PHAR 6224
Pharmacogenomics: Genetic Basis for Variability in Drug Response
Spring 2017
2 Credits
Tuesdays 3:35-5:30pm

Course Director: Pamala Jacobson, PharmD Professor
Experimental and Clinical Pharmacology
WDH 7-151
Minneapolis, MN 55455
jacob117@umn.edu
612-624-6118

Course Faculty: Jeff Bishop, PharmD, Associate Professor
Experimental and Clinical Pharmacology
14-271 Moos Tower
Minneapolis, MN 55455
jrbishop@umn.edu
612-625-5435

Jacob Brown, PharmD, Assistant Professor
Pharmacy Practice and Pharmaceutical Sciences
115 Life Sciences, 1110 Kirby Drive
Duluth, MN, 55812
jtbrown@d.umn.edu
218-726-6028

Bonnie LeRoy, MS, CGC, Professor
College of Biological Sciences; Genetics, Cell Biology, and Development
Director, Graduate Program of Study in Genetic Counseling, MCB 5-104
Minneapolis, MN 55455
Leroy001@umn.edu

Amit Mitra, PhD, Postdoctoral Fellow
College of Biological Science and Institute of Human Genetics
mitra008@umn.edu

William S Oetting, PhD, Professor
Experimental and Clinical Pharmacology
14-255 Moos Tower
515 Delaware St SE
Minneapolis, MN 55455
oetti001@umn.edu
612-624-1139
Robert Straka, Pharm.D, Professor
Experimental and Clinical Pharmacology
WDH 7-115
Minneapolis, MN
strak001@umn.edu
612-625-5663

Brian VanNess, PhD, Professor
College of Biological Sciences and Institute of Human Genetics
2231 6th St SE
Room 3-131 CCRB
Minneapolis, MN 55455
vanne001@umn.edu
612-624-9944

Michael Walters, Ph.D, Research Associate Professor
Institute for Therapeutics Discovery & Development
717 Delaware St SE, Room 609
Minneapolis, MN 55455
mwalters@umn.edu
612-626-6864

Sophia Yohe, MD, Assistant Professor
Department of Laboratory Medicine and Pathology
Rm D219-7 Mayo
420 Delaware St SE
Minneapolis, MN 55455
yohe001@umn.edu

Teaching Assistants:
Duluth
Axel Vazquez-Deida
vazqu103@d.umn.edu

Twin Cities
David Hottman
Hott0017@umn.edu

Rooms:
College of Pharmacy
Twin Cities WDH 7-193
Duluth 165 LSci

Meeting Time:
Tuesdays, 3:35-5:30pm

Course Description:
Phar 6224 is a 2 credit elective course oriented towards 2nd and 3rd year pharmacy and graduate students. This
course consists of lectures and in class discussions designed to introduce the theory and practice of pharmacogenomics. The goal of the course is to give students an understanding of the principles of human genetics and genomics as they apply to improving the problems in drug therapy optimization and patient care. The genetic basis of variability in drug response can contribute to drug efficacy and toxicity, adverse drug reactions and drug-drug interactions. As such, pharmacists need an understanding of the genetic component of patient variability to deliver effective individualized pharmaceutical care. Understanding of the basics of pharmacogenomics will enable students to better understand and manage the new genomics based tools as they become available as well as make best treatment choices. The principles covered in this course will prepare pharmacists and clinical scientists to critically evaluate, interpret and apply this information.

**Learning Objectives:**

At the conclusion of the course, the student will be able to:

1. **Explain** the basic principles of human genetics and heredity as they apply to inter-individual variation in medication treatment response.
2. **Apply** the principles of molecular and cellular biology to explain the genetic basis of variability in drug response.
3. **Describe** the various biochemical/molecular biology methods used to determine genotype and polymorphic variability.
4. **Discuss** how genetic variability in genes encoding drug metabolizing enzymes, drug transporting proteins, and drug receptors (targets) can contribute to variability in drug disposition and action, leading to changes in pharmacokinetics, pharmacodynamics and clinical outcome.
5. **Recognize** the societal and ethical implications of genetic testing and the resultant individualization of drug therapy.
6. **Apply** pharmacogenomic concepts to a particular drug therapy to solve relevant problems in pharmaceutical care.
7. Critically **evaluate** the current and future literature in the area of pharmacogenomics.
8. **Identify** key sources and genetic data-bases with information relevant to pharmacogenomics.

