



BISC 461: Biotechnology and Chemical Biology in Modern Biomedical Research

Section 13464D

Spring 2024, Tuesdays 4:00-5:50 PM

Location: RRI 221

Instructor: Lin Chen

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Office Hours: Monday 2:00-3:00PM

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Course Description

This course will review recent advances of biotechnology and chemical biology in biomedical research, emphasizing how the development of novel experimental and computation tools can be inspired by new inquiries of biology and catalyze the breakthroughs in basic research and biotech/pharmaceutical industry. Milestone papers of biotechnology breakthroughs will be selected. Each week a different student will present one of the papers selected and will be responsible for explaining the technology used in the paper and the experiments that were performed. In addition, the student will lead a discussion on the relative merits of the paper.

Learning Objectives

By the end of the course, the students will be able to critically read and evaluate scientific papers and present their understanding and ideas in a group discussion setting. Many of the topics covered by the papers represent major techniques and approaches currently used in biomedical research. A general understanding of these techniques will be beneficial to students' future learning and development in biomedical research. Although the selection of papers is not meant to be comprehensive, by reading and discussing these exemplary papers, a general goal of this course is to nurture a curiosity-driven, problem-solving, and multidisciplinary approach to science.

Course Notes

Required Readings and Supplementary Materials

Week 1 (Jan. 9): Structure and Function of the Genome

Reza Kalhor, Harianto Tjong, Nimanthi Jayathilaka, Frank Alber, and Lin Chen
“Genome architectures revealed by tethered chromosome conformation capture and population-based modeling”
Nature Biotechnology, 30, 90-98, 2012

Week 2 (Jan. 16): Capturing Chromosome Conformation: 3C

Dekker J, Rippe K, Dekker M, Kleckner N
“Capturing Chromosome Conformation”,
Science, 295, 1306, 2002

Week 3 (Jan. 23): Capturing Chromosome Conformation: HiC

Erez Lieberman-Aiden, Nynke L van Berkum, Louise Williams, Maxim Imakaev, Tobias Ragooczy, Agnes Telling, Ido Amit, Bryan R Lajoie, Peter J Sabo, Michael O Dorschner, Richard Sandstrom, Bradley Bernstein, M A Bender, Mark Groudine, Andreas Gnirke, John Stamatoyannopoulos, Leonid A Mirny, Eric S Lander, Job Dekker
“Comprehensive mapping of long-range interactions reveals folding principles of the human genome”
Science, 326, 289, 2009

Week 4 (Jan. 30): Capturing Chromosome Conformation: Roles of Proteins

Maxwell R Mumbach, Adam J Rubin, Ryan A Flynn, Chao Dai, Paul A Khavari, William J Greenleaf, Howard Y Chang
“HiChIP: efficient and sensitive analysis of protein-directed genome architecture”
Nature Methods, 13, 919, 2016

Week 5 (Feb. 6): Mapping genome-wide protein-DNA interactions: ChIP-seq

David S Johnson, Ali Mortazavi, Richard M Myers, Barbara Wold
“Genome-wide mapping of in vivo protein-DNA interactions.”
Science, 316, 1497–1502. 2007.

Week 6 (Feb. 13): Mapping genome-wide protein-DNA interactions: Cut&Run

Skene P.J., and Henikof, S
“An efficient targeted nuclease strategy for high-resolution mapping of DNA binding sites”
Elife, 6, e21856, 2017

Week 7 (Feb. 20): Mapping genome-wide protein-DNA interactions: Ongoing Research

Chen Lab
“Bi-functional photo-crosslinking (BFPX) for genome-wide study of protein-nucleic acid interactions”
To be published, 2024

Week 8 (Feb. 27): Click reaction in living systems

Nicholas J. Agard, Jennifer A. Prescher, and Carolyn R. Bertozzi
“A Strain-Promoted [3 + 2] Azide-Alkyne Cycloaddition for Covalent Modification of Biomolecules in Living Systems”

J. AM. CHEM.SOC. 126, 15046-15047, **2004**

Or

Baskin et al.,

“Copper-free click chemistry for dynamic *in vivo* imaging

Proc Natl Acad Sci U S A. 104:16793–16797, **2007**

Additional reading (optional)

Huisgen, R. 1,3-Dipolar Cycloadditions. Past and Future. *Angew. Chem. Int. Ed.* 1963 , 2 (10), 565–598.

Kolb, H. C.; Finn, M. G.; Sharpless, K. B. Click Chemistry: Diverse Chemical Function from a Few Good Reactions. *Angew. Chem. Int. Ed.* 2001, 40 (11), 2004–2021.

