BC563: Molecular Genetics – Fall 2022

Module #1 – DNA replication, DNA repair and genomic editing
Module #3 – Transcription mechanisms and regulation

Instructor for Modules #1 and #3:
Thomas (Tom) Santangelo (thomas.santangelo@colostate.edu).

PLEASE do not use CANVAS-based messaging for email contact but rather directly email the instructor at thomas.santangelo@colostate.edu.
Responses to emails will generally be provided within 36 hours. Messages sent outside of normal working hours (nights/weekends) may require longer response times.

Phone: 970-491-3150 Office: 383 Molecular and Radiological Biosciences

CSU Graduate School anticipates that 3 additional hours of outside classwork will be completed each week per credit hour. BC563 students should thus expect to spend ~8-12 hours on assignments and reading material each week.

Office Hours are available by scheduled appointment.
I am enthusiastic towards student learning and encourage questions and appointments. Given the demands of time for both students and faculty, individual meetings are best established via email contact. The GTA for the course, **Gustavo Mendez**, will establish regular office hours and post information to discussion boards on Canvas.

Date	Topic
Mon Aug 22	Course overview and expectations DNA Replication (A quick review to modern questions)
Wed Aug 23	Primary literature #1 (Quiz 1 and Critique 1 due prior to class)
Mon Aug 29	DNA repair (Problem Set 1 due)
Wed Aug 31	Primary literature #2 (Quiz 2 and Critique 2 due prior to class)
Mon Sept 5	No class – Labor Day
Wed Sept 7	Genome editing (CRISPR and classical genetics) (Problem Set 2 due)
	Final assessment for Module 1 will be due before the start of Module 2
Mon Oct 3	Transcription (A quick review to modern questions) (
Wed Oct 5	Primary literature #3 (Quiz 3 and Critique 3 due prior to class)
Mon Oct 10	RNA polymerase along the genome (Problem Set 3 due)
Wed Oct 12	Primary literature #4 (Quiz 4 and Critique 4 due prior to class)
Mon Oct 17	A detailed view of the transcription cycle (Problem Set 4 due)
Wed Oct 19	Regulatory mechanism of transcription
	Final assessment for Module 3 will be due before the start of Module 4

Teaching format
Modules 1 and 3 of BC563 in the Fall of 2022 will be taught in a traditional face-to-face format. The course meets on Monday and Wednesdays from 3:00 pm until 4:50 pm.

Lectures will be presented face-to-face in real-time. Whenever possible, lectures and discussions will be recorded via Echo360 technologies and subsequently posted to the Canvas course page. Recordings are not guaranteed, nor is the quality of any recording guaranteed to any minimal standard, and all students should thus plan on attending each class in person to maximize educational gains. To maintain copyright restrictions and ensure that private information, privileged information, and images (including potential screen captures of students and their surroundings) remain private, all recordings and course materials CAN NOT be copied, shared, or posted to public repositories, social media accounts, or any digital platform. There are NO exceptions to this policy and a violation of this policy may result in disciplinary and/or legal action from CSU, faculty and/or students of BC563, copyright owners of the manuscripts and images presented in the course, textbook distributors, etc. Simply stated, materials on Canvas are private information. Releasing recordings or images of lectures and course materials beyond the restricted boarders of Canvas is NOT permitted.

The requirement for real-time discussions of manuscripts requires real-time participation of BC563 students. You should ensure that you are prepared to discuss your opinions and thoughts regarding techniques/manuscripts with your peers. Students are expected to generate and present images in person.

Learning outcome and goals

Module 1 is designed to explore state-of-the-art techniques and informational gains surrounding DNA replication, DNA repair and genomic editing (primarily via CRIPSR-engineering and modern genetic techniques) through investigation of the primary literature. The module builds upon the foundational information presented in undergraduate coursework and does not aim to repeat this information. ***The material presented in module 1 is not meant to be a refresher of previous coursework on molecular genetics and assumes that you have mastered the general concepts of i) DNA replication, ii) the replisome components and functions, iii) the basis of replication initiation and termination in eukaryotes and prokaryotes (archaea and bacteria), iv) the importance and differences of direct repair, base excision repair, nucleotide excision repair, transcription-coupled DNA repair, and homologous DNA repair mechanisms, including non-homologous end joining, v) the basis of CRISPR-immunity systems in prokaryotes and vi) a general understanding of selectable and counter-selectable marker systems employed in modern genetics.***

