

Course Title: Pharmacogenomic and Genomic Data Analysis
Transcript Title: PGx-Genomic Analysis
PHA 6449

Departments of Pharmacotherapy and Translational Research
Center for Pharmacogenomics, University of Florida
Credits: 3 hours

Spring Semester 2020

Course Syllabus

COURSE DESCRIPTION: Pharmacogenomics is the study of how an individual's genetics influence responses to drugs, while genomics is the study of genes and their functions. This course will focus on pharmacogenomics and human genomics, particularly disease genomics. This course will include utilization of key knowledge from the central dogma of molecular biology, the human genome, HapMap and 1000 genomes projects, genomic, transcriptomic, and metabolomics approaches, other considerations in design of human pharmacogenomic and disease genomic investigations, and approaches to defining functional effects of biological candidate biomarkers (SNPs, RNA, metabolites). This course will use the framework of pharmacogenomics and human genomics to lay the foundation for understanding other types of omic and pharmaco-omic study designs and analyses. The course will use a combination of lectures, discussions of assigned literature, small group discussions, analysis projects and student-led presentations. This course is intended as a graduate course with a maximum of 12 students.

Pre-requisites: 1 semester of statistics (PHC 6052/6053 or similar) OR PCB 5065 (Advanced Genetics) (preferably both) OR instructor approval.

Learning Objectives: The goal of this course is to provide students with the knowledge and skills to undertake pharmacogenomics/genomics research. The students will learn the basics of designing a pharmacogenomics or a genomics study using genomic, transcriptomic and metabolomics approaches. The students will also gain hands-on experience of how to apply for access to publically available data and how to perform a pharmacogenomics or genomics GWAS analysis using real data. The focus on GWAS analyses will provide students with a skill set that may be applied to many other types of 'omic' data.

CLASS PERIOD/ROOM: Pre-Recorded Lectures: 0-2 hours per week
Live Lecture and Discussion: 1-2 hour per week – Monday 3-5pm
Small group discussion: 0-1 hour per week – Wednesday 3-5pm

As of March 10th, 2020 – all classes will meet online via Zoom

COURSE COORDINATORS: Yan Gong, Ph.D. (gong@cop.ufl.edu)
Caitrin McDonough, Ph.D. (cmcdonough@cop.ufl.edu)

FACULTY: Timothy Garrett, Ph.D (tgarrett@ufl.edu)
Julio Duarte, Pharm.D., Ph.D. (juliod@cop.ufl.edu)
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INVITED SPEAKER: Sonal Singh, PhD. (sonal.singh@takeda.com)
Takeda Pharmaceutical Company.

TEXT: There is no required text. The instructors will provide the required readings.

GRADING AND EXAMS:

The course grade will be determined as follows:

• Written report of pharmacogenomics study/oral presentation	25%/5%
• Association analysis written report/oral presentation	15%/5%
• Association analysis follow-up written report/oral presentation	15%/5%
• Final written exam	10%
• Class participation/completion of required readings	20%

Grades will be assigned as follows:	92.50-100%	A
	89.50-92.49%	A-
	86.50-89.49%	B+
	82.50-86.49%	B
	79.50-82.49%	B-
	76.50-79.49%	C+
	72.50-76.49%	C
	69.50-72.49%	C-
	66.50-69.49%	D+
	62.50-66.49%	D
	59.50-62.49%	D-
	< 59.50%	E

Information on the current UF grading policy for assigning grade points may be found at:
<https://catalog.ufl.edu/ugrad/current/regulations/info/grades.aspx>

ACCOMMODATIONS FOR STUDENTS WITH DISABILITIES: Students requesting classroom accommodation must first register with the Dean of Students Office. The Dean of Students Office will provide documentation to the student who must then provide this documentation to the instructor when requesting accommodation.

ACADEMIC HONESTY: UF students are bound by The Honor Pledge which states, “We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honor and integrity by abiding by the Honor Code. On all work submitted for credit by students at the University of Florida, the following pledge is either required or implied: “On my honor, I have neither given nor received unauthorized aid in doing this assignment.” The Honor Code (<http://www.dso.ufl.edu/scer/process/student-conduct-honor-code/>) specifies a number of behaviors that are in violation of this code and the possible sanctions. Furthermore, you are obliged to report any condition that facilitates academic misconduct to appropriate personnel. If you have any questions or concerns, please consult with the instructor of TAs in this class.

