Pharmacogenomics
PHA 6449
Departments of Pharmacotherapy and Translational Research
Center for Pharmacogenomics, University of Florida
Credits: 3 hours (Pending with the Office of the Registrar)

Spring Semester

Course Syllabus

COURSE DESCRIPTION: Pharmacogenomics is the study of how an individual's genetics influences responses to drugs. This course will focus on pharmacogenetics and pharmacogenomics research design, including 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 pharmacogenomics investigations, and approaches to defining functional effects of pharmacogenetic candidates. This course will use the framework of pharmacogenomics 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, 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 or pharmaco-'omic' research. The students will learn the basics of designing a pharmacogenomics 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 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: Lecture: 2 hours per week – Mondays 3:00 -5:00 PM; HSC MSB Room PG-19
Small group discussion: 1 hour per week – Wednesday 3:00-5:00PM

COURSE COORDINATOR: **Yan Gong, Ph.D. (gong@cop.ufl.edu)**
CO-COORDINATOR: **Caitrin McDonough, Ph.D. (cmcdonough@cop.ufl.edu)**

FACULTY:
Larisa Cavallari, Pharm.D. (LCavallari@cop.ufl.edu)
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Mohamed Shahin, Ph.D. (mhossam@cop.ufl.edu)

INVITED SPEAKER: **Hobart Rogers, Pharm.D (Hobart.Rogers@fda.hhs.gov)**

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 oral exam 10%

- Class participation/completion of required readings 10%
- Human Genetics Quizzes 10%

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/sccr/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 iTheniticate software, to ensure the work represents each students 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.

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 is the recommended source, 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 8-9 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 8-9 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 ~10 minutes long.

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

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 Rouby 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 Oct 7;8(10):e76984. PubMed PMID: 24116192.

McDonough CW, El Rouby NM, Magvanjav O, Sa ACC, Dave C, Kawaguchi-Suzuki M, Mei W, Shen Y, Singh R, Solayman M, Tucker AN, Bailey KR, Boerwinkle E, Chapman AB, Turner ST, Cooper-DeHoff RM, Gong Y, Johnson JA. Genetic Variants Influencing Plasma Renin Activity in Hypertensive Patients from the Pharmacogenomics Evaluation of Antihypertensive Responses (PEAR) Study. In Revision. *Circ Cardiovascular Genet*.

Conrado DJ, Gonzalez D, Gong Y, Shahin MH, Lobmeyer M, Cooper-DeHoff RM, Boerwinkle E, Turner ST, Chapman AB, Gums JG, Johnson JA. Genetic Predictors of Heart Rate Response to beta-blockers in the Pharmacogenomic Evaluation of Antihypertensive Responses (PEAR) Study. In Revision. *JAHA*.

Singh S, Alghamdi W, Arwood M, Bargal S, de Oliveira F, Dumeny L, Li W, Mehanna M, Fredette N, Stockard B, Yang G, Shahin M, Bailey KR, Beitelshees AL, Boerwinkle E, Chapman AB, Gums JG, Turner ST, Gong Y, McDonough CW, Cooper-DeHoff RM, Johnson JA. Genome wide association study to identify pharmacogenomic variants associated with chlorthalidone induced glucose change in African Americans. Journal of the American Heart Association. In Revision. *JAHA*.

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.

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Course Schedule Spring 2018

Week	Lecture Topics and Discussion Schedule	Instructor
Week 1 Jan 8th	Course introduction and Overview of pharmacogenetics and pharmacogenomics Study designs in pharmacogenetics and phenotype selection and Identifying biological candidate genes.	Gong
	Home Study: 1) Intro to PGx and Quiz 2) Principles of Genetic Medicine, Part 1 and Quiz	
Week 2 *WED Jan 17th*	Linkage disequilibrium, HapMap, 1000 Genomes & ENCODE; Controlling for population structure in genetic association analyses	McDonough
	Home Study: Principles of Genetic Medicine, Part 2 and Quiz	
Week 3 Jan 22nd	Introduction to 1st project, and NCBI dbGaP TagSNPs, pfSNPs, and other web tools and databases	McDonough
	Home Study: Database Tools for Pharmacogenomics, and Quiz	
Week 4 Jan 29th	Genome-wide association studies in pharmacogenomics (discussions)	Gong & McDonough
Jan 31st	Small Group Discussions – dbGaP projects	
Week 5 Feb 5th	Association analysis: GWAS and meta-analysis; Intro to 2nd project Computer hands-on training: PLINK	Gong McDonough
Feb 7th	Small Group Discussions – dbGaP projects	
Week 6	Feb. 12th: no class due to College Research Showcase	
Feb 14th	Computer hands-on training: Genomic QC with PLINK Association analysis: Imputation	McDonough Sonal Singh
Week 7 Feb 19th	**Student presentations of dbGaP pharmacogenomics study** **dbGaP Papers are due at the start of class**	All
Feb 21st	Small Group Discussions – GWAS analysis	
Week 8 Feb 26th	Association analysis: meta-analysis Analysis Q&A	Gong Gong & McDonough
Feb 28th	Small Group Discussions – Association I Projects	
Week 9	**Spring Break (March 5th – March 9th)**	

Week 10 March 12th	Next-generation sequencing; Whole genome sequencing, Whole Exome sequencing (discussions)	Duarte
March 14th	Small Group Discussions – Association I Projects	
Week 11 March 19th	Application of Transcriptome and RNAseq in PGx Epigenetics and pharmacogenomics, DNA methylation analysis	Duarte DeRemer
	NO SMALL GROUP DISCUSSION – ASCPT (March 21st-24th)	
Week 12 March 26th	**Genetic association analysis presentations** **Genetic association analysis papers are due at the start of class**	All
March 28th	Small Group Discussions – Follow-up Association Projects	
Week 13 April 2nd	Application of Metabolomics in Pharmacogenomics	Garrett
April 4th	Small Group Discussions – Follow-up Association Projects	
Week 14 April 9th	Integrated analysis of multiple types of genomic data	Mohamed Shahin
April 11th	Small Group Discussions – Follow-up Association Projects	
Week 15 April 16th	Pharmacogenomics: Regulatory Issues Pharmacogenomics: Translation to Practice	Rogers (FDA) Cavallari
April 18th	Small Group Discussions – Follow-up Association Projects	
Week 16 April 23rd	**Association analysis hits: strongest candidates presentations** **FINAL ORAL EXAM** (conducted at the end of each students presentation) **Final Papers are due at the start of class**	All 3 hours (2-5pm OR 3-6pm)