9. **Describe** study designs and statistical techniques used in pharmacogenomics.

**Textbook:**

**Prerequisites:**
College of Pharmacy professional student in Duluth or Twin Cities in the second or third year of the Pharm.D. program, Experimental and Clinical Pharmacology graduate students and others with permission.

**Course Format:**
Class format will be traditional lecture/discussion or seminar format, in class discussion of assigned materials, hands on activities using databases and clinical case studies where the discussion in based around a situation (problem) that a clinician may encounter that requires application of the knowledge of genetic variability and drug response and an oral presentation on a pharmacogenomic topic.

**Exams and assignments:**
There will be one **midterm exam** during the semester. This exam will be worth 30 points. The **final exam** will be comprehensive, i.e., it will cover material from the entire semester and will be worth 30 points. There will also be class assignments/homework (20 points total) and two quizzes (10 points each). Exams and quizzes will be given in class. Oral group presentation on a pharmacogenomic topic (20 points). **Total possible points over the semester are 120.**

**Oral Group Presentation:**
Students will work together in groups to select and deliver a short presentation on a contemporary pharmacogenomic topic. Potential topics will be provided. The time allowed for these Powerpoint presentations will be dependent upon course enrollment. Four hours of class time will be devoted to this exercise.

**Grading Policy:**
Students who have questions regarding the grading of the midterm exam or quizzes must submit them in writing to the instructor within one week following the return of the exam or quiz grades.
Grades will be assigned according to the following:

<table>
<thead>
<tr>
<th>Grade</th>
<th>%Range</th>
<th>Grade</th>
<th>%Range</th>
<th>Grade</th>
<th>% Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>93-100</td>
<td>B</td>
<td>80-82</td>
<td>D</td>
<td>60-69</td>
</tr>
<tr>
<td>A-</td>
<td>90-92</td>
<td>C+</td>
<td>77-79</td>
<td>F</td>
<td>Less than 60</td>
</tr>
<tr>
<td>B+</td>
<td>87-89</td>
<td>C</td>
<td>73-76</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>83-86</td>
<td>C-</td>
<td>70-72</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Honor Code: Each student is bound by the following specific provisions as part of the honor code: Academic misconduct is any unauthorized act which may give a student an unfair advantage over other students, including but not limited to: falsification, plagiarism, misuse of test materials, receiving unauthorized assistance and giving unauthorized assistance. Specifically, each student will be required to do her/his own work on all assessments unless otherwise stated.

Make-Up Policy: A make up assignment or exam may be allowed only under one of the following circumstances: illness, verified by a note from a medical doctor; a family emergency, verified by note from the professional person in attendance; a university of Minnesota-sponsored event, verified by a note from the leader of the sponsoring organization.

Disability Accommodations: Students with a documented disability (eg. physical, learning, psychiatric, vision, hearing, etc.) already registered with the Disability Resource Center must contact the course director within the first week of class to discuss your accommodations. Accommodations take advance planning to implement. Students who do not present documentation from Disability Services a minimum of one week before an assessment will adhere to original/traditional expectations for that assessment. Please contact Disability Services to quantify and arrange the necessary accommodations: Twin Cities: http://ds.umn.edu/ 612-626-1333 Duluth: http://www.d.umn.edu/access/ 218-726-8217 All discussions concerning this issue will remain confidential. English as a second language is not considered a disability by the College of Pharmacy and this course will not accommodate requests for additional exam time based on this criterion.

