the scientific community) recommends students get the COVID vaccine and booster. Please direct your questions or concerns about vaccines to the Curry Health Center.
Topics

Review and Overview of Cells and Biochemistry (Alberts, Chapters 1 and 2)

Oral questions will be used to assess how well students are prepared for this class.

Review and Overview of Methods (Alberts, Chapters 8 and 9)

Students will be asked in class to explain different methods used to manipulate nucleic acids and proteins, and to visualize cells. These chapters are a good first review or source for methods.

Cell structure, lipids and membrane traffic (Alberts, Chapters 10-13)

Reviews


Primary papers


Two related papers together:


Single paper:


Signal transduction and intracellular localization (Alberts, Chapters 15 as well as 12, 13, and 16)

Reviews


Primary papers


**The cytoskeleton and membranes (Alberts, Chapters 16 and 19)**

Reviews


Primary papers


**The Cell Cycle (Alberts Chapters 17 and 20)**

Reviews


Primary papers

Two related papers together:


**Programmed cell death (Alberts Chapter 18)**

**Reviews**


**Primary papers**


**Asymmetric Cell Division and Cell Fate (Alberts Chapters 17 and 21)**

**Reviews**


**Primary papers**


**RNA and Regulation of gene expression (Alberts Chapters 4, 6 and 7)**

**Reviews**


Primary papers


**Stem cells and chromatin modifications (Alberts Chapters 7 and 22)**

Reviews


Primary paper


**Stem Cells and Organoids (Alberts Chapter 22)**

Reviews


Primary Paper


**CRISPR and Gene Drive**

Reviews


**Primary Papers**


**Endoplasmic Reticulum: ER Sorting and The Unfolded Protein Response (Alberts Chapter 12)**

**Reviews**


**Primary papers**


**Alzheimer’s Disease**

**Reviews**


**Primary papers**


**Nervous System Evolution**

**Review**


**Primary paper**