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## BCH 584.01: Nucleic Acids

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#### Syllabus

# BCH584 Nucleic Acids

Instructor: Dr. Stephen Lodmell

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Email: stephen.lodmell@umontana.edu

Office Hours: Arrange Class place & time: TBD

This course will provide an advanced-level overview of the chemistry, structure and function of nucleic acids and the major biological processes that employ nucleic acids. The course will emphasize critical reading of current literature in the various subdisciplines of nucleic acids biochemistry. Research and review papers will be selected by the instructor as well as by the students to supplement the material covered in the text.

Major topics to be covered will be nucleotides, DNA, and RNA structure and chemistry, synthesis of nucleic acids (DNA replication and transcription of RNA), mechanisms of translation, and the principles of interactions of the nucleic acids with proteins and small nucleic acid binding molecules.

Following several weeks of core material, we will focus on specific topics to be explored in depth. Students will have a significant role in the selection and presentation of these topics, including one or two in-class presentations per student.

Important dates for Autumn semester (from the University calendar):

| September 2 (Thursday) | Organizational meeting 3-4pm ISB103b    |
|------------------------|---|
| September 6 (Monday)   | Labor Day Holiday, no classes held      |
| November 11 (Thursday) | Veterans Day Holiday, no classes held   |
| November 24-26 (WThF)  | Thanksgiving Holiday, no classes held   |
| December 10 (Friday)   | Last day of classes for Autumn Semester |
| December 13-17         | Final exams                             |

## Learning outcomes for Nucleic Acids

The purpose of this course is to provide a firm foundation in the structures and functions of the nucleic acids at an advanced level. Toward this end, upon completion of this course:

- 1. Students will understand nucleotide/nucleoside structure, properties, chemistry and functions.
- 2. Students will understand DNA and RNA structure.
- 3. Students will understand prokaryotic and eukaryotic DNA replication mechanisms.
- 4. Students will understand prokaryotic and eukaryotic RNA transcription mechanisms.
- 5. Students will understand prokaryotic and eukaryotic translation (protein synthesis) mechanisms.
- 6. Students will become expert at topics of their choice related to nucleic acids, and will present the topic to the class.
- 7. Students will gain experience writing an NIH-style research proposal related to their special topic of choice.

Possible topics for in-depth study:

Nucleotides as signaling molecules

Next-generation sequencing technologies and applications

DNA damage and repair

Protein interactions with Nucleic Acids

Recognition of DNA sequences by nucleases, transcription factors, DNA repair molecules, viral RNA or DNA interactions with host or viral proteins, etc.

Binding motifs of RNA/protein ligand pairs (r-proteins, helicases, synthetases, etc.)

RNA (or DNA) mediated catalysis

Natural (self splicing, RNase P)

"new" biochemically-evolved activities

Small non-coding RNAs (microRNAs, IncRNAs, snRNAs, snoRNAs, pRNAs, etc.: control of gene expression, RNA processing, and development)

Gene expression variation through alternative splicing

Origins of Life/ the RNA world

RNA interference/ siRNA

Gene editing/ CRISPR

Telomere structure and function in chromosome maintenance, cancer, and aging

Chromatin structure and the control of gene expression (DNA looping, topoisomerases, etc)

Ribosome structure and function

Control of mRNA translation via riboswitches, siRNAs, miRNAs

### Grading:

- 1. Midterm examination 20%
- 2. Oral presentation(s) 20%
- 3. Class participation, assignments, quizzes, and written analyses of papers and peer reviewing of grant proposals **20%.** Participation by every student in oral discussions of research papers, review papers, student presentations, and grant reviews is expected during every class period.
- 4. Research proposal (first draft) 20%
- 5. Review of peers research proposals 10%
- 6. Response/revisions based on written and in-class critiques of research proposal: 10%

The midterm examination will be an in-class closed-book exam covering material from the first half of the semester.

The oral presentation(s) (one or two, depending on class size) will cover a topic agreed upon by the student and instructor and will complement the subject material in the course outline. The presentation will consist of a critical review of two related original research papers (see specific instructions) and will involve class discussion during and after the presentation. The accompanying written assignment will be in the form of a research proposal of 7 pages maximum (see specific instructions). While the research proposal does not necessarily have to pertain exactly to the oral presentation, it is assumed that the background research done for the oral presentation could be put to good use here as well.

Active class participation is essential to the development of skills for critical analysis of scientific information, and is essential to the success of this type of course. Reading the assigned articles before class is mandatory and will be judged by class participation and/or the completion of assignments requiring careful reading of the assigned articles prior to class.