Tornøe, C. W.; Meldal, M. Peptidotriazoles: Copper(I)-Catalysed 1,3-Dipolar Cycloadditions on Solid Phase. In *Peptides 2001*, proc. Am. Pept. symp.; American Peptide Society; American Peptide Society; Kluwer Academic Publishers: San Diego, 2001; pp 263–264.

Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. A Stepwise Huisgen Cycloaddition Process: Copper(I)-Catalyzed Regioselective “Ligation” of Azides and Terminal Alkynes. *Angew. Chem. Int. Ed.* 2002 , 41 (14), 2596–2599.

Week 9 (Mar. 5): Directed Evolution – Engineering Enzymes

Chen, K and Arnold, FH

“Tuning the activity of an enzyme for unusual environments: sequential random mutagenesis of subtilisin E for catalysis in dimethylformamide.”

Proc Natl Acad Sci U S A. 90:5618-5622. **1993**

Additional reading (optional)

Wu et al.,

“Machine learning-assisted directed protein evolution with combinatorial libraries” **Proc Natl Acad Sci U S A.** 116 (18) 8852-8858, **2019**

Week 10 (Mar. 19): Directed Evolution – Engineering binding proteins

Smith GP

“Filamentous fusion phage: novel expression vectors that display cloned antigens on the virion surface”.

Science, 228: 1315–7, **1985**

Week 11 (Mar. 26): Directed Evolution – Impact and Engineering antibodies

McCafferty J, Griffiths AD, Winter G, Chiswell DJ

Phage antibodies: filamentous phage displaying antibody variable domains.

Nature, 348:552-554, **1990**

Week 12 (Apr. 2): Genome editing tools– The discovery and application of the CRISPR/Cas system

Martin Jinek, Krzysztof Chylinski, Ines Fonfara, Michael Hauer, Jennifer A.

Doudna, Emmanuelle Charpentier

“A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity.”

Science, 337(6096): p. 816-21. **2012**

Additional reading (optional):

Deltcheva, E., et al.,

CRISPR RNA maturation by trans-encoded small RNA and host factor RNase III.

Nature, 471 (7340): p. 602-7, **2011**

Jinek et al., "RNA-programmed genome editing in human cells" *eLife*, 2013;2:e00471.

Cong et al., "Multiplex Genome Engineering Using CRISPR/Cas Systems". *Science*, 2013, **339** (6121): 819–823.

Mali, P., et al., RNA-guided human genome engineering via Cas9. *Science*, 2013. 339 (6121): p. 823-6.

Week 13 (Apr. 9): Genome editing tools – Improving editing precision

Komor AC, Kim YB, Packer MS, Zuris JA, Liu DR.

"Programmable editing of a target base in genomic DNA without double-stranded DNA cleavage.

Nature, 533(7603): p. 420-4. **2016**

Week 14 (Apr. 16): Genome editing tools – new applications

Xin Liu, Yuannyu Zhang, Yong Chen, Mushan Li, Feng Zhou, Kailong Li, Hui Cao, Min Ni, Yuxuan Liu, Zhimin Gu, Kathryn E. Dickerson, Shiqi Xie, Gary C. Hon, Zhenyu Xuan, Michael Q. Zhang, Zhen Shao, and Jian Xu

"In Situ Capture of Chromatin Interactions by Biotinylated dCas9"

Cell, 170, 1028, **2017**

Week 15 (Apr. 23) : Transcription errors, RNA damages and diseases beyond DNA mutations – new questions that demand new tools

Marc Vermulst et al.,

"Transcription errors induce proteotoxic stress and shorten cellular lifespan"

Nat Commun, 6, 8065, **2015**

Additional reading:

Michael A. Lodato et al.,

"Somatic mutation in single human neurons tracks developmental and transcriptional history"

Science, 350(6256): 94–98. **2015**

Deborah A. Kreuzer and John M., Essigmann

"Oxidized, deaminated cytosines are a source of C-T transitions in vivo"

Proc. Natl. Acad. Sci. USA, Vol. 95, pp. 3578 –3582, **1998**

Lindah, T. and B. Nyberg,

"Heat-induced deamination of cytosine residues in deoxyribonucleic acid."

Biochemistry, 13(16): p. 3405-10. **1974**

Description and Assessment of Assignments

The grades for the course will be determined by the presentation (50%), class participation (10%) and questions (40%). Each week, every student must email 3 questions about each paper that is being discussed in that week's class to the instructor prior to the class. These questions will be graded and will constitute 40% of the final grade.

Disclaimer: It may be necessary to make some changes in the syllabus during the semester.

Statement on Academic Conduct and Support Systems

Academic Integrity:

The University of Southern California is a learning community committed to developing successful scholars and researchers dedicated to the pursuit of knowledge and the dissemination of ideas. Academic misconduct, which includes any act of dishonesty in the production or submission of academic work, comprises the integrity of the person who commits the act and can impugn the perceived integrity of the entire university community. It stands in opposition to the university's mission to research, educate, and contribute productively to our community and the world.

