Keck School of Medicine of USC

BIOC 581: Toolbox for Biochemistry and Molecular Biology (4 units)

Fall 2018—Monday/Wednesday, 12 - 3pm (extra time allowed to complete group exercises in class)
Location: Harkness Assembly Room, 2nd Floor, Clinical Sciences Center, CSC250

Course Coordinator: Pragna Patel, Ph.D.
Office: CSC 266
Office Hours: Will be posted on Blackboard
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Instructors will respond to emails/phone messages within 48 hours

Course Description

The purpose of this course is to explore the principles and applications of traditional and state-of-the-art methods in molecular biology and biochemistry with live/video demonstrations of techniques when appropriate. The course is inclusive of specific topics that will be of interest to the MS and PhD students engaged in research that employs molecular biology and biochemistry methods.

While this course is open to any MS or PhD student at USC, it will be required of all first year students in the Master's degree program in the Department of Biochemistry and Molecular Biology. It is needed to comprehensively and systematically provide the critical foundation of knowledge required for additional required and elective courses that they will take in subsequent semesters. Currently offered courses do not cover many of the topics that will be covered in this course including a detailed survey of DNA cloning methods, flow cytometry, genome editing, functional applications of next-generation sequencing including RNA-seq and ChIP-Seq, and RNA interference. It has become apparent that knowledge of the latter approaches is critical to successful performance in the required as well as several elective courses taken by these students in the succeeding semesters.

Learning Objectives

Upon completion of the course, each student will be able to:

- Demonstrate comprehension and fluency with traditional and state-of-the-art molecular biology and biochemistry terminology and methods
- Understand and assimilate information in published research articles and oral seminar presentations.
- Analyze and interpret data relevant to biochemistry and molecular biology techniques.

- Identify appropriate techniques to achieve a given molecular biology or biochemistry goal.
- Propose solutions to resolve problems in the laboratory involving biochemistry and molecular biology techniques.

Each of these competencies is expected of students who will embark upon a focused Master's thesis project in the lab of faculty members in the Department of Biochemistry and Molecular Biology and graduate from the Program. A major objective of this Master's degree program is to increase the awareness of current research advances in molecular biology and biochemistry by conducting bench-research. This course by offering a systematic comprehensive education in both traditional and state-of-the-art methods will equip the students to not only engage in bench research more effectively but also enhance their ability to comprehend current research literature and seminar presentations.

Prerequisite(s): There are no prerequisite course requirements.
Co-Requisite (s): There are no co-requisite course requirements.
Concurrent Enrollment: Students in the MS program in Biochemistry and Molecular Biology will be taking BIOC599 – 511 concurrently.
Recommended Preparation: Students will be expected to have a fundamental knowledge of DNA, RNA and protein equivalent to an undergraduate molecular biology course.

Course Notes

Class structure

1. Before class, students will be required to view papers/videos that provide basic background on the class topic, followed by a short (3-5 questions) online quiz addressing basic information from the papers/videos. The quiz will be auto-graded by Blackboard or hand-graded and the grade fed directly into the Blackboard gradebook.
2. Classes will begin with a short introductory lecture, followed by a short period of group work to answer a question (or questions) central to the day's topic. The question(s) will be provided to the students prior to the introductory lecture, to help them focus during the introductory lecture. Student work will be assessed by cold-calling students or group representatives.
3. A longer lecture will provide further details and examples of the day's topic. The lecture will proceed for ~30 mins followed by a 20 min period of group work that will involve solving a problem or interpreting data. The lecture will resume for an additional 30 min and a second period of group work 20 min as before will close the class. Students will be broken into groups (no more than 3 students/group) and as stated, given cases/problems to address. Each student will submit the solved problem on paper or on Blackboard and it will be graded for completion (completed/not completed) and will serve as a means of recording attendance/participation. Student groups will be set by the instructor, and changed periodically (every four lectures). Group representatives may be called upon to explain their group's response, as time allows.