Guidelines for writing your research proposal are below, as are guidelines for your peer review of classmates' research proposals. You will be assigned two or three research proposals on which to carry out a written NIH-style review. We will then conduct a mock NIH-style study section review of all of the grant proposals, where the Primary and Secondary reviewers will orally present their critiques of each grant proposal and then discussion will be open to all panel participants, including the author of each grant. Your reviewer activities will count 10% toward the final grade, and each author is expected to use the written and oral criticisms of their grant proposal to revise their original proposal and resubmit it along with an Introduction page, that describes the changes that have been made. The responsiveness to criticisms in the revised proposal will count 10% toward the final grade.

## General University policies concerning written assignments:

In working through homework assignments, students are encouraged to work together to solve problems, to share information or resources, and to test each other's understanding of the material. Those are all acceptable forms of collaboration. However, the written work that each student turns in must be his or her own. Only in this way can faculty judge individual understanding of concepts or information. A good rule of thumb for students to follow is to work together up to the point of committing words to paper. At that stage, each student must work independently. A second key guideline is that once a student has written an out-of-class assignment, it must not be shown to another student in the course. Assignments from two or more students that have significant overlap, in the professional judgment of the faculty member, will be regarded as reflecting a violation of the expectation that students turn in independent assignments. Please note that direct copying of sentences from any published without proper citation is considered plagiarism. THIS INCLUDES THE INTERNET. Be sure to put the information in your own words and be aware that the instructor will check literary and Internet resources. Violations will be dealt with according to the Student Conduct Code.

## Accessibility, disabilities, and special accommodations:

The University of Montana assures equal access to instruction through collaboration between students with disabilities, instructors, and the Office for Disability Equity (ODE). If you anticipate or experience barriers based on disability, please contact the ODE at: (406) 243-2243, ode@umontana.edu, or visit www.umt.edu/disability for more information. Retroactive accommodation requests will not be honored, so please, do not delay. As your instructor, I will work with you and the ODE to implement an effective accommodation, and you are welcome to contact me privately if you wish. Any questions please contact me.

# Guidelines for the Oral Presentation BCH 584, Fall 2021

The presentation should be regarded more as a workshop than a formal seminar, as participation of the audience is essential. The oral presentation plus discussion will last 60 to 75 minutes and should be divided into the following general sections:

- Introduction. A brief overview of the subject matter should be presented with enough background information to set the stage for the body of the talk. The introduction may be based upon as many research or review articles as the presenter deems necessary, but this portion of the talk will be limited to 10-15 minutes maximum.
- 2. **Presentation and discussion of two related research articles.** This is the body of the talk and should last approximately 45 minutes. Experimental data from both papers will be carefully analyzed with respect to the purpose of the experiment, the specific results obtained, the authors' interpretation of the data, and other possible interpretations of the individual or collective data sets.
- 3. Model, conclusions, and prospects. In the last 10-15 minutes of the talk, the presenter will summarize with an integrated model of the system, or discuss the relative features of two or more competing models from different laboratories. In addition, the presenter will suggest experiments that could be done to help advance the field. Your synthesis of the information, development of models and new hypotheses, and vision for further research in the field will be a primary determinant of your score on the presentation. Remember that interactive discussion between presenter and audience at this point could benefit the presenter in the preparation of the written research proposal (see guidelines below). Involve your audience and invite participation!

### Timetable for oral presentations:

- 2-4 weeks prior to talk. Arrange to meet with me outside class time about your talk.
  Bring a detailed outline of your talk, including a list of 5-10 papers that you feel best
  embody the current state of progress in the field and copies of the two papers that
  you plan to present. I will work with you on the organization of the talk or problems
  you may have encountered, if any.
- One week prior to talk. I will distribute copies of your papers to all class members.
   Your talk should be in near-final form. Each student is expected to have carefully
   read these articles before coming to class, and should be prepared to discuss the
   papers. It is recommended that class members write down questions and
   comments about the papers before coming to class. If class participation is
   inadequate for active critical analysis of the research, written analyses of the papers
   will be routinely collected from class members prior to each presentation.

## Guidelines for the Written Research Proposal

The major written assignment will be in the form of a research proposal and should probably originate from the research you did for your talk. In the research proposal, you may incorporate some aspects of the oral presentation, including some input you may have received from the class during discussion of your papers, but it should be written in a formal research proposal style. The size of this proposal (not including references) will be strictly limited in size to 7 single-spaced pages (with font size no smaller than 11 point and "normal" margins), so you must be concise. Focus your proposal carefully. As a general guideline, you should aim to resolve a scientific problem within two years, using about two laboratory workers. Don't be too ambitious, or the proposal will not appear feasible to your reviewers. If you need help at any point during the preparation of your proposal, arrange to meet with me. Proposals can take lots of time to prepare, so start working on it early.

