

USC Mann

Alfred E. Mann School of Pharmacy
and Pharmaceutical Sciences

Fall 2023: BPSI 412: Targeted and Precision Medicines FINAL

Instructors

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Course Weight: 4 Units

Day/Time/Location: Mon, Wed/12:30-1:50pm/KAP 159

Catalog Description: Precision medicine utilizing data from basic science, clinical, personal, environmental and population settings; understanding biological processes and disease mechanisms; develop precise diagnostics, therapeutics and prevention.

Introduction

Fundamental principles of analyzing and visualizing biomedical data using code; Introduction to tools and software packages for data analysis, featuring interactive notebooks based on Python. Analysis of next-generation sequencing data.

Review of examples of targeted and precision medicines utilizing data from basic science, clinical, personal, environmental and population settings; understanding biological processes, biomarkers, and disease mechanisms; development of precise diagnostics, therapeutics and preventions.

Most medical treatments have been designed for the "average patient" as a one-size-fits-all-approach, which may be successful for some diseases. Precision medicine, alternatively called

"personalized medicine", represents an innovative approach to tailoring disease prevention and treatment by considering differences in people's genes, and impact of their environments or lifestyles. The goal of precision medicine is to target the right treatments at the right dose to the right patients at the right time (The Four Rights, Margaret A. Hamburg, M.D. former FDA commissioner, "Path to Personalized Medicine" N Engl J Med 2010; 363:301-304).

Advances in precision medicine have already led to powerful new discoveries and FDA-approved treatments that are tailored to specific characteristics of individuals, such as a person's genetic makeup, or the genetic profile of an individual's disease. Drug products such as Xalkori®, Lorbrena®, Zelboraf®, Lumakras®, and Krazati® are a few examples, and will be case-studied in BPSI 412. The era of precision medicine is rapidly unfolding. Staying ahead of the curve in this emerging field requires a solid foundation of knowledge and training. This encompasses our ability to harness all available data and technology tools at our disposal to prevent and treat human illness and improve human health.

Objectives

The objective of this course is to train students in the state-of-the-art tools and methods for bioinformatics analysis of next generation data. Secondary objectives include studies of example drugs from pharma or biotech (small molecules or biologics) as medical modalities, that have been discovered, developed, and approved based on principles of targeting specific genetic drivers of disease. Primary and secondary objectives will render a global understanding around expertise in bioinformatics, pharmacology, diagnostics, and regulation which facilitate bringing precision drugs to patients.

Students are expected to learn how to:

- Analyze the large-scale biomedical data using commonly used interactive python-based libraries and packages.
- Use various visualizations techniques to display real-world biomedical data in real-time.
- Use open source biological and genomics databases for basic information and analysis.
- Run bioinformatics analysis of next generation sequencing data using high-performance computing.
- Describe the current state of knowledge and emerging trends in precision medicine in clinical practice.
- Relate mutated cancer-relevant genes to drug pharmacology and mechanism of action, as well as emergence of resistance.
- Interpret pharmacogenetic data and present information to individuals of varying levels of knowledge.
- Determine whether a variant is "somatic" by comparison with the germline DNA.
- Understand the heterogeneous nature of most tumors.

Deliverables, Evaluation and Grading

Evaluation will be based on one midterm examination, a final examination, five course quizzes, and three writing assignments (critical report and discussion).

Description	Points	Weight
Up-to 10 Quizzes (normalized pts) Includes class participation	50 pts	(20%)
Midterm presentation/report	50 pts	(20%)
Homework	25 pts	(10%)
Individual data analysis project	50 pts	(20%)
Final research term paper	75 pts	(30%)
Total	250 pts	(100%)

20% Quizzes: There will be up-to 10 quizzes over the course of the semester. Each quiz will be worth a number normalized fraction of the total 50 pts, but all quizzes will contribute to 20% cumulative fraction of the final grade. The quizzes may be based on questions testing students understanding of lecture and reading material and may include multiple choice, T/F and fill-in the blank questions. There will be no makeups allowed for unexcused missed quizzes.

20% Midterm presentation/report: There will be 1 midterm for this course that will be due following first 8 weeks. The midterm will consist of a presentation/report. Near the midpoint of the course, students will present their findings to the class. The presentations should be 5-8 minutes but no more than 10 minutes in length. This assignment will help students to generate a critical assessment of key topics in this course, to develop a suitable argument, and to convey their ideas and interpretations through writing.

10% Homework assignments will be given throughout the course to facilitate mastering techniques and methods for real world genomic data analysis in discovery and design of precision drugs.

30% Individual data analysis project: students will prepare and present an analysis of real world genomic data from public repositories. They will be evaluated on completeness and accuracy of their methodology application and thoroughness of sourcing data from public data-banks.

30% Final research term paper (literature survey): will be in the form of a research term paper due during exam week. The assignment will include critical analysis and research of existing or emerging precision medicines or their coupled diagnostics devices. Submission will demonstrate the students' knowledge regarding topics covered in the course and allow students to express their ideas based on facts derived from the course.