Pedagogical techniques

- Group work within class to promote student engagement, information retention, and peer-networking
- Pre-class exercises posted and an associated short assignment graded on Blackboard to help students (particularly international students) gain basic background information to assist their understanding of the lecture
- Posting lecture videos and/or slide decks after the class on Blackboard, so students may view them independently
- Consciously recalling information from previous lectures to assist students in practicing with the information
- Live demonstrations of instrumentation used will be conducted for mass spectrometry and video demonstrations will be conducted for flow cytometry and transgenic mice/knockout mice production
- Instruction in critical analysis of empirical research articles to develop critical thinking skills that is then assessed by a quiz requiring analysis of data in a research paper without access to the text of the Results section of the paper
- Use of a smart phone app/clicker technology for formative assessment during the lectures

Technological Proficiency and Hardware/Software Required

Students will need a laptop computer or tablet with internet access to use Blackboard in the classroom. They will also need a smartphone to respond to queries in class.

Required Readings and Supplementary Materials

1) Short Protocols in Molecular Biology (2 volume set) 5th Edition, F. Ausubel et al. Editors. Wiley Press.
2) Molecular Cloning: A Laboratory Manual (Fourth Edition): Three-volume set by Michael R. Green, Joseph Sambrook. Cold Spring Harbor Press.
3) Additional reading pertinent to each lecture will be posted in PDF format or as a link to an online video on Blackboard prior to and/or after the lecture.

Description and Assessment of Assignments

This is a one-semester course with a letter grade issued at the end of the semester. This grade is based on five elements (1) pre-class assignments after reading/viewing assignments (2) group exercises during class (3) two quizzes (4) mid-term and final examinations (5) final project. Items 1 and 2 are essential participation grades and designed primarily for learning, not assessment or evaluation. Item 5 likewise is designed to allow a student to complete at their own pace while developing a curiosity about different journals and different fields that use the methods covered in the course and to stimulate students to listen to a lecture with an ear for application.

Grading Criteria:

A) Attendance: 100% attendance is expected. More than 1 session missed without a legitimate excuse or > 3 sessions where the student arrives late (>15 minutes), leaves early or is missing from the course without an excuse is grounds for a failing grade. Advance notice for any absence is required unless an unexpected severe illness or similarly serious event precludes such advance planning or notification. If that is the case, Dr. Patel and the course lecturer should be notified by email.

B) Pre-class assignments: Students will be expected to read the assigned topics or watch a video(s) before the actual class to enhance comprehension of the material in class. They will take a short quiz in Blackboard and will earn full points for completion of the assignment by the posted deadline. Additional homework assignments may also be given at the discretion of the lecturers.

C) In-class participation: Typically, two problem-solving exercises will be assigned during class and students will work in groups and submit the responses to the instructor on paper or on Blackboard. Full credit will be earned for submission of the exercise by the posted deadline.

D) Final Project: Students will be given a semester-long assignment that they can do at their pace where they will select a research article of their choice that represents data generated using at least six of the methods learnt in the course and answer simple questions such as "Why did they use Method X?", "What other method could they have used instead of Method X?". This project will be due just before the final exam.

E) Quizzes: There will be two quizzes – the first one (based on lectures 1 - 6) will be offered to give students an idea of the mode of assessment in the course and will also allow them to prepare for the mid-term exam (which will cover lectures 1 – 10). The second one will be before the final exam and will assess a student's ability to apply the method taught in the course on how to read a paper critically.

F) Mid-term and Final Exams: These exams will be partly open-computer and partly closed-book written exams given on a scheduled time/date. Exam formats will include a few multiple choice questions, and short-answer questions that will assess the understanding of topics covered in this course.

Grading Breakdown

Preclass Assignments (100% given for submission by deadline)	5%
Group exercises (100% given for submission by deadline)	15%
Quizzes	25%
Mid-Term Examination	20%
Final Examination	20%
Final project	15%
TOTAL	**100%**

Final grade will be based upon the following percentage:

>95%	**A**
>87-95%	**A-**
>80-87%	**B+**
>75-80%	**B**
>70-75%	**B-**

66-70%	**C**
61-65%	**D**
<60%	**F**

Assignment Submission Policy

Before class, students will be required to view papers/videos that provide basic background on the class topic, followed by a short (3 question) online quiz addressing basic information from the papers/videos. The quiz will be autograded by Blackboard and the grade fed directly into the Blackboard gradebook. In-class assignments will be emailed to the instructor and will be used to determine the class participation grade.

Additional Policies

Using electronic devices such as smart phones or tablets for conducting personal business during class is prohibited.

