

Biology 423 Syllabus Spring 2018
Lab Experiments in Genetics

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Friday afternoons after 3:30 are optimal.

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Course co-requisite: Biol 423L. Biol 423 and 423L should be taken at the same time. Together they compose a Course-based Undergraduate Research Experience (CURE)

Course prerequisite: Biol 202 Genetics and Molecular Biology or equivalent.

Instruction hours:

Section 001: Mondays 1:00 - 5:00 p.m. in Wilson room 132

Section 002: Tuesdays 1:00 - 5:00 p.m. in Wilson room 132

Students will be expected to return to the lab classroom outside of the instruction hours to complete their experiments. This will apply every week of instruction. The extra times will be at the student's discretion. The lab classroom will be available outside instruction hours for this purpose.

Course Description: Biol 423 and Biol432L combine to make a Course-based Undergraduate Research Experience (CURE) that is accepted as an elective biology course with lab for the Biology Major This course combination offers students the chance to engage in cutting-edge genetic research related to an ongoing federally-funded research project in the lab of a UNC faculty member. The three hour lecture course is intermingled with the co-requisite 1 hour laboratory course so that both will be held in the same four hour block. Students will use the time to discuss the biological problem of study and relevant research publications, to learn techniques commonly used in genetic research, to evaluate and discuss possible research approaches to investigate the biological problem of study, to perform genetic research and to produce reports of their results in a conventionally accepted format. Students will work with the instructor and the collaborating research faculty to develop their own research plans. They will carry out the work flow that they have designed and as their final exam, they will produce a report useful to the research collaborator.

Laboratory exercises will be done in small groups of two or three students. They will share data to produce reports and they can coordinate coming in after instruction hours to complete experiments for other group members.

Target Audience: This course is designed for undergraduates with an interest in Genetics and Genome Biology. Students must have completed Biol 202 Genetics and Molecular Biology, or an equivalent course.

Diversity statement: The Department of Biology values the perspectives of individuals from all backgrounds reflecting the diversity of our students. We broadly define diversity to include race, gender identity, national origin, ethnicity, religion, social class, age, sexual orientation, political background, and physical and learning ability. We strive to make this classroom and this department an inclusive space for all students. **Course materials are all available on Sakai**

Text book: All reading materials will be available on Sakai at the course site.

Copyright policy All course materials including your class notes and in-class assignments are covered by University Copyright Policy, @<http://www.unc.edu/campus/policies/copyright%20policy%2000008319.pdf>. This means it is illegal and an honor code offense to share your notes or any other course materials with anyone not directly affiliated with this particular class, i.e., no uploading materials to non-class sharing sites.

The course project for Spring 2018 comes from an ongoing NIH-sponsored research project led by two scientists in the Biology Department at UNC, Drs. Kerry Bloom and Elaine Yeh, studying chromosome structure and DNA repair mechanisms using yeast. Every eukaryotic chromosome has one centromere. When chromosomes have been copied and cells divide, the two chromosome copies are each directed into one of the two daughter cells via connections between the cytoskeleton and the centromere. In cancer cells, chromosomes are often rearranged and in some cases, chromosomes with two centromeres, or dicentric chromosomes, are formed. When cells with a dicentric chromosome divide, that chromosome could be directed to travel to both daughter cells at once. The chromosomes then break before cell division can be completed. The resulting daughter cells have too few or too many copies of genes on the chromosome. The Bloom lab has developed a yeast strain carrying one chromosome with a second, inducible centromere. The activation of the second centromere leads to cell death as the yeast cells reproduce. This strain of yeast has been used to study DNA repair mechanisms, define DNA sequences essential to centromere structure and to identify proteins that bind centromeres to guide them to daughter cells. The goal of this course will be to create mutant yeast that can survive activation of the second (inducible) centromere and to identify the DNA changes that cause the mutations.

The course goals will be divided into three consecutive modules: A) Mutation and selection of mutants. B) characterization of mutants to distinguish those affecting centromere DNA sequence from those affecting the sequence of proteins that affect the function of the centromere. C) Ultimately we will go through an example of mapping by genome sequence comparison to identify genes that contain the mutations students have identified.

Attendance: Instruction periods cannot be made up at another time but students may come to the lab room to work independently to finish experiments as necessary. If students cannot attend an instruction period because of another commitment such as an interview for professional advancement, an arrangement can be made in advance with the instructor. Contact her by email with the date you will have to miss, preferably in advance of that date. Students are excused in case of illness. The instructor must be informed of the circumstance to avoid losing participation points.

Grading: Weekly participation in lab activities and group discussion: Participation grades will depend on discussion of answers to homework assignments and instructor questions in lecture and on active participation in laboratory exercises. 5% of final grade.