Module 3 is designed to explore current structural techniques, single-molecule to genome-wide approaches and biochemical assays to explore the processes involved in transcription through investigation of the primary literature. The module builds upon the foundational information presented in undergraduate coursework and does not aim to repeat this information. ***The material presented in module 3 is not meant to be a refresher of previous coursework on molecular genetics and assumes that you have mastered the general concepts of i) transcription as the process of generating an RNA transcript, ii) the composition and function of multi-subunit RNA polymerases, iii) the basis of transcription initiation, elongation and termination in eukaryotes and prokaryotes (archaea and bacteria), iv) the***

importance of genome organization of controlling gene expression, v) the basis of mRNA maturation, RNA modifications, and export and vi) a general understanding of the role of activators, coactivators, repressors and chromatin-remodeling factors.

The suggested textbook, "Molecular Biology – Principles of Genome Function, 2nd Edition"; by Craig, Cohen-Fix, Green, Greider, Storz and Wolberger offers chapters that refresh and reinforce basic concepts. While concepts presented in the text should be familiar to, and more often be mastered by students prior to the start of the course, some review of important foundational concepts will take place in class. Once foundational concepts are briefly reviewed, however, we will primarily explore the methodologies, approaches, and critically evaluate the results obtained in current primary literature articles to investigate the utility of modern approaches to establish new information regarding the molecular biology of cells. ***Modules 1 and 3 are thus very different from previous courses that perhaps stressed facts over interpretations and methods. This format 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 BC463 or equivalent upper-level molecular biology and genetics courses are strongly encouraged to discuss their suitability with the instructor before they sign up for or continue with 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 many of the contents rather abstract.

Mode of instruction
This course is a mixture of lectures and student-lead discussions of the primary literature. Modules 1 and 3 will be presented in a traditional, face-to-face format.

Reading assignments
For the primary literature assignments, each student will be tasked with description of a key concept, key deficiency, or a partial or full figure(s) from each paper and will lead the discussion on that figure. ***Every student needs to be prepared to present each concept and/or figure***. Figures and key concepts will NOT be pre-assigned and the flow of describing the manuscripts will not necessarily follow the flow of the paper. In addition to descriptions/interpretations of the figures, each paper will require at least one student to present a historical background and/or perspective; there is little point in addressing the details of a manuscript without knowing the context of why the science under study is important. Each manuscript under discussion will require at least one student(s) to serve as a critical evaluator of the techniques employed – would the experimental details be better investigated with a different technique? Would the data have been better analyzed with an alternative statistically approach? How would funding restrictions (or unlimited funding) have changed the experimental workflow? 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.

The instructor and GTA will have each figure available to display during the discussion to aid in the presentation. Students are encouraged to prepare slides that define key concepts and prepare notes that will permit them to rapidly respond to requests for information during the group discussions.

Should students not be able to participate in the group discussion, alternative assignments will be arranged.

Student Evaluation
There will be a final, take-home assessment. There will also be graded take home problem sets, Canvas-based short quizzes and manuscript critiques. These problems will draw on your knowledge from the entire class and we will discuss the solutions to the problems in class.

The point distribution is as follows

Final assessment (take-home)	30 points
Discussion leading/participation in literature discussions (Two @ 5 pts)	10 points
Canvas-based short definition quizzes (Two @ 5 pts)	10 points
Primary literature (Two written critiques @ 15 pts)	30 points
Homework (Two problem sets @10 points)	20 points
Total points	**100 points**

Final grades
Students who receive 100-90% of available points will earn an A.
Students who receive 89-80% of available points will earn a B.
Students who receive 79-70% of available points will earn a C.
Students who receive 69-60% of available points will earn a D.
Students who receive less than 60% of available points will earn a F.

Note that CSU does not use C-, D+, or D- grades. This course will not assign + or – designations for any grades.

Academic Integrity & CSU Honor Pledge
This course will adhere to the CSU Academic Integrity/Misconduct policy as found in the General Catalog and the Student Conduct Code.

