USC School of Pharmacy

BPSI 402: Biopharmaceutics I

Coordinator: Hovhannes J. Gukasyan, PhD
Associate Professor, Department of Pharmacology and Pharmaceutical Sciences
University of Southern California
Email: gukasyan@usc.edu
Office Phone: (323) 442-1362
Office Location: HSC campus PSC 716
Office Hours: by appointment

Instructors: Daryl L. Davies, PhD
Professor, Department of Clinical Pharmacy
University of Southern California
Office: HSC campus PSC 506
Email: ddavies@usc.edu
Office Phone: (323) 442-1427
Office hours: by appointment

Course Weight: 4 Units (two weekly 1.5-hour sessions; plus computer simulations lab ad libitum complete drug discovery practice assignment and case study report)

Catalogue description: Comprehensive overview of industrial approaches to drug discovery; *in vitro* and *in vivo* assays and *in silico* simulations/modeling, exploratory biopharmaceutics.

Day/Time/Location: T/Th, 2:00-3:20pm, KAP 145

Introduction and Purpose

Biopharmaceutics I is a multidisciplinary course encompassing areas of study that employ basics of general chemistry, biology, and biochemistry addressing identification and refinement of early molecular substrate to an optimized candidate worthy of clinical trials. This introductory course – and a precursor to BPSI 403/Biopharmaceutics II - will provide students with a comprehensive overview of industrial approaches to drug discovery. It will focus on all modalities (small molecules, biologics, and other complex non-biological systems). Full spectrum of the course covers the classical division of pharmaceutical research into four phases, commencing with target identification and ending with preclinical.

We will build an understanding on how *in vitro* and *in vivo* assays are used to identify and validate drug targets and apply progressive modeling and simulation tools to improve molecular pharmacology of compounds. Modeling, computational methods and quantitative structure activity relationships (in chemistry, biology, and informatics) have become integral to the design

and development of new drugs. Handling large amounts of data to build learning models is poised towards launching artificial intelligence capability in drug discovery. Influencing key aspects of the discovery process, including molecular design, pharmacological and toxicological biochemistry assessment, comprise the linchpins to any new drug molecule and its future chances of becoming a medicinal product.

Applied biochemistry and biology concepts will be used to exemplify approaches in discovery of new drugs in a pragmatic, bio-pharmaceutical industrial context. Case studies to be enclosed in this course will include principals of drug design and pharmacology. Students will utilize computer aided virtual "blind" docking to proteins playing having roles as disease targets (i.e., computer lab) to study potency and selectivity of newly designed molecules. Concepts of translation of discovery-centric molecular parameters from virtual pre-clinical research to higher species will be introduced. Students' understanding of basic pharmacology and toxicology principles will be reinforced preparing them to apply knowledge gained in the design, implementation, and management of drug discovery in a variety of modality and strategy settings.

"Drug Discovery in the Modern Age: How We Got Here and What Does It Mean?" will be introduced, with case-study driven historical background, and current status of drug discovery. Students will be able to understand the basic concepts and tenets underlying modern drug discovery, how they have evolved, and various approaches and strategies to modern drug discovery. Beginning with a focus on TARGET SELECTION, then VALIDATION, discovery of drugs in BPSI 402 discusses the central dogma of industrial approaches to drug discovery. To help prepare the student for the ever-changing environment, this course will present foundational and newly advancing modeling and simulation technologies to provide knowledge regarding critical aspects of medicinal product development.

Objectives

BPSI 402, Biopharmaceutics I, is a recommended prerequisite of BPSI 403, Biopharmaceutics II. In Biopharmaceutics I, students will learn industrial, semi-automation, and digital approaches in drug discovery, question the productivity of each strategy, i.e., high-throughput technologies for screening millions of compounds against the large numbers of new targets from genomics, use of CADD in the same, and drug repositioning. Recognizing the need for greater productivity, bio-pharmaceutical organizations are demanding significantly greater throughput from existing resources. Translational aspects will be introduced to facilitate understanding interspecies relationships in safety and efficacy. (1) Target identification, by which the hypothesis of the involvement of a particular molecular target is postulated; (2) lead identification, delivery of several chemical lead series that show a demonstrable effect on the disease target of interest; (3) bearing on the optimization of the structure-activity relationships (SARs) around specific pharmacophore classes; and finally, (4) optimized lead compounds to enter preclinical/clinical testing where their overall selectivity and toxicity profiles are assessed as a precursor – will be covered.

Upon successful completion of this course, the student should be able to understand and explain:
- Drug targets: what are they, where they come from, how are they related to disease?