BIOC 581_2018_Course Schedule
Mondays and Wednesdays, 1-3 pm, Harkness (CSC250)

Monday August 20, 2018	**Overview of databases and resources available for Mol Biol**. Hands-on exercises with NCBI databases; Literature databases: Pubmed vs Google Scholar; OMIM, Web of Science.	Patel
Wednesday August 22, 2018	**DNA Manipulation, Amplification and Detection:** Enzymes to modify, label amplify or quantify nucleic acids; Polymerase chain reaction (PCR) and applications incldg. hybrid PCR, quantitative PCR, real time PCR, digital PCR	Patel
Monday August 27, 2018	**DNA Cloning I:** Applications of cloning, vectors, transformation methods, plasmid purification systems, traditional cloning methods	Patel
Wednesday August 29, 2018	**DNA Cloning II:** Applications of advanced cloning and mutagenesis; Gateway & PIPE, sequence and ligation-independent cloning, Gibson cloning, Type IIs cloning; site-directed/insertion/deletion mutagenesis	Patel
Wednesday September 5, 2018	**cDNA and Genomic Libraries:** Construction and handling of cDNA libraries; whole genome libraries, targeted strategies such as exome and regional capture, circulating cell-free genomic libraries	Patel
Monday September 10, 2018	**First-Generation Sequencing and Global Gene Expression:** Introduction to Maxam-Gilbert, Sanger and automated Sanger sequencing; microarray analysis	Allayee
Wednesday September 12, 2018	**Next-generation sequencing platforms:** Comparison of the different sequencing technologies and new methods based on sequencing (e.g. single cell analyses)	Campo
Monday September 17, 2018	**Genomic Profiling Methods:** Functional assays using NGS: ChIP-seq, Whole genome Bisulfite-seq, ATAC-seq, and RNA-seq	Farnham
Wednesday September 19, 2018	**DNA Variation Detection:** Technology approaches for detection of single nucleotide and structural variants; determination of allele-specific expression using coding variants	Allayee
Monday September 24, 2018	**Transfection and stable cell line production:** approaches for introduction of DNA into mammalian cells ($CaCl_2$, lipofection, electroporation and lentivirus-mediated); various selection methods including G418, hygromycin & puromycin, single clone isolation	Frenkel
Wednesday September 26, 2018	**Mid-term exam**	Patel
Monday October 1, 2018	**Transgenic and Knock-out mice:** constructs, generation of founders, breeding basics, Cre-lox applications	Maxson
Wednesday October 3, 2018	**RNA Interference and genetic screens:** RNA interference (RNAi) mechanisms and tools, genetic screening methods, technical considerations in using RNAi	Frenkel
Monday October 8, 2018	**Genome editing:** Zinc-finger technology, TALEN, CRISPR/Cas9 systems	Cannon
Wednesday October 10, 2018	**Antibody production, characterization and uses:** Monoclonal antibodies (mAbs) - mouse and rabbit hybridomas, B cell IgG cloning and recombinant single domain mAbs; polyclonal antibodies; antibodies to protein post-translational modifications and peptides, characterization and validation of antibodies.	Rice
Monday October 15, 2018	**Protein Purification:** Strategies for protein purification, basic principles of purification (solubilization, centrifugation, differential precipitation, column chromatography). Protein quantification and stabilization.	Comai