Homework Assignments: Assignments will be designed to help students understand the research problem being investigated. Assignments will include reading primary research papers and preparing descriptions, answering questions posed by the instructor and solving representative problems. Homework Assignments will be posted as a word file in the resources folder for each week. Answers will be due posted to the Assignment section of the course Sakai web page by 5 pm Friday at the end of the week. Students and instructors will discuss the answers the following week in class. Students will be allowed to amend and resubmit your answers until 5 pm Wednesday the week we discuss the answers in class. Preliminary answers will be graded mostly on whether a good attempt to find the answer was made. Student's discussion in class will be part of the grade. Generally, each student should answer at least one question in class. Your resubmission will be graded for content. 10% of final grade.

Preliminary research plan: At the midpoint of the course students will design a proposal for the way to continue their investigation for Module B. Students will submit the preliminary research proposal to the instructor for comments and grading. Students are allowed to discuss the proposals but each student must submit an individual plan. The plans presented will be discussed in the lecture class and a final work plan will be agreed on. 10% of final grade.

Weekly work plan: Each student will prepare a work outline for each lab period to be submitted before starting work. Students are encouraged to collaborate to produce the final work plan but each student must submit their own work plan.

The work plan will be submitted by email to the instructor before the beginning of the class period. 5% of final grade.

Module report: A report on the results of module A will be submitted within 2 weeks of completing the research. This will include 1) an introduction section, 2) a results section including illustrations and tables representing the experimental design used and the resulting data and 3) a discussion section summarizing the relevance of the result to the rest of the project. Students are expected to share data with their lab partners but they must prepare their own reports including their own figures and tables even though the figures and tables will have the same information as their lab partners. Students are encouraged to discuss the interpretation of their results with any member of the class and students may be requested to share data and interpretations with other class members by the instructor. See the course Sakai site for instructions on how to prepare lab reports. 20% of final grade

Module Quiz: One week after completing module A and B, students will have a closed book quiz in short answer, multiple choice format to evaluate their mastery of the genetic principles used in the module. The honor code will apply to each quiz. Students are not permitted to collaborate on the quiz. 20% of final grade (10% each)

Final report: At the end of the semester, students will prepare a report on the results of the full semester. The report will have the same format used for directed undergraduate research projects (Biol 395), which is similar to the module report. The rules on collaboration are the same as for module reports. The final report will be submitted at the beginning of exam week, April 30. **This report will be prepared outside of the final exam period but it will serve as the final exam.** 30% of final grade.

Penalty for handing research plans or reports in late: All homework, proposals and research reports must be submitted on Sakai or by email to the instructor by 5 pm on the due date. Work handed in late but within 24 hours of the due date will be graded for 50% of the points. Work submitted later will not be graded. Exceptions can be made in unusual circumstances by arrangement (email to instructor, preferably **before** due date)

There will be no make-up exams. In exceptional circumstances, a student may arrange to take a Quiz at a date different from the scheduled date. The same applies to homework and reports.

Regrade requests: Lab reports and homework: Regrade requests must be submitted within one week of receiving the graded work. Students must submit a graded file with grader's comments to the instructor. The complaint must be described in writing. It can be submitted by email with the graded PDF attached.

The instructor reserves the right to regrade the entire paper, not just evaluate the complaint.

Quizzes: Regrade requests must be submitted in writing to the instructor with the exam within one week of receiving the graded work. The instructor reserves the right to regrade the entire test. If the problem is incorrect addition of marks, students may discuss that directly with the instructor (after class is fine).

Time line: This is a suggested timeline. It is essential to be time flexible in the context of a CURE. Therefore, the instructor reserves the right to modify the timeline as the course progresses.

Week 1: Jan. 16-19: Because of the MLK holiday Monday's section cannot meet so Tuesday's section will also not meet. There will be a reading assignment and an associated homework assignment for both sections. The assignment will be in the Assignment folder in the Sakai site for the class.

Week 2: Jan 22-26: First class

Discussion of Homework: yeast biology, yeast genetics. Chromosome structure. Mitosis and Cell division

Introduction to lab class and project for this semester

Lab Safety

Sterile technique, making media, Yeast culture techniques.

Compare viability of dicentric chromosome strain on two sugars.

Discuss experiment for next week and how to set up a work outline.

Homework assignment for next week. Centromere structure in detail (McKinley and Cheeseman, Bloom Annual review paper fig 2) Brock and Bloom 1994 Figures 2-5.

Week 3: Jan 29-Feb 2:

Discuss Homework: Dicentric chromosomes, breakage and repair, structure of a centromere and kinetochore. Brock and Bloom Table 1 Discuss work plans for today.

Calculation of viability on two sugars results from last week. Discuss how to keep data in your notebook.