All students are expected to submit assignments that represent their own original work, and that have been prepared specifically for the course or section for which they have been submitted. You may not submit work written by others or "recycle" work prepared for other courses without obtaining written permission from the instructor(s).

Other violations of academic integrity include, but are not limited to, cheating, plagiarism, fabrication (e.g., falsifying data), collusion, knowingly assisting others in acts of academic dishonesty, and any act that gains or is intended to gain an unfair academic advantage.

The impact of academic dishonesty is far-reaching and is considered a serious offense against the university. All incidences of academic misconduct will be reported to the Office of Academic Integrity and could result in outcomes such as failure on the assignment, failure in the course, suspension, or even expulsion from the university.

For more information about academic integrity see [the student handbook](#) or the [Office of Academic Integrity's website](#), and university policies on [Research and Scholarship Misconduct](#).

Please ask your instructor if you are unsure what constitutes unauthorized assistance on an exam or assignment, or what information requires citation and/or attribution.

Students and Disability Accommodations:

USC welcomes students with disabilities into all of the University's educational programs. The Office of Student Accessibility Services (OSAS) is responsible for the determination of appropriate accommodations for students who encounter disability-related barriers. Once a student has completed the OSAS process (registration, initial appointment, and submitted documentation) and accommodations are determined to be reasonable and appropriate, a Letter of Accommodation (LOA) will be available to generate for each course. The LOA must be given to each course instructor by the student and followed up with a discussion. This should be done as early in the semester as possible as accommodations are not retroactive. More information can be found at osas.usc.edu. You may contact OSAS at (213) 740-0776 or via email at osasfrontdesk@usc.edu.

Support Systems:

[Counseling and Mental Health](#) - (213) 740-9355 – 24/7 on call

Free and confidential mental health treatment for students, including short-term psychotherapy, group counseling, stress fitness workshops, and crisis intervention.

[988 Suicide and Crisis Lifeline](#) - 988 for both calls and text messages – 24/7 on call

The 988 Suicide and Crisis Lifeline (formerly known as the National Suicide Prevention Lifeline) provides free and confidential emotional support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week, across the United States. The Lifeline is comprised of a national network of over 200 local crisis centers, combining custom local care and resources with national standards and best practices. The new, shorter phone number makes it easier for people to remember and access mental health crisis services (though the previous 1 (800) 273-8255 number will continue to function indefinitely) and represents a continued commitment to those in crisis.

[Relationship and Sexual Violence Prevention Services \(RSVP\)](#) - (213) 740-9355(WELL) – 24/7 on call

Free and confidential therapy services, workshops, and training for situations related to gender- and power-based harm (including sexual assault, intimate partner violence, and stalking).

[Office for Equity, Equal Opportunity, and Title IX \(EEO-TIX\)](#) - (213) 740-5086

Information about how to get help or help someone affected by harassment or discrimination, rights of protected classes, reporting options, and additional resources for students, faculty, staff, visitors, and applicants.

[Reporting Incidents of Bias or Harassment](#) - (213) 740-5086 or (213) 821-8298

Avenue to report incidents of bias, hate crimes, and microaggressions to the Office for Equity, Equal Opportunity, and Title for appropriate investigation, supportive measures, and response.

[The Office of Student Accessibility Services \(OSAS\)](#) - (213) 740-0776

OSAS ensures equal access for students with disabilities through providing academic accommodations and auxiliary aids in accordance with federal laws and university policy.

[USC Campus Support and Intervention](#) - (213) 740-0411

Assists students and families in resolving complex personal, financial, and academic issues adversely affecting their success as a student.

[Diversity, Equity and Inclusion](#) - (213) 740-2101

Information on events, programs and training, the Provost's Diversity and Inclusion Council, Diversity Liaisons for each academic school, chronology, participation, and various resources for students.

[USC Emergency](#) - UPC: (213) 740-4321, HSC: (323) 442-1000 – 24/7 on call

Emergency assistance and avenue to report a crime. Latest updates regarding safety, including ways in which instruction will be continued if an officially declared emergency makes travel to campus infeasible.

[USC Department of Public Safety](#) - UPC: (213) 740-6000, HSC: (323) 442-1200 – 24/7 on call

Non-emergency assistance or information.

[Office of the Ombuds](#) - (213) 821-9556 (UPC) / (323-442-0382 (HSC)

A safe and confidential place to share your USC-related issues with a University Ombuds who will work with you to explore options or paths to manage your concern.

[Occupational Therapy Faculty Practice](#) - (323) 442-2850 or otfp@med.usc.edu

Confidential Lifestyle Redesign services for USC students to support health promoting habits and routines that enhance quality of life and academic performance.