Wednesday October 17, 2018	**Analysis of Proteins and Detection of Protein-Protein Interactions:** Electrophoresis, isoelectric focusing, 2D gels, immunoblotting, immunoprecipitation, protein motifs and domains. Methods to detect protein-protein interactions: co-immunoprecipitation, in vitro pull-down assays and yeast two-hybrid system. Protein expression systems (E. coli, yeast, insect and mammalian cells), epitope/affinity tags (6x His, GST, HA, myc).	Comai
Monday October 22, 2018	**Flow Cytometry:** Introduction to the technique of flow cytometry and cell sorting, detecting fluorescent cells through expressed antigens and endogenous fluorescent molecules	Boyd
Wednesday October 24, 2018	**Microscopy:** Light, Fluorescence, confocal microscopy; principles and applications	Lansford
Monday October 29, 2018	**Physical Methods for Biochemistry:** pH, dialysis and filtration, spectrophotometry (absorbance spectroscopy, fluorescence spectroscopy, fluorescence transfer, circular dichroism), centrifugation, radioactivity	Siemer
Wednesday October 31, 2018	**Mass Spectrometry - Basic Principles:** instruments and analytical methods; principles of identification of analytes and analysis of data. Specific examples with peptides and post-translational modifications (PTMs).	Katz
Monday November 5, 2018	**Visualizing DNA, RNA and Proteins:** in situ hybridization (ISH), fluorescence ISH, immunohistochemical detection methods; colored fluorescence protein reporters; fluorescence resonance energy transfer (FRET)	Frey
Wednesday November 7 , 2018	How to read a scientific paper: Part I	Patel
Monday November 12, 2018	**Seminar:** Application of the approaches learnt in the course	Bajpai
Wednesday November 14, 2018	How to read a scientific paper: Part II	Patel
Monday November 19, 2018	Invited speaker: Discussion of scientific paper from previous class	Patel
Wednesday November 26, 2018	No class (Thanksgiving break)	
Monday November 28, 2018	In-class assignment: Analysis of a paper using the techniques learnt in class (counts towards class grade)	Patel
Wednesday December 3, 2018	**Q and A: Review session**	Patel/TA
Wednesday December 5, 2018	**Final exam**	Patel

Lecturers

Name	Location	Email address
Pragna Patel, Ph.D.	CSC 266	pragna@usc.edu
Hooman Allayee, Ph.D.	CSA 202	hallayee@usc.edu
Daniel Campo, Ph.D.	CEM 206(UPC)	dcampo@usc.edu
Peggy Farnham, Ph.D.	NRT 511 B	pfarnham@usc.edu
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Robert Maxson, Ph.D.	NOR 5334	maxson@usc.edu
Paula Cannon, Ph.D.	HMR 413A	pcannon@usc.edu
Judd Rice, Ph.D.	NRT 6506	juddrice@usc.edu
Lucio Comai, Ph.D.	CSC 264	comai@usc.edu
Jeffrey Boyd, Ph.D.	BCC 205	boydjeff@usc.edu
Rusty Lansford, Ph.D.	CHLA	lansford@usc.edu
Ansgar Siemer, Ph.D.	ZNI	asiemer@usc.edu

Jonathan Katz, Ph.D.	CSC 244	katzj@usc.edu

Statement on Academic Conduct and Support Systems

Academic Conduct
Plagiarism – presenting someone else's ideas as your own, either verbatim or recast in your own words – is a serious academic offense with serious consequences. Please familiarize yourself with the discussion of plagiarism in *SCampus* in Part B, Section 11, "Behavior Violating University Standards" https://policy.usc.edu/student/scampus/part-b. Other forms of academic dishonesty are equally unacceptable. See additional information in *SCampus* and university policies on scientific misconduct, http://policy.usc.edu/scientific-misconduct.

Discrimination, sexual assault, intimate partner violence, stalking, and harassment are prohibited by the university. You are encouraged to report all incidents to the *Office of Equity and Diversity/Title IX Office* http://equity.usc.edu and/or to the *Department of Public Safety* http://dps.usc.edu. This is important for the health and safety of the whole USC community. Faculty and staff must report any information regarding an incident to the Title IX Coordinator who will provide outreach and information to the affected party. The sexual assault resource center webpage http://sarc.usc.edu fully describes reporting options. Relationship and Sexual Violence Services https://engemannshc.usc.edu/rsvp provides 24/7 confidential support.

Support Systems
A number of USC's schools provide support for students who need help with scholarly writing. Check with your advisor or program staff to find out more. Students whose primary language is not English should check with the *American Language Institute* http://ali.usc.edu, which sponsors courses and workshops specifically for international graduate students. *The Office of Disability Services and Programs* http://dsp.usc.edu provides certification for students with disabilities and helps arrange the relevant accommodations. If an officially declared emergency makes travel to campus infeasible, *USC Emergency Information* http://emergency.usc.edu will provide safety and other updates, including ways in which instruction will be continued by means of Blackboard, teleconferencing, and other technology.

Emergency Preparedness/Course Continuity in a Crisis
In case of a declared emergency if travel to campus is not feasible, USC executive leadership will announce an electronic way for instructors to teach students in their residence halls or homes using a combination of Blackboard, teleconferencing, and other technologies.