Discussion of how to present data using R computer package.

Presentation of genotypes used in course.

Comparison of *RAD52+* and *rad52-* viability on two sugars.

Examine yeast under the microscope. Dr. Kerry Bloom assists.

Homework assignment for next week: Mutation with UV light. Read yeast and mutation pdf. Investigate *RAD52* gene and what the protein does.

Week 4: Feb 5-9: Discuss homework: Evaluate viability results from last week and determine statistically significant differences between strains using ANOVA in R package.

Workshop on UV mutagenesis. All groups will do a time course for survival on non-selective media. Also plate on dextrose selective media.

Discuss work plan for next week. Plates needed. Goals for a second mutagenesis experiment.

Homework assignment for next week: Read Kramer et al 1994 to see broken chromosomes and centromere damage in *rad52* background. Prepare an outline for next week's mutation experiment.

Week 5: Feb 12-16: Discuss homework. What kind of mutations do we expect to get based on reading? What does RAD52 protein do? How does that change mutations we expect to see?

Evaluate time course from last week. Prepare a table for report. Decide on optimal conditions. Make a survival curve and a mutants per 100 curve.

Do Mutation experiment. - students do on their own.

Prepare description of the experiment for your report.

Discussion of how to characterize mutants further

Set up matings to alpha strain of yeast - Prepare plates for mating and to select diploids.

Homework: read Myhre and Bloom, 2003 paper. What kind of *in trans* mutations might we get?

Week 6: Feb 19-23:

Discuss reading. Go over Myhre and Bloom paper in detail. Dr. Bloom will give a lecture on his interests in dicentric chromosome studies.

Collection of mutants

Streak mutants onto selective media and non-selective media.

Set up matings with mutants if possible.

Discuss how to proceed to characterize mutants: segregation analysis, sequencing, introduce centromere plasmids.

Workshop on proposal preparation

If time permits, prepare plasmids for transformation.

Week 7: Feb 26-March 2: Quiz on module A.

Confirm phenotypes by dilution and plating on selective and non-selective media

Discuss what controls to use. Discussion of how to distinguish mutant types: Test heritability of mutations by retesting dextrose resistance compared to parents with growth on non-selective media as control. Up to 10 mutants per group. Do matings with same 10 mutants and wild type control and select diploids from the matings by end of week

Workshop on reference manager Mendeley

Workshop on DNA prep and gel electrophoresis. Make DNA from parent strains.

Workshop on writing a report on results. Prepare report for next week.

Set up cultures for DNA preps of mutants next week.

Week 8: March 5-9: Reports on Module A due

Discuss writing a proposal for characterizing mutants.

Workshop on yeast data base and designing primers. PCR principles.
Students prepare DNA from their mutants and design primers.
Discuss format for preparation of proposal on what to do to characterize mutants.
Preliminary proposals due at end of the week.

March 12-16 Spring break

Week 9: March 19-23: Final Proposals for characterization due next week. Peer discussion this week.

Workshop on PCR, PCR cleanup and sequencing

Students can prepare PCR reactions from their mutants.

Workshop on function annotation: Compare mutant and wildtype centromere sequences.

Start cultures for yeast transformation and genomic DNA prep of mutants as necessary.

Start sporulation of diploids for segregation analysis and mapping.

Week 10: March 26-29: PCR clean-up and send to sequencing.

Workshop on sequence analysis and genome annotation.

Workshop on plasmid prep and prep cultures for yeast transformation

Sporulation of diploids,

Week 11: April 2-6:

Yeast transformation

Separate haploid spores and select, evaluate segregation and select for sequence mapping (on plates or in liquid)

Discuss QEP Expo presentations

Week 12: April 9-13: Quiz on transformation, plasmid stability, PCR methods, DNA sequence analysis and other progress so far.

Evaluate results of yeast transformation. Set up CEN stability tests,

Analyze DNA sequences.

Prepare evaluation for final report.

Select spores for sequence mapping using control strains.

Workshop on principles of sequence mapping.

Week 13: April 16-20: Evaluate CEN stability tests. Document results.

DNA for mapping and prep libraries for genome sequencing.

Workshop on library prep for genome sequencing.

Week 14: April 23-27: PCR sequences should be ready. Comparison of DNA sequences between mutants and parents. Annotate function.

SNP analysis of data from sequence mapping done previously.

April 26: 3-5 QEP Expo presentations. Format to be determined.

Week 15: Final exam: Final Report summarizing results from full course program due April 30. Official exam time is Tuesday May 8 at 4 pm.

The instructor reserves the right to make changes to the syllabus, including project due dates and test dates when unforeseen circumstances occur. These changes will be announced as early as possible so that students can adjust their schedules.