Plagiarism: Plagiarism is defined as the practice of taking someone else’s work or ideas and passing them off as one’s own. Plagiarism is not tolerated at the University of Florida or in this class. All written assignments will be examined for originality using iThenticate software, to ensure the work represents each student’s own words, and that proper citation is used. If a written assignment is found to be plagiarized (e.g. large portions of the work are directly copied from another source), the incident will be reported to the University, and procedures outlined by the students’ graduate program will be followed.

STUDENT ASSIGNMENTS

Projects/papers/presentations:

Note: All written reports are due at the start of class on the oral presentation days.

Genomic or Pharmacogenomics project. For this project, you will be expected to find a publically available dataset with genome-wide SNP data (GWAS data), and drug information (NIH dbGaP, UK biobank, the Million Veterans Program are the recommended sources, and will be covered in class). You will select your primary

drug response phenotype from the phenotypes available in the study you are working with. You will select additional phenotypes that you would want to include as covariates in your analysis. You will identify the sample size, genetic information available (or other 'omic information available), your study design, the limitations in your study design that arise from using a publically available dataset, which was not necessarily collected with pharmacogenomic questions in mind, and ways that you plan to overcome these limitations. You will use the provided modified template for a dbGaP proposal for the written report, and you should include appropriate references. The oral presentation should be ~8 minutes summarizing your written dbGaP proposal. You may also use other 'omics data available within dbGaP, or other 'omic data from similar databases (with instructor approval) to complete this assignment. The question, hypothesis and phenotype still must be pharmaco – omic based.

Association analysis project – Part 1. To gain experience with pharmaco-omic analyses and the types of large datasets these analyses use, you will conduct a pharmacogenomic GWAS analysis. You will be given data from the Pharmacogenomic Evaluation of Antihypertensive Responses (PEAR) study for association analysis. It is expected that you will each be given directly typed or imputed data from either the whole genome, or part of the genome, and will be given the relevant covariates and drug response phenotype data. To conduct this analysis, you will need to learn PLINK software at the website: <http://pngu.mgh.harvard.edu/~purcell/plink/index.shtml> or a similar analysis tool. Additionally, you will need a HPC account (<http://www.hpc.ufl.edu/help/account-request/>), you should list your graduate advisor as the faculty member.

You will then summarize in both an oral and written report your analysis approach and statistically-strongest findings, including typical graphical representations of your findings. Your oral presentation should be ~8 minutes.

Association analysis project – Part 2. The second part of your association analysis project will be to 1) describe the 3 strongest biological candidates/regions from your analysis, identifying the genes that make the region strong and why, 2) describe the LD in the top regions, and whether your top SNPs, or any LD/tag SNPs, are putative functional SNPs, and 3) summarize what you would consider your strongest 5 SNPs, based on all of the above, to move forward to replication in an independent cohort. Again, this will be summarized in a written and oral presentation. The oral presentation should be ~8 minutes long.

****Project requirements may change slightly depending on the students' knowledge level**

Final Written Exam - We will be posting 5 essay questions on the course website. You must answer 4 of the 5. Using approximately 200-250 words per question. Provide proper references for the answers. This can be open book/open note, but you must work alone, and use your own words. You will submit your documents through the course website, via TurnItIn.

Note: Prior offerings of this course have resulted in publication of the course project with all the participating students included as coauthors:

McDonough CW, Gillis NK, Alsultan A, Chang SW, Kawaguchi-Suzuki M, Lang JE, Shahin MH, Buford TW, El Roubi NM, Sá AC, Langaee TY, Gums JG, Chapman AB, Cooper-DeHoff RM, Turner ST, Gong Y, Johnson JA. [Atenolol induced HDL-C change in the pharmacogenomic evaluation of antihypertensive responses \(PEAR\) study](#). PLoS One. 2013;8(10):e76984. doi: 10.1371/journal.pone.0076984. eCollection 2013. PubMed PMID: 24116192; PubMed Central PMCID: PMC3792156.