Academic integrity lies at the core of our common goal: to create an intellectually honest and rigorous community. Because academic integrity, and the personal and social integrity of which academic integrity is an integral part, is so central to our mission as students, teachers, scholars, and citizens, I will ask that you affirm the CSU Honor Pledge as part of completing your work in this course.

Any coursework materials that are submitted that do not adhere to the CSU Honor Pledge will receive zero credit and will be reported to the administration.

Primary literature critiques
A typed, on-line submitted critique of the papers discussed in class will be due at the start of face-to-face discussion and will be graded. ***Please target the overall length of your critiques to approximately 800 words. Use Ariel 12-point font with 1-inch margins.*** Critique writing assignments allow you 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 for publication quality work should also depend on the journal to which the manuscript has been submitted: Science, Cell or Nature (highest quality and of general interest); a top-notch, but more specialized journal (such as 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 all demand different rigor. Is the manuscript too flawed to be published at all in its present form? Whatever the recommendation, the review should highlight strengths/weaknesses of the paper, the rationale for the recommendation chosen, and suggestions for improvement.

The written review must be your thoughts and must be written using complete sentences (no bullets, abbreviations, or jargon). Your reviews should mimic reviews of manuscripts actually under consideration and should be drafted as such. The first paragraph (5-6 sentences) should start by describing the field and the context that the manuscript might impact the field. You must tell the authors and editors that you are knowledgeable about the field, you understand the knowledge gaps of the field, you understand the main techniques employed, etc. Something akin to "Proper gene regulation is necessary to permit cell differentiation, but the mechanisms underlying regulation at the level of transcription/translation/genome architecture/etc/etc are not completely understood. The current manuscript addresses a significant gap in the field, particularly x, y, or z". Conclude the first paragraph with a statement whether you as a reviewer would accept the paper as is, accept with revisions (major and/or minor), or reject the paper.

In the second paragraph you explain your decision. If there are significant flaws, state the flaw(s) and back up your criticism with specific points. You should comment on the techniques, analyses and interpretations of the results for points that you feel the manuscript fails to carefully or correctly address. You should suggest orthogonal approaches that would bolster experimental results and findings. The second paragraph typically makes broad statements to justify your decision and is the core of your review. Although central to the review, you are generally pointing out the most significant advances or deficiencies in the work. Be careful about asking for additional experimentation. Think about the timeline for your request. Do not simply point out weaknesses, but rather devise alternative and/or better ways to test the hypothesis (at least in your opinion).

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. Late critiques will not be accepted. **Critiques are graded on a four-tier scale: 15 pts for excellent, 10 points for good, 5 points for fair, 0 points for poor or incomplete work**. Critiques will not receive any intermediate evaluations; that is, critiques that boarder on excellent/good will not receive 12.5 points but will be ranked either within excellent (15 points) or good (10 points). Your participation in the critique will be scored as zero should you not contribute meaningfully, or as five points when you contribute meaningfully to the discussion. It is your responsibility to ensure that you participate in the discussions. The GTA and instructor will make every effort to encourage participation from all present while limiting any single party from dominating the discussion.

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. In a real review your summary paragraph(s) would 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.

Grading of problems sets and final evaluations.
Canvas-based short quizzes typically have five questions, each asking you to define or explain a key concept. Definitions of key concepts will receive 1, 0.5, or zero credit each, only, for a maximum score of 5 points total. Late assignments will not be accepted.

Problem sets consist of short essay questions with no obvious correct answer. Your responses will receive 5, 4, 3, 2, 1 or zero credit only. No half-points will be assigned. Late assignments will not be accepted.

The final evaluation is a composite of key concepts and short essay questions and will be graded with the same rigor and point system as the quizzes and problem sets. Late assignments will not be accepted.

Important information for students: All students are expected and required to report any COVID-19 symptoms to the university immediately, as well as exposures or positive tests from a non-CSU testing location.