- Understand principles of drug target discovery or identification.
- Criteria for drug target validation. Is there a difference in drug discovery when it comes to validation of a drug target, as opposed to clinical treatment of a disease condition?
- What are different modalities of drugs in a discovery setting?
- Are all modalities equal when it comes to drug discovery?
- Are all targets "druggable"?
- What are hits? What are leads? What are candidates?
- What are druggable attributes in drug discovery?
- What is the mode of action or mechanism of action and how is it different from efficacy?
- What is potency as opposed to selectivity?
- What is pharmacology as opposed to toxicology?
- Use of:
  - Databased such as PubMed, PubChem, PDB, ChemiIDPlus Advanced, and Clinicaltrials.gov
  - Software such as Autodock Veena® and CB-Dock® for molecular docking; ChemDraw®/ChemSketch®/Marvin Sketch®/Online etc. for molecular editing.
- Interpret drugs bound to targets and mode of binding / cavity location / size

Assignments and Grading:

Class participation:	10 pts	(~3.3 %)
10 quizzes @ 10 pts each:	100 pts	(~33.3%)
Drug discovery project report:	90 pts	(30 %)
Cumulative final exam:	100 pts	(~33.3 %)
Total:	300 pts.	

Class Participation and Attendance (10 pts): On a scale of 10, 0-indicating no participation, 10-indicating best participation. You can therefore increase the probability of getting a higher mark by being proactive in terms of asking (relevant) questions in class and/or contributing to discussions.

Attendance at all classes is expected. Participation will include asking and answering questions and being actively involved in the discussion. It is expected that the students read the assigned papers prior to the lecture and be prepared to discuss background, current understanding, treatments, and gaps in knowledge for the topic in each lecture.

There will be 10 quizzes over the course of the semester that will primarily be based testing students' understanding of key concepts. The final exam, cumulative (100 points) will include multiple choice questions and/or T/F questions centered around all the quizzes taken over the course of 15 weeks. Notes, books, calculators, electronic dictionaries, regular dictionaries, cell phones or any other aids are not allowed during exams.

Double-spaced report, not more than 5 pages including figures and references, based on drug discovery case study (deliverable) will be due by **5pm PST on the day of the final** via posting on Blackboard or via email to gukasyan@usc.edu. The report will focus on designing a new drug against a specific target, with rationale on target selection, validation, and quantitative structure

activity vina score (Vina. An empirical scoring function calculates the affinity, or fitness, of protein-ligand binding by summing up the contributions of several individual terms) improvement demonstration.

Additional details will be presented during week one of the class and included in the Week 1 PPT slides.

Students will be asked to complete an anonymous critical evaluation of the course at its completion.

Course Readings

Required Readings

Handen, P.D.,.J.S. (Ed.). (2005). Industrialization of Drug Discovery: From Target Selection Through Lead Optimization (1st ed.). CRC Press. https://doi-org.libproxy2.usc.edu/10.1201/9781420028072

Chapters from required textbooks will be supplemented with a variety of source materials, including articles from scientific journals and public websites. Case studies will be critically reviewed, and emerging "hot" topics discussed.

Additional text that students may find helpful:
1. Drug Design: Principles and Applications, Grover, A. ISBN 9789811051876, https://books.google.com/books?id=n2AwDwAAQBAJ, 2017, Springer Singapore
2. Smith and Williams' Introduction to the Principles of Drug Design and Action. Smith, H.J., Williams, H. ISBN 9781135299750, https://books.google.com/books?id=4XmmDwAAQBAJ, CRC Press, 2005.

Additional textbooks are not mandatory, however students interested in drug discovery process should consider purchasing them to expand comprehension related principles. The students will be able to use identified chapters in the text to support their learning process throughout the semester.

Other course materials including but not limited to the syllabus, supplemental reading assignments and additional handouts will be posted on http://blackboard.usc.edu/. The students will also be encouraged to use the online discussions among students via Blackboard.

Recommended Supplemental Readings

Online learning Etiquette (if applicable)

- o If it is not possible to have you webcam on during the entire class, do you best to have it on when speaking
- o Turn off your microphone when not speaking
- o If you need to step away from your computer during class (e.g. get a drink of

water, use the bathroom, attend to a family member/pet) please do so quietly and without disturbing your classmates. Return to the class when you can.
- o Be aware the contents of conversations typed into the chat box, even private conversations, are visible by the instructors

Course Outline

This course will be in the format of a directed seminar/lecture under the guidance of the instructor for the specific session. During each weekly session, the instructor will engage the students with questions and draw comments or interpretations primarily based on the assigned reading. Students are expected to ask questions and participate in an interactive fashion.

