USC Dornsife College of Letters, Arts and Sciences

QBIO-110g – Drug discovery: from genes to medicines (4 units)

Spring 2023

Lectures: 11:00-12:20 pm TTh
Location: RRI-101

Discussion: 5:00-6:20 pm Th
Location: RRI-101

Instructor: Dr. Vsevolod "Seva" Katritch
Office Hours: 3:00-4:30pm Tue, and by appointment
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Course Description (short)

The course will explore the science of modern drug discovery and development, its key challenges and pitfalls in the personal health and socioeconomic context.

Course Description (full)

Modern drug discovery starts with a deep understanding of biological mechanisms, coded in our genes or genes of the pathogens, and involves major technological breakthroughs in structural and functional biology, chemistry, imaging, computational and other technologies on the way to clinical applications. Students will develop an appreciation of this complex and rapidly evolving multistage process of drug discovery and development, learn about its key challenges and pitfalls in the personal health and socioeconomic context.

Learning Objectives

Upon the successful completion of this course, students will be able to describe and explain the key aspects and stages of modern target-based drug discovery and development, and how they are rooted in advances in basic science and impact society. Specific learning objectives include understanding of the following concepts:

- Why do we need new drugs – a historical perspective
- Key biotechnology and "omics" platforms involved in drug discovery: Recombinant DNA, PCR, CRISPR etc.
- Target discovery and validation. Proteins and different types of protein targets (enzymes, receptors, channels/transporters, etc) and druggable sites. Structural biology revolution, NMR, X-ray, and cryo-EM
- Different types of therapies: small mol/peptides, antibodies/protein therapeutics, aptamers, degraders, DNA-binding, RNA- binding, gene therapies etc. Different interaction classes: covalent, allosteric, biased etc.
- Process of small molecule hit discovery and hit-to-lead optimization. Combinatorial and high-throughput chemistry.
- Computer-assisted drug discovery and machine learning (AI) in drug discovery. Structure-based vs. Ligand-based.
- Animal models and their relevance to disease and therapeutic effects. Transgenic and knockout animals.
- Medicinal chemistry optimization, delivery route and formulation, dosage, toxicity, and side effects. Therapeutic window and pharmacodynamics. Translational medicine, biomarkers and imaging.
- Scientific and ethical principles of clinical trials, Phase I-II-III. Patient cohorts and equity. Placebo and side effects.

- Drug approval, marketing, and post-market evaluation.
- Drugs and healthcare - recent therapeutic breakthroughs and major pitfalls (opioids, molnupiravir).
- Future of drug discovery in modern society – rapid response to emerging pathogens, personalized drugs, smarter drugs, and alternatives to drugs.

Required Materials

- Basic Principles of Drug Discovery and Development (2nd Edition, 2021) by Benjamin Blass. ISBN-13: 978-0128172148

New, used, and electronic copies are available from various online resources. eTextbook version can be rented.

Optional Materials

- Drugs: From Discovery to Approval (3rd Edition, 2015) by Rick Ng. ISBN-13: 978-1118907276
- The Drug Hunters: The Improbable Quest to Discover New Medicines (2018) by Donald R. Kirsch and Ogi Ogas. ISBN-13 : 978-1628727180

Description and Grading of Assignments

Written Exams will be administered in person on specific days during the class period (see Course Schedule below). Exams will be used to access all of the learning objectives. Exams may include multiple choice, multiple answer, true or false, fill-in-the-blank, short answer, or essay questions. A request to take a make-up exam must be accompanied by evidence of a university-sanctioned excused absence (*e.g.,* a letter from a doctor, athletic release, etc.) and must be made before the date of the scheduled exam. Make-up exams may be given in a different format from that of the scheduled exam (*e.g.,* essay).

In-Class Work will be unscheduled and used to access all learning objectives. Work may include small group assignments, polls, a summary of lecture points, open-note or closed-note quizzes, problem solving in groups, a submitted question of a "muddy point," or other individual assignments to be submitted or reported on by the end of class. When working in groups, all members will receive the same score for the work product. Students who miss an assignment as a result of either arriving late or leaving early will not have the opportunity to make up the work. However, the lowest three in-class assignments will be dropped to allow for occasional absences.

The ***term paper*** will be a 4 – 5 page (double-spaced) "cause and effect" literature review research paper on a specific drug of your choice. The paper will include various aspects of the discovery and development of this drug and citations from recent primary research articles. A detailed description of the term paper and the rubric for grading will be provided at a later time. The term paper is due before the Final Exam and will be submitted on Blackboard for grading by the course grader.