If you suspect you have symptoms, or if you know you have been exposed to a positive person or have tested positive for COVID, you are required to fill out the COVID Reporter (https://covid.colostate.edu/reporter/). If you know or believe you have been exposed, including living with someone known to be COVID positive, or are symptomatic, it is important for the health of yourself and others that you complete the online COVID Reporter. Do not ask your instructor to report for you. If you do not have internet access to fill out the online COVID-19 Reporter, please call (970) 491-4600. You may also report concerns in your academic or living spaces regarding COVID exposures through the COVID Reporter. You will not be penalized in any way for reporting. When you complete the COVID Reporter for any reason, the CSU Public Health office is notified. Once notified, that office will contact you and, depending upon each situation, will conduct contact tracing, initiate any necessary public health requirements and notify you if you need to take any steps.

For the latest information about the University's COVID resources and information, please visit the **CSU COVID-19 site**: https://covid.colostate.edu/.

Resources & Policies

Canvas Information & Technical Support
Canvas is the place where course content, grades, and communication will reside for this course.

Login: canvas.colostate.edu Support: info.canvas.colostate.edu

For passwords or any other computer-related technical support, contact the Central IT Technical Support Help Desk.

Voice: (970) 491-7276 Email: help@colostate.edu

The Technical Requirements page identifies the browsers, operating systems, and plugins that work best with Canvas.

Further information about Academic Integrity is available at CSU's Academic Integrity - Student Resources.

Universal Design for Learning/Accommodation of Needs
I am committed to the principle of universal learning. This means that our classroom, our virtual spaces, our practices, and our interactions be as inclusive as possible. Mutual respect, civility, and the ability to listen and observe others carefully are crucial to universal learning.

If you are a student who will need accommodations in this class, please contact me (thomas.santangelo@colostate.edu) to discuss your individual needs. Any accommodation must be discussed in a timely manner. A verifying memo from The Student Disability Center may be required before any accommodation is provided. The Student Disability Center (SDC) has the authority to verify and confirm the eligibility of students with disabilities for the majority of accommodations. While some accommodations may be provided by other departments, a student is not automatically eligible for those accommodations unless their disability can be verified and the need for the accommodation confirmed, either through SDC or through acceptable means defined by the particular department. Faculty and staff may consult with the SDC staff whenever there is doubt as to the appropriateness of an accommodative request by a student with a disability.

The goal of SDC is to normalize disability as part of the culture of diversity at Colorado State University. The characteristic of having a disability simply provides the basis of the support that is available to students. The goal is to ensure students with disabilities have the opportunity to be as successful as they have the capability to be.
Support and services are offered to student with functional limitations due to visual, hearing, learning, or mobility disabilities as well as to students who have specific

physical or mental health conditions due to epilepsy, diabetes, asthma, AIDS, psychiatric diagnoses, etc. Students who are temporarily disabled are also eligible for support and assistance.

Any student who is enrolled at CSU, and who self-identifies with SDC as having a disability, is eligible for support from SDC. Specific accommodations are determined individually for each student and must be supported by appropriate documentation and/or evaluation of needs consistent with a particular type of disability. SDC reserves the right to ask for any appropriate documentation of disability in order to determine a student's eligibility for accommodations as well as in support for specific accommodative requests. The accommodative process begins once a student meets with an accommodation's specialist in the SDC.

Copyrighted Course Materials
Please refer to Faculty Manual - Section J for rights and responsibilities related to creative works.

Undocumented Student Support
Any CSU student who faces challenges or hardships due to their legal status in the United States and believes that it may impact their academic performance in this course is encouraged to visit Student Support Services for Undocumented, DACA & ASSET for resources and support. Additionally, only if you feel comfortable, please notify me such that I might pass along any additional resources I may possess.

Food Insecurity
Any CSU student (along with faculty and staff) who is experiencing food insecurity can receive support from the Rams Against Hunger program. Services include a food pantry, a meal-swipe program, pocket pantries, and in-person assistance with navigating federal aid eligibility. The RAH page includes numerous resources as well as county, state and federal programs which are described and linked.

