**BC663: Advanced Gene Expression – Spring 2019**

**Biochemistry and Molecular Biology**

**Instructor: Tom Santangelo (thomas.santangelo@colostate.edu)**
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**Office: 383 Molecular and Radiological Biosciences**
**2 credits; meets Tuesday and Thursday 9:00 – 10:50 AM in Room 312 MRB**

*CSU Graduate School anticipates that 3 additional hours of outside classwork will be completed each week per credit hour. BC663 students should thus expect to spend ~12 hours on assignments and reading material each week.*

**Office Hours: immediately after each class or by scheduled appointment**

| | Date | Topic |
|---|---|---|
| 1 | Jan 22 Tues | Course overview<br>New paradigms in gene expression |
| 2 | Jan 24 Thurs | Model organisms: a comparative perspective |
| 3 | Jan 29 Tues | Primary literature 1 |
| 4 | Jan 31 Thurs | Primary literature 2 |
| 5 | Feb 5 Tues | Recombinant DNA methods – Part 1: cloning |
| 6 | Feb 7 Thurs | Recombinant DNA methods – Part 2: real-time PCR, high-throughput sequencing and genome editing |
| 7 | Feb 12 Tues | Transcriptional Regulation Methods I<br>Problem Set 1 due |
| 8 | Feb 14 Thurs | Primary literature 3<br>Critique due |
| 9 | Feb 19 Tues | Transcriptional Regulation Methods II<br>Problem Set 2 due |
| 10 | Feb 21 Thurs | Primary literature 4<br>Critique due |
| 11 | Feb 26 Tues | Transcriptional Regulation Methods III<br>Problem Set 3 due |
| 12 | Feb 28 Thurs | Primary literature 5<br>Critique due |
| 13 | March 5 Tues | Chromatin |
| 14 | March 7 Thurs | Primary literature 6<br>Critique due |
| 15 | March 12 Tues | **Exam (ALL class)** |
| 16 | March 14 Thurs | Primary literature 7 (no critique due) |

**Important Note:**

- **The schedule above is a tentative guideline. Please check the website for current deadlines and up-to-date scheduling information throughout the semester.**

**Learning outcome and goals:**

This graduate course is designed to explore state-of-the-art techniques and informational gains surrounding gene expression by exploring the primary literature. The course builds upon the foundational information presented in BC563 (Molecular Genetics), with BC663 designed under the assumption that all materials from BC563 have been mastered by students entering the

course. We will primarily explore the methodologies, approaches, and critically evaluate the results obtained in current primary literature articles. This course is thus very different from previous courses that perhaps stressed facts over interpretations and methods. This graduate level course is designed to better inform you on new technologies, help you to critically evaluate manuscripts with written reviews, and delve deeper into regulatory mechanisms underlying gene expression.

As future scientists it is essential that you learn how to design experimental approaches to ask questions of nature and how to interpret the answers you obtain. In addition, you must learn how to effectively read the primary literature so that you can decide for yourself with regards to conflicting views, and how to communicate your scientific opinion both orally and in writing. Papers have been chosen for their exposition of methods, or classical experimental design, or specific approaches. The primary goal is to train your ability to access, digest and evaluate the literature, not to be encyclopedic in its coverage of the field.

*Students who have not taken BC563 or equivalent graduate-level courses are strongly encouraged to discuss with the instructor before they sign up this course. In addition, this course is designed for students who have been exposed to working in the wet lab and whom are involved in research projects. Those with no real-lab experience will find the contents rather abstract.*

**Mode of instruction:**
This course is a mixture of lectures, and student-lead discussions of the primary literature.

**Reading assignments:**
For the primary literature assignments, each student will be assigned one figure from each paper and will lead the discussion on that figure in class. The emphasis of the discussion should be on the hypotheses tested, and the methods utilized. Please be prepared to provide additional information beyond that provided solely in the manuscript.

**Student Evaluation:**
There will be one in class exam. There will also be take home problem sets and critiques. These problems will draw on your knowledge from the entire class and we will discuss the solutions to the problems in class. The students will also be evaluated by their peers on their performance in leading the discussion on their assigned figures as well as participating in the discussion of the other figures. The critiques of each paper will be graded as well.

**The point distribution is as follows:**

| | |
|---|---|
| Exam | 100 points |
| Discussion leading/participation | 70 points |
| Primary literature (Presentations/Critiques) | 110 points |
| Problem Sets | 120 points |
| Total points | 400 points |

A total number score of 360 or better will earn an A, 320-359 will earn a B, 280-319 will be a C.

**Primary literature**
A typed critique of the papers discussed in class will be due at the start of class and will be graded. ***Please target the overall length of your critiques to approximately 600-800 words. Use Ariel 12-point font with 1 inch margins.*** The written review must be your thoughts on the paper and must be written using complete sentences (no bullets, abbreviations, or jargon). Please include

the major point of the paper, a major strength and a major weakness. Include whether you as a reviewer would accept the paper, accept with revisions, or reject the paper. Explain your decision. Be careful about asking for more work. Think about the timeline for your request. Do not simply point out figure legends or layout as a weakness, but rather devise alternative and/or better ways to test the hypothesis. Late critiques will not be accepted. You are also expected to participate in the discussion of these papers and may also be called upon to describe the experimental approach and the results of a random figure in the paper. Critiques will be evaluated on scientific content, ***AND*** spelling and grammar.

Critique writing assignments allow the student to practice written evaluation of papers. Each critique should answer the central question: "Does the experimental rigor, novelty, presentation, and general interest of the manuscript in question warrant its publication? Your scale should also depend on the journal to which it has been submitted: in Science or Nature (highest quality and of general interest); a top-notch, but more specialized journal (such as Cell, Genes & Development, EMBO J., or PNAS); a somewhat less visible, but high quality journal (such as J. Biol. Chem, J. Bacteriology, J. Molecular Biology, Nucleic Acids Research, or Molecular Microbiology), a second-tier journal. Is the manuscript too flawed to be published at all in its present form?

Whatever the recommendation, the review should highlight strengths and weaknesses of the paper, the rationale for the recommendation chosen, and suggestions for improvement.

The overall goal of the critique is to evaluate the quality and importance of the work. Criticisms of writing, format or suggestions for future experiments are okay, but do not substitute for a balanced scientific critique. A good review format is to devote one or two paragraphs to description of the experimental approach and major findings and conclude this part with a statement of your overall evaluation of the paper. This might be a statement of the biggest problem you have with it or it might be a statement that the work is of high interest and impeccably done. In either case the summary paragraph(s) should be followed with a specific list of items that support and clarify your position on the paper. Journals typically ask that this be a numbered list so as to simplify evaluation of an author's response to it. In this list you should include both major points pertaining to the overall evaluation (usually first) and any minor points you wish to raise about format, writing, etc. Somewhere in the review include a specific recommendation about whether the paper is suitable for the particular journal. This part of your review is something you would normally include in a cover letter or evaluation sheet to the editor, rather than in the comments that would be passed along to the authors.