Week & Date	Speakers	Subtopics to be Included	Assigned and Supplemental Reading
Week 1 Aug 23, 25	Gukasyan, HJ	▪ Welcome Orientation ▪ "Druggable" Property Space: Desired properties and qualities of an ideal candidate? Safety, Efficacy, Delivery	Syllabus, PowerPoint Slides
Week 2 Aug 30, Sep 1	Gukasyan, HJ	▪ Drug Discovery in the Modern Age: How We Got Here and What Does It Mean? ▪ The Regulatory Age	Handen Ch.1, 2
Week 3 Sep 6, 8	Gukasyan, HJ	▪ Drug Discovery in the Modern Age: How We Got Here and What Does It Mean? ▪ The Regulatory Age	Handen Ch.1, 2
Week 4 Sep 13, 15	Gukasyan, HJ	Industrialisation, Not Automation Applications of Computer-Aided Drug Design	Handen Ch. 3 Abhinav Ch. 9
Week 5 Sep 20, 22	Gukasyan, HJ	Compound Management Applications of Computer-Aided Drug Design	Handen Ch. 4 Abhinav Ch. 9
Weeks ~3-5	Computer lab work	Setting up drug files and protein target files, create a workflow for modification of templates, create a workflow for tracking Vina scores	Liu Y, et al. **CB-Dock: a web server for cavity detection-guided protein-ligand blind docking.** Acta Pharmacol Sin. 2020;41(1):138-144.
Week 6 Sep 27, 29	Gukasyan, HJ	High-Throughput Screening Applications of Computer-Aided Drug Design	Handen Ch. 5 Abhinav Ch. 9
Week 7 Oct 4, 6	Gukasyan, HJ	Parallel Lead Optimization Applications of Computer-Aided Drug Design	Handen Ch. 6 Abhinav Ch. 9
Week 8 Oct 11	Gukasyan, HJ	Knowledge Management Fall Recess	Handen Ch. 7
Week 9 Oct 18, 20	Gukasyan, HJ	Knowledge Management	Handen Ch. 7
Week 10 Oct 25, 27	Gukasyan, HJ	Cheminformatics Approaches in Modern Drug Discovery	Abhinav Ch. 9
Week 11 Nov 1, 3	Gukasyan, HJ	Cheminformatics Approaches in Modern Drug Discovery Understanding the Value of Research	Abhinav Ch. 9 Handen Ch. 8
Weeks 6-11	Computer lab work	Produce simple two dimensional correlations tracking simple structure modifications vs. Vina score and cavity size location	Yang Liu, et al. **CB-Dock2: improved protein–ligand blind docking by integrating cavity detection, docking and homologous template fitting**. Nucleic Acids Research, 2022, vol. 50, is. W1, p. W159–W164.
Week 12* Nov 8, 10	Gukasyan, HJ	Collaboration in a Virtual and Global Environment	Handen Ch. 9
Week 13* Nov 15, 17	Gukasyan, HJ	From Genome to Drug: Ethical Issues	Handen Ch. 10
Week 14* Nov 22	Gukasyan, HJ	From Genome to Drug: Ethical Issues ADMET Properties: Overview and Current Topics Thanksgiving Recess	Handen Ch. 10 Abhinav Ch. 8
Week 15 Nov 29, Dec 1	Gukasyan, HJ	Pharmacogenetics and Personalized Medicine ADMET Properties: Overview and Current Topics	Abhinav Ch. 10 Abhinav Ch. 8
Weeks 12-15	Computer lab work	Compose a brief report with literature based background on target, disease, drug starting point and individual lead optimization experimental results. Explain final candidate selection in terms of best Vina score, and draggability criteria.	Save final discovered drug candidate molecule and report for BPSI 403 if planning to take second half of Biopharmaceutics (e.g. II).
Dec 7th-14th	Finals Week	Final Exam TBD; reports due by 5pm on day of Final Exam	

*Place holder for possible biopharmaceutical industry guest lectures

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" policy.usc.edu/scampus-part-b. Other forms of academic dishonesty are equally unacceptable. See additional information in SCampus and university policies on Research and Scholarship Misconduct.

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
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 for Equity, Equal Opportunity, and Title IX (EEO-TIX) - (213) 740-5086
eeotix.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 for Equity, Equal Opportunity, and Title for appropriate investigation, supportive measures, and response.

The Office of Student Accessibility Services (OSAS) - (213) 740-0776
osas.usc.edu
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) 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, Equity and Inclusion - (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.

*Occupational Therapy Faculty Practice - (323) 442-33*40 or otfp@med.usc.edu
chan.usc.edu/otfp
Confidential Lifestyle Redesign services for USC students to support health promoting habits and routines that enhance quality of life and academic performance.