Title IX/Interpersonal Violence
For the full statement regarding role and responsibilities about reporting harassment, sexual harassment, sexual misconduct, domestic violence, dating violence, stalking, and the retaliation policy please go to: Title IX – Sexual Assault, Sexual Violence, Sexual Harassment.
If you feel that your rights have been compromised at CSU, several resources are available to assist:

- Student Resolution Center, 200 Lory Student Center, 491-7165
- Office of Equal Opportunity, 101 Student Services, 491-5836

A note about interpersonal violence: If you or someone you know has experienced sexual assault, relationship violence and/or stalking, know that you are not alone. As instructors, we are required by law to notify university officials about disclosures related to interpersonal violence. Confidential victim advocates are available 24 hours a day, 365 days a year to provide support related to the emotional, physical, physiological and

legal aftermath of interpersonal violence. Contact the Victim Assistance Team at: 970-492-4242.

Religious Observances
CSU does not discriminate on the basis of religion. Reasonable accommodation should be made to allow individuals to observe their established religious holidays.
Please see CSU's Religious Observances Calendar.
Students seeking an exemption from attending class or completing assigned course work for a religious holiday will need to fill out the Religious Accommodation Request Form and turn it in to the Division of Student Affairs, located on the second level of the Administration building.

Once turned in, the Division of Student Affairs will review the request and contact the student accordingly. If approved, the student will receive a memo from the Dean of Students to give to their professor or course instructor.

Students are asked to turn in the request forms as soon as the conflict is noticed.

Similarly, unanticipated conflicts requiring a religious observance, such as a death in the family, can also be reviewed.

CSU Principles of Community

Inclusion: We create and nurture inclusive environments and welcome, value and affirm all members of our community, including their various identities, skills, ideas, talents and contributions.

Integrity: We are accountable for our actions and will act ethically and honestly in all our interactions.

Respect: We honor the inherent dignity of all people within an environment where we are committed to freedom of expression, critical discourse, and the advancement of knowledge.

Service: We are responsible, individually and collectively, to give of our time, talents, and resources to promote the well-being of each other and the development of our local, regional, and global communities.

Social Justice: We have the right to be treated and the responsibility to treat others with fairness and equity, the duty to challenge prejudice, and to uphold the laws, policies and procedures that promote justice in all respects.

Diversity and Inclusion
Respect for Diversity: It is my intent that students from all diverse backgrounds and perspectives be well served by this course, that students' learning needs be addressed both in and out of class, and that the diversity that students bring to this class be viewed

as a resource, strength and benefit. It is my intent to present materials and activities that are respectful of diversity: gender, sexuality, disability, age, socioeconomic status, ethnicity, race, and culture. Your suggestions are encouraged and appreciated. Please let me know ways to improve the effectiveness of the course for you personally or for other students or student groups.

Student Parents/Guardians/Caregivers
I realize that student parents/guardians and caregivers face distinctive challenges in succeeding academically, and I'm committed to supporting those of you who are parents/guardians to achieve our course's learning outcomes. If you encounter challenges in meeting course expectations, please contact me as soon as possible (beforehand if feasible or as soon afterward as you reasonably can if not). If you need to bring your child or person you care for to class, for example because you're nursing or planned childcare became unavailable, I encourage you to do so if it's feasible for you to participate in class and support your child or person in your care without compromising the educational opportunities of your peers.

Finally, know that pregnant and parenting students are guaranteed equal educational opportunities by Title IX; know your rights, the protections provided, and how to advocate for yourself.

Student Case Management
Student case management is available to help students with extenuating life circumstances and connect them with resources. In some cases, after you and I discuss your situation, I may request verifiable documentation for class absences from the SCM office if you request considerations for absences or missed coursework.

Mental Health and Wellness
CSU is a community that cares. You are not alone. CSU Health Network Counseling Services has trained professionals who can help. Your student fees provide access to a wide range of support services.

Call Counseling Services at (970) 491-6053, and they will work together with you to find out which services are right for you.

Visit https://health.colostate.edu/about-counseling-services to learn more and https://health.colostate.edu/mental-health-resources/ for additional student mental health and well-being resources. An extensive set of mental health resources is available to CSU students: https://health.colostate.edu/mental-health-resources/

If you are concerned about a friend or peer, use **Tell Someone** by calling (970) 491-1350 or visiting https://supportandsafety.colostate.edu/tell-someone/ to share your concerns with a professional who can discreetly connect the distressed individual with the proper resources. Rams Take Care of Rams. Reach out and ask for help if you or someone you know is having a difficult time.