Grading Breakdown

Assignment	Points	% of Grade
Pop Quizzes/In-Class Work	200	20
Midterm 1	200	20
Midterm 2	200	20
Final Exam	200	20
Term Paper	200	20
Total	1000	100

Grading Scale

Letter Grade	Point Ranges	Grade Point Value
A	930-1000	4.000
A-	900-929	3.667
B+	870-899	3.333
B	830-869	3.000
B-	800-829	2.667
C+	770-799	2.333
C	730-769	2.000
C-	700-729	1.667
D+	670-699	1.333
D	630-669	1.000
D-	600-629	0.667
F	<600	0.000

Individual exams, quizzes, in-class assignments, and the term paper will be scored but not assigned a letter grade. Only the final point tally will be used to assign a letter grade.

Late Work

All in-class assignments will be due by the end of class and cannot be made up if missed. Similarly, all pre-lecture and homework assignments will have published due dates and will not be accepted late. However, the lowest three assignments of each will be dropped to allow for occasional in-class absences and missed pre-lecture or homework assignment deadlines.

Communication Policies

Students are *strongly* encouraged to raise any questions in regard to all matters involving course content or policy during Discussion section led by your TA. Should you have a question about specific course content and cannot attend Discussion, students are encouraged to submit their question to the course blog. Should you need to communicate with the instructor, please email the instructor from your USC email account *making sure to include in the subject line the course number and your full name* (expect significant delays or no response if this information is omitted). Simple questions will be answered by email but for more complex discussions students may be instructed to visit office hours. Best attempts will be made to answer all emails within 48 hours, 72 hours over a weekend and the work day following a holiday. Note that the instructor may not respond to nonemergency emails 24 hours preceding an exam and may not respond to emails sent from non-USC accounts.

To promote independence and critical thinking, students are encouraged to work through the following process for obtaining answers to course-related questions before contacting the instructor. First, consult the course syllabus. If you cannot find the answer you need, next please ask the question at Discussion section with your TA. If you still cannot find a satisfactory answer, email the instructor using your USC email *making sure to include the course number in the subject*

line. In your email, please indicate the steps you have gone through to seek the answer for your question. Use your USC email account for all correspondence with the instructor.

Technology Policies

It is expected that students will use any internet-enabled device(s) to participate in activities guided by the instructor alone. Such activities include looking up terms, doing research, and completing in-class work. Please make sure all electronic devices are silenced so as not to disturb classmates or the instructor during class. Use of electronic devices for other purposes during class is strongly discouraged and you may be asked to put a device away should your instructor deem it to be disruptive. If you require an internet-enabled device, please see the "Technological Proficiency and Hardware/Software Required" section above.

Attendance

Attendance of lectures is mandatory given in-class assignments cannot be made up unless a student has been excused from such an assignment due to a university-sanctioned excuse (*e.g.,* illness, religious holiday, athletic event, etc.). If remote students are allowed to enroll and if they live in a time zone in which attending class would be extremely inconvenient, they need to contact the instructor to make other arrangements for the assessment of in-class skill sets.

Classroom Norms

At all times, students are expected to promote and support a positive learning environment, to listen actively and attentively, to follow best practices of inclusivity, to be respectful of the instructors' and fellow students' views and opinions, and to only provide *constructive* criticisms and critiques when asked to do so.

Sharing of Course Materials Outside of the Learning Environment is Strictly Prohibited

USC has a strict policy (SCampus Section 11.12[B]) that prohibits sharing of *any* synchronous and asynchronous course content outside of the learning environment. Any student who violates this policy will be prosecuted to the maximum extent allowable by the USC Student Conduct Code, including failure of the course and suspension from the University.

Distribution or use of notes or recordings based on university classes or lectures without the express permission of the instructor for purposes other than individual or group study is a violation of the USC Student Conduct Code. This includes, but is not limited to, providing materials for distribution by services publishing class notes. This restriction on unauthorized use also applies to all information, which had been distributed to students or in any way had been displayed for use in relationship to the class, whether obtained in class, via email, on the Internet or via any other media. (See Section C.1 Class Notes Policy).

Tentative Course Schedule

	Date	Lecture Topic	Blass (2nd edition)
Week 1a	Jan10	Introduction: Big picture	
Week 1b	Jan12	History: 7000 years of drug discovery	Ch. 1
Week 2a	Jan17	Modern times: Key technologies	Ch. 2
Week 2b	Jan19	Key protein targets: structure, function, biology, druggable sites	Ch. 3
Week 3a	Jan24	Target Discovery and validation: "omics" approaches	-
Week 3b	Jan26	Finding a needle: In vitro screening	Ch. 4
Week 4a	Jan31	Rational approaches: Structure-based and fragment-based	-