#### Organize your proposal as follows:

- 1. **Title and Project Summary.** On a separate page write one paragraph of no more than 200 words that describes in general terms the problem, the approach, and the rationale -- why is it important to do this research? This page does not count toward the 7 page limit.
- 2. **Specific Aims.** State concisely what you plan to do, with the assumption that the reader is somewhat experienced in the field. The Specific Aims should be numbered so that they can be referred to in the rest of the proposal. The Specific Aims section should be self-contained and on exactly one page.
- 3. **Significance.** The significance section addresses first and very briefly the global importance/significance of the problem you want to study, e.g. to help toward curing a disease. More importantly, you should address the potential significance/impact of the research you have proposed. In other words, describe how your successful completion of the specific aims will push your particular field forward, and how it will help to fill existing knowledge gaps. This section should be half to one page.
- 4. **Innovation.** Write a paragraph about how your project is innovative (novel, unique) in terms of approach or that the particular research you are proposing is somehow really different than what people have tried before. NIH *loves* innovation.
- 5. **Research Strategy.** You can use the space in your Research Strategy for background information, preliminary results that are important for the basis for your research, and a detailed description of the lines of experiments you will propose. Background provides the setting for the problem that you plan to address. It is not necessary to review and cite all of the literature in the field, only the research that has been done that will help the reader to understand your research problem and why you need to study it. But, be careful to cite all the literature that is crucial for the evaluation of your ideas. For example, if there are conflicting models, or if there is a research

paper out that addressed a similar problem but that you do not believe, you must cite these and explain your position rather than ignore them. A proposal reviewer who realizes that you have not cited all potentially relevant research could conclude that you have not done your homework and the proposal may be fatally flawed. You can also include in this section Preliminary Results, where you can give details of some specific experiments that lead up to your proposed experiments. In a 'real' proposal, these would be details of experiments you (or a collaborator) have performed, which may or may not be published. In the present case, you will use published experiments that you feel are the most immediately relevant to your proposed experiments. Finally and most importantly in this section, you should elucidate your **Experimental design.** Here, explain carefully how you plan to address each of the Specific Aims. You must include enough detail to convince the reader that you know how to use the proposed technology. Discuss what you hope to learn with each experiment, and what difficulties you may experience, either technically with the experimental procedure, or with the interpretation of results.

**Figures** are helpful, but figures and text of your Specific Aims plus your Research Strategy cannot exceed 7 pages.

A **bibliography** of literature cited in the text should be added after the Experimental Design section and <u>does not count in the page limit</u>. Use full citations including titles of papers.

This is a model research grant proposal, and as such, it should be free of typographical errors, spelling mistakes and grammatical errors. Proofread your proposal carefully, and ask a friend or colleague to read it as well. With the level of competition for grants today, reviewers need reasons to fault a proposal; a sloppily assembled application makes an easy target for rejection!

Good luck and good research!

## Guidelines for Peer Reviewing Research Proposals

You will be assigned to be primary reviewer on one of your peers grants and secondary reviewer on another grant.

In an NIH grant review panel, each grant is assigned, upon review, a score in the range 1-9 for Overall Impact, which is the composite score based on the individual scored criteria of Significance, Innovation, Approach, Investigator, and Environment. Note that the Overall Impact does not have to be the numerical average of the scores given to the individual scored criteria. For example, if the perceived Significance of a project gets a very low score, even if all of the other metrics are very good, it would probably still get a low Overall Impact rating, because the research was not anticipated to make a big impact in the field.

#### For your reviews:

- a. Address the strengths and weaknesses for each review criterion on the Review Critique template. Provide score-driving strength or weakness for each criterion unless the score is 1 (exceptional, no weaknesses) or 9 (poor, no discernable strengths), respectively. Your written critiques should reflect your numerical criterion scores.
- b. Your bulleted comments should provide context and an explanation based on the project (e.g., refer to a Specific Aim). While brevity is acceptable, bullets should express complete thoughts and be sufficient to inform the applicant. A bullet can be a single sentence or a whole paragraph, depending on the complexity of the issue being addressed.
- c. Write a paragraph summarizing the factors that informed the <u>Overall Impact</u> score
- d. Primary reviewers should write a brief summary of the project under consideration. Do not repeat the applicant's description verbatim.

Your grade on your critiques will be based on how well you informed yourself on the grant proposal, the relevant literature in the field (i.e. to ensure that the work proposed will fill a knowledge gap, will make a significant advance in the field, is innovative, etc.). Keep the reviews relatively brief, but let me know that you have done your homework and studied both the proposal and the 'state of the art' in the field that the proposal addresses!

Good luck and happy reviewing!