Course Readings:

1. Cai, W., Liu, Z., Miao, L., & Xiang, X. 2020 Pharmacogenomics in Precision Medicine. Singapore: Springer Nature.
2. Refer to "Readings" column for access through digital library

Fall Course Outline:

Week	Date	Lecture	Readings
Week 1	Mon. Aug. 21	The Path to Personalized Medicine (HG)	N Engl J Med 2010; 363:301-304 DOI: 10.1056/NEJMp1006304
Week 1	Wed. Aug. 23	The story of Crizotinib, case study on biology (HG)	Soda, M., Choi, Y., Enomoto, M. et al. Identification of the transforming EML4–ALK fusion gene in non-small-cell lung cancer. Nature 448, 561–566 (2007). https://doi.org/10.1038/nature05945
Week 2	Mon. Aug. 28	Introduction to modern computational data-driven research	
Week 2	Wed. Aug. 30	Overview of fundamental software tools and platforms to analyze biomedical data	
Labor Day, University Holiday, Monday September 4, 2023			
Week 3	Wed. Sept. 6	The story of Crizotinib Part 2, target engagement. (HG)	https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/202570s021lbl.pdf
Week 4	Mon. Sept. 11	Google Colab Lab 1	
Week 4	Wed. Sept. 13	Lorlatinib, case study on cancer biology. (HG)	1. Nat Cancer. 2022 Jun;3(6):710-722. doi: 10.1038/s43018-022-00399-6. Epub 2022 Jun 20. 2. Clin Cancer Res. 2021 May 15;27(10):2899-2909. doi: 10.1158/1078-0432.CCR-21-0032. Epub 2021 Mar 8.
Week 5	Mon. Sept. 18	Lorlatinib, case study on target engagement. (HG)	Cancer Discov. 2018 Jun;8(6):714-729. doi: 10.1158/2159-8290.CD-17-1256. Epub 2018 Apr 12. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210868s000lbl.pdf
Week 5	Wed. Sept. 20	Alectinib and Ceritinib case studies on cancer biology. (HG)	1. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208434s003lbl.pdf 2. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211225s000lbl.pdf
Week 6	Mon. Sept. 25	Vemurafenib case study on target engagement and differentiation	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3623294/

		from other melanoma drugs (HG)	
Week 6	Wed. Sept. 27	Drugging the undruggable Ras: mission possible? - PMC (nih.gov) (HG)	https://doi.org/10.1038%2Fnr4389
Week 7	Mon. Oct. 2	Fundamental concepts of biomedical data cleansing, manipulation, and wrangling through Python libraries.	
Week 7	Wed. Oct. 4	Implementation of code-driven visualization for real world biomedical data.	
Week 8	Mon. Oct. 9	Python pandas Lab 2 - Data Management Overview	
Fall Recess, Thursday Oct. 12 to Friday. Oct. 13, 2023			
Week 9	Mon. Oct. 16	Targeting Mutant Kirsten Rat Sarcoma Viral Oncogene Homolog in Non-Small Cell Lung Cancer: Current Difficulties, Integrative Treatments and Future Perspectives - PMC (nih.gov) (HG)	https://doi.org/10.3389%2Fphar.2022.875330
Week 9	Wed. Oct. 18	Fundamental concepts of bioinformatics analysis of next generation sequencing (NGS) data	
Week 10	Mon. Oct. 23	Analysis of NGS data using bioinformatics tools (1)	
Week 10	Weds. Oct. 25	Analysis of NGS data using bioinformatics tools (2)	
Week 11	Mon. Oct. 30	UNIX Lab 4- Running bioinformatics tools with UNIX command line	
Week 11	Wed. Nov. 1	Bioinformatics Lab 5- Analysis of NGS data from public genomic repositories using bioinformatics tools	
Week 12	Mon. Nov. 6	Sotorasib and adagrasib, KRAS story, a cancer biology approach (HG)	Targeting KRAS in non-small-cell lung cancer: recent progress and new approaches - PubMed (nih.gov)
Week 12	Weds. Nov. 8	Sotorasib and adagrasib, KRAS story, a cancer biology approach, investigating the ultimate target for cancer (HG)	Therapeutics Targeting Mutant KRAS - PubMed (nih.gov)
Week 13	Mon. Nov. 13	Sotorasib target engagement and differentiation (HG)	1. label (fda.gov) 2. label (fda.gov)

Saturday, December 2 to Tuesday, December 5, 2023 – Study Days

**FINAL EXAM/SUBMISSIONS:
FRIDAY, DECEMBER 8, 11 am to 1 pm**

***note** topics are subject to change, there may be special lectures from invited guests from various biotech/pharma organizations which will replace assigned topics (TBD).

Course Content Distribution and Synchronous Session Recordings Policies

USC has policies that prohibit recording and distribution of any synchronous and asynchronous course content outside of the learning environment. Recording a university class without the express permission of the instructor and announcement to the class, or unless conducted pursuant to an Office of Student Accessibility Services (OSAS) accommodation. Recording can inhibit free discussion in the future, and thus infringe on the academic freedom of other students as well as the instructor. ([Living our Unifying Values: The USC Student Handbook](#), page 13).

Distribution or use of notes, recordings, exams, or other intellectual property, based on university classes or lectures without the express permission of the instructor for purposes other than individual or group study. This includes but is not limited to providing materials for distribution by services publishing course materials. 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. ([Living our Unifying Values: The USC Student Handbook](#), page 13).

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.