Shahin MH, Conrado DJ, Gonzalez D, Gong Y, Lobmeyer MT, Beitelshes AL, Boerwinkle E, Gums JG, Chapman A, Turner ST, Cooper-DeHoff RM, Johnson JA. [Genome-Wide Association Approach Identified Novel Genetic Predictors of Heart Rate Response to \$\beta\$ -Blockers](#). J Am Heart Assoc. 2018 Feb 24;7(5). doi: 10.1161/JAHA.117.006463. PubMed PMID: 29478026; PubMed Central PMCID: PMC5866313.

Singh S, McDonough CW, Gong Y, Alghamdi WA, Arwood MJ, Bargal SA, Dumeny L, Li WY, Mehanna M, Stockard B, Yang G, de Oliveira FA, Fredette NC, Shahin MH, Bailey KR, Beitelshes AL, Boerwinkle E,

Chapman AB, Gums JG, Turner ST, Cooper-DeHoff RM, Johnson JA. [Genome Wide Association Study Identifies the *HMGC2* Locus to be Associated With Chlorthalidone Induced Glucose Increase in Hypertensive Patients](#). J Am Heart Assoc. 2018 Mar 9;7(6). doi: 10.1161/JAHA.117.007339. PubMed PMID: 29523524; PubMed Central PMCID: PMC5907544.

McDonough CW, Magvanjav O, Sá ACC, El Rouby NM, Dave C, Deitchman AN, Kawaguchi-Suzuki M, Mei W, Shen Y, Singh RSP, Solayman M, Bailey KR, Boerwinkle E, Chapman AB, Gums JG, Webb A, Scherer SE, Sadee W, Turner ST, Cooper-DeHoff RM, Gong Y, Johnson JA. [Genetic Variants Influencing Plasma Renin Activity in Hypertensive Patients From the PEAR Study \(Pharmacogenomic Evaluation of Antihypertensive Responses\)](#). Circ Genom Precis Med. 2018 Apr;11(4):e001854. doi: 10.1161/CIRCGEN.117.001854. PubMed PMID: 29650764; PubMed Central PMCID: PMC5901893.

Shahin MH, Conrado DJ, Gonzalez D, Gong Y, Lobmeyer M, Beitelshes AL, Boerwinkle E, Gums JG, Chapman AB, Turner ST, Cooper-DeHoff RM, Johnson JA. [β₂-Adrenergic Receptor Gene Affects the Heart Rate Response of β-Blockers: Evidence From 3 Clinical Studies](#). J Clin Pharmacol. 2019 Nov;59(11):1462-1470. doi: 10.1002/jcph.1443. Epub 2019 May 14. PubMed PMID: 31090079.

Final oral examination. Following your association analysis (Part 2) presentation, you will be asked questions related to this assignment, but will also be asked questions that will serve as your final oral examination (i.e. questions can derive from anywhere in the course).

Required Readings. Students are expected to complete all required readings PRIOR to class, and a portion of their grade will be based on class participation and their ability to discuss the required readings.

Class Attendance. Attendance to all class sessions, and to all other students' oral presentations is expected. If you need to miss a class session, you need to make **ADVANCED** arrangements with the course coordinators. All unexcused absences will receive a 'zero' for that week's participation grade.

Late assignments. Assignments turned in late will receive a penalty:

1 hr to 24 hrs late: 20% deduction

25 hrs to 48 hrs late: 50% deduction

Assignments will not be accepted past 48 hrs, and the student will receive a zero.

These requirements for class attendance and make-up exams, assignments, and other work in this course are consistent with university policies that can be found in the online catalog at:

<https://catalog.ufl.edu/ugrad/current/regulations/info/attendance.aspx>.

Class demeanor: Students are expected to be engaged and participate during class. We also expect minimal cell phone usage and internet usage during class.

Course and instructor evaluations. Students are expected to provide feedback on the quality of instruction in this course based on 10 criteria. These evaluations are conducted online at <https://evaluations.ufl.edu>. Evaluations are typically open during the last two or three weeks of the semester, but students will be given specific times when they are open. Summary results of these assessments are available to students at <https://evaluations.ufl.edu>.