Week 4b	Feb2	Rational approaches: In silico screening	-
Week 5a	**F**eb7	**MIDTERM EXAM 1**	-
Week 5b	Feb9	Hit to Lead optimization	Ch. 5
Week 6a	Feb14	Medicinal chemistry	Ch. 5
Week 6b	Feb16	In vitro properties measurements and predictions	Ch. 6
Week 7a	Feb21	In vivo pharmacokinetics	Ch. 6
Week 7b	Feb23	Animal models: why and how	Ch. 7
Week 8a	Feb28	Animal models of specific disease	Ch. 7
Week 8b	Mar2	How to make sure the drug is safe	Ch. 8
Week 9a	Mar7	Antibody drug discovery	Ch. 9
Week 9b	Mar9	New approaches to drugs: stem cells, gene therapies, RNA, etc	-
Week 10a	Mar 21	Basics concepts of Clinical Trials	Ch. 10
Week 10b	Mar23	**MIDTERM EXAM 2**	-
Week 11a	Mar28	Translational medicine, biomarkers and imaging technologies	Ch. 11
Week 11b	Mar30	Postmarket and major drug pitfalls	Ch. 11
Week 12a	Apr4	Economics of drug discovery	Ch. 12
Week 12b	Apr6	Intellectual property: why	Ch. 13
Week 13a	Apr11	Case studies: cancer	Ch. 14
Week 13b	Apr13	Case studies: cardiovascular	Ch. 14
Week 14a	Apr18	Case studies: psychiatric	Ch. 14
Week 14b	Apr20	Case studies: neurodegenerative	Ch. 14
Week 15a	Apr25	Case studies: Covid-19	-
Week 15b	Apr27	Future of drug discovery	-
May 9th		**FINAL EXAMINATION**	

Academic Accommodations

Any student requesting academic accommodations based on a disability are required to register with Disability Services and Programs (DSP) each semester. A letter of verification for approved accommodations can be obtained from DSP. Please be sure the letter is delivered to the instructor as early in the semester as possible. DSP is located in Student Union (STU) 301 and is open 8:30 a.m. – 5:00 p.m. Monday – Friday. The phone number for DSP is (213) 740-0776.

Academic Integrity and Conduct

Students who violate University standards of academic integrity are subject to disciplinary sanctions, including failure of the course and suspension from the University. Given that dishonesty in any form harms not only the individual but other students and the University, academic integrity policies will be strictly enforced. Please familiarize yourself with the Academic Integrity guidelines found in the current SCampus (Student Handbook).

Plagiarism, *i.e.,* 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" policy.usc.edu/scampus-part-b. Other forms of academic dishonesty are equally unacceptable. Additional information can be found in SCampus as well as university policies on scientific misconduct (policy.usc.edu/scientific-misconduct).

Academic Integrity Violations

Academic dishonesty/misconduct, e.g., plagiarism, cheating, unauthorized collaboration, etc., will not be tolerated. All academic integrity violations will result in a grade sanction and will be reported to the Office for Student Judicial Affairs. It is your responsibility to "reasonably" protect your own work from the plagiarism of others.

If plagiarism is detected on a group project, all members of the group will be held responsible.

You are expected to be familiar with the Academic Integrity guidelines found in the current SCampus. An electronic version is available at http://usc.edu/scampus.

Disruptive and Threatening Student Behavior

Behavior that persistently or grossly interferes with classroom activities is considered disruptive behavior and may be subject to disciplinary action. Such behavior inhibits other students' ability to learn and the instructor's ability to teach. A student responsible for disruptive behavior may be required to leave class pending discussion and resolution of the problem and may be reported to the Office of Student Judicial Affairs for disciplinary action.

Support Systems

Counseling and Mental Health - (213) 740-9355 – 24/7 on call
studenthealth.usc.edu/counseling
Free and confidential mental health treatment for students, including short-term psychotherapy, group counseling, stress fitness workshops, and crisis intervention.

National Suicide Prevention Lifeline - 1 (800) 273-8255 – 24/7 on call
suicidepreventionlifeline.org
Free and confidential emotional support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week.

Relationship and Sexual Violence Prevention Services (RSVP) - (213) 740-9355(WELL), press "0" after hours – 24/7 on call studenthealth.usc.edu/sexual-assault
Free and confidential therapy services, workshops, and training for situations related to gender-based harm.

Office of Equity and Diversity (OED) - (213) 740-5086 | Title IX – (213) 821-8298
equity.usc.edu, titleix.usc.edu
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
usc-advocate.symplicity.com/care_report
Avenue to report incidents of bias, hate crimes, and microaggressions to the Office of Equity and Diversity |Title IX for appropriate investigation, supportive measures, and response.

The Office of Disability Services and Programs - (213) 740-0776 dsp.usc.edu
Support and accommodations for students with disabilities. Services include assistance in providing readers/notetakers/interpreters, special accommodations for test taking needs, assistance with architectural barriers, assistive technology, and support for individual needs.

USC Campus Support and Intervention - (213) 821-4710 campussupport.usc.edu
Assists students and families in resolving complex personal, financial, and academic issues adversely affecting their success as a student.

Diversity at USC - (213) 740-2101
diversity.usc.edu
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
dps.usc.edu, emergency.usc.edu
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) 442-120 – 24/7 on call dps.usc.edu
Non-emergency assistance or information.

Office of the Ombuds - (213) 821-9556 (UPC) / (323-442-0382 (HSC)
ombuds.usc.edu
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.