**Pharmacogenomics
PHA 6449
Course Schedule Spring 2020**

Week	Lecture Topics and Discussion Schedule		Instructor
	Monday	Wednesday	
Week 1 Jan 6	Live Lectures: 1. Course introduction 2. Overview of genomics and pharmacogenomics 3. Study designs in disease genetics and Pharmacogenomics 4. Introduction to 1 st project and publically available data sources	No Small Group Discussion	Gong & McDonough
Week 2 Jan 13 Jan 15	Pre-recorded Lectures (watch before the live discussion): 1. Linkage disequilibrium, HapMap, 1000 Genomes & ENCODE; 2. Controlling for population structure in genetic association analyses Live Discussion: Overview of online databases and web tools	Small Group Discussions – Public data source genomic/PGx study	McDonough
Week 3 MLK Day Jan 20 Jan 22	No Class Monday Jan 20 th – MLK Day Pre-recorded Lectures: 1. Genetic association analysis 2. Power calculation for GWAS	Live Discussion (ALL: 3-4pm): Group discussion of Genome-wide association studies in disease genetics and pharmacogenomics	Gong & McDonough
Week 4 Jan 27 Jan 29	Live Lectures: 1. Intro to 2 nd project 2. Brief PLINK installation and tutorial 3. Computer hands-on training: PLINK 4. Q&A for power calculations.	Small Group Discussions – Public data source genomic/PGx study	Gong McDonough
Week 5 Feb 3	Student presentations of Public datasource genomics/PGx study	Small Group Discussions – Public data source genomic/PGx study	All McDonough
Week 6 Feb 10 Feb 12	No Class Monday Feb 10 th due to Research Showcase – all COP students and trainees are expected to attend the Research Showcase	Public datasource genomic/PGx study Papers are due at the start of class Live Lectures and Hands-on Training (ALL: 3-5pm): 1. Imputation 2. Continued hands-on training: PLINK	Gong & McDonough

Week 7 Feb 17 Feb 19	Live Lecture: 1. Meta-analysis and rare variant analysis 2. GWAS Meta-analysis QC Live Discussion: Analysis Q&A	Small Group Discussions – PLINK/GWAS analysis	Gong & McDonough
Week 8 Feb 24 Feb 26	Live lectures: 1. Next-generation sequencing 2. Application of Transcriptome and RNAseq in PGx Live Discussion: Sequencing applications in Disease genetics and PGx	Small Group Discussions – PLINK/GWAS analysis	Duarte
Week 9	Spring Break		
Week 10 March 9 March 11	Live Lecture: Introduction to Metabolomics Live training: Metabolomics analysis using MetaboAnalyst	Small Group Discussions – PLINK/GWAS analysis VIA ZOOM	Garrett
Week 11 March 16 March 18	Live ZOOM lectures: 1. Epigenetics and pharmacogenomics, DNA methylation analysis (3-4pm) 2. GWAS follow-up analysis 3. Analysis project 2 guidelines	Discussion if needed please email Dr. Gong and Dr. McDonough if you want to attend VIA ZOOM	Langae Gong & McDonough
Week 12 March 23 March 25	Genetic association analysis presentations via ZOOM Genetic association analysis papers are due by 3pm on Canvas Email presentations to Gong/McDonough by 2pm	No Small Group Discussion	All
Week 13 March 30 April 1	Live Zoom Lecture: MicroRNA Live Zoom Discussion: Applications of metabolomics, epigenetics, methylation, mircoRNA in PGx OR project discussion	Small Group Discussions – Follow-up Association Projects via Zoom	Marwa Gong & McDonough
Week 14 April 6 April 8	Live Zoom Lecture: Proteomics Live Zoom Discussion: Paper examples	Small Group Discussions – Follow-up Association Projects via Zoom	TBD
Week 15 April 13 April 15	Live Lecture through Zoom : Integrated analysis of multiple types of genomic data Live Lectures through Zoom : Other Data sources (EHR, Claims) and other analyses (PheWAS, PRS, MR) Final Written Exam will be released on April 13th	Small Group Discussions – Follow-up Association Projects via Zoom	Sonal (invited) Gong & McDonough
Week 16 April 20	Association analysis hits: strongest candidates presentations via ZOOM Final Written Exam due by 11:59pm on Canvas Final Papers are due at 3pm on Canvas Email presentations to Gong/McDonough by 2pm		All 3 hours (2-5pm OR 3-6pm)