<table>
<thead>
<tr>
<th>Minneapolis Campus</th>
<th>Duluth Campus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disability Services</td>
<td>Disability Services</td>
</tr>
<tr>
<td>McNamara Alumni Center</td>
<td>256 Kirby Student Center</td>
</tr>
</tbody>
</table>
Course evaluation: Students will have an opportunity to complete online course evaluations for course instructors and the overall course. We value your opinion.
<table>
<thead>
<tr>
<th>Dates</th>
<th>Topic</th>
<th>Instructor</th>
<th>Lecture No.</th>
<th>Hrs In/out class</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/17/17</td>
<td>Introduction. Course expectations, sequencing of material, course schedule. Introduction to human genome, evolving concepts of genes/locus. Introduction to genetic variation, types of variants, SNPs, coding and cis/trans regulatory variants, insertion/deletions, copy number variants</td>
<td>Pamala Jacobson</td>
<td>William Oetting</td>
<td>1/1</td>
</tr>
<tr>
<td>1/17/17</td>
<td>From DNA to a clinical result. Whole genome and whole exome sequencing, bioinformatics, creation of reports for clinicians.</td>
<td>William Oetting</td>
<td>2</td>
<td>1/1</td>
</tr>
<tr>
<td>1/24/17</td>
<td>Pharmacogenomics in Psychiatry Part 1. Variants affecting drugs used for psychiatric indications.</td>
<td>Jeff Bishop</td>
<td>3</td>
<td>1/1</td>
</tr>
<tr>
<td>1/24/17</td>
<td>Pharmacogenomics in Psychiatry Part 2.</td>
<td>Jeff Bishop</td>
<td>4</td>
<td>1/1</td>
</tr>
<tr>
<td>1/31/17</td>
<td>Pharmacogenomics in Cardiology Part 1. Variants affecting drugs used for cardiovascular indications such as Acute Coronary Syndromes, dyslipidemia and others.</td>
<td>Robert Straka</td>
<td>5</td>
<td>1/1</td>
</tr>
<tr>
<td>1/31/17</td>
<td>Pharmacogenomics in Cardiology Part 2. HOMEWORK ASSIGNMENT</td>
<td>Robert Straka</td>
<td>6</td>
<td>1/1</td>
</tr>
<tr>
<td>2/7/17</td>
<td>Genetic Counseling Counseling on genetic findings, tools to assist in counseling, how to explain genetic and genetic variation to patients, disease risk vs pharmacogenomic variants, future</td>
<td>Bonnie LeRoy</td>
<td>7</td>
<td>1/1</td>
</tr>
<tr>
<td>2/7/17</td>
<td>Drug development in the post-genomic era. Use of genetics in development of new therapies in pharmaceutical industry (e.g. imatinib, crizotinib, herceptin).</td>
<td>Michael Walters</td>
<td>8</td>
<td>1/1</td>
</tr>
<tr>
<td>2/14/17</td>
<td>Pediatric Pharmacogenomics Part 1. Variants affecting common drugs used in children and special considerations of genetics in this population (e.g ADHD, PPIs, codeine, asthma)</td>
<td>Jacob Brown</td>
<td>9</td>
<td>1/1</td>
</tr>
<tr>
<td>Date</td>
<td>Activity</td>
<td>Instructor</td>
<td>Lecture Range</td>
<td>Pages</td>
</tr>
<tr>
<td>------------</td>
<td>--------------------------------------------------------------------------</td>
<td>---------------------</td>
<td>---------------</td>
<td>-------</td>
</tr>
<tr>
<td>2/14/17</td>
<td>Pediatric Pharmacogenomics Part 2. <strong>HOMEWORK ASSIGNMENT</strong></td>
<td>Jacob Brown</td>
<td>10</td>
<td>1/1</td>
</tr>
<tr>
<td>2/21/17</td>
<td><strong>In class Quiz (15 min)</strong> <strong>Covers lectures 1-10</strong></td>
<td>Pamala Jacobson</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2/21/17</td>
<td>Clinical consequences of pharmacogenomic based drug interactions. The impact of how genetic variants modify the severity of a drug interaction.</td>
<td>Robert Straka</td>
<td>11</td>
<td>1/1</td>
</tr>
<tr>
<td>2/21/17</td>
<td>Hands on exercise with genomics databases PharmGKB, NCBI, 1000genomes, hapmap, etc</td>
<td>Amit Mitra</td>
<td>12</td>
<td>1/1</td>
</tr>
<tr>
<td>2/28/17</td>
<td>Hands on exercise with genomics databases PharmGKB, NCBI, 1000genomes, hapmap, etc <strong>HOMEWORK ASSIGNMENT</strong></td>
<td>Amit Mitra</td>
<td>13</td>
<td>1/1</td>
</tr>
<tr>
<td>2/28/17</td>
<td>PGx cases and interpretation of genetic results</td>
<td>Jeff Bishop/Jacob Brown</td>
<td>14</td>
<td>1/1</td>
</tr>
<tr>
<td>3/7/17</td>
<td>PGx cases and interpretation of genetic data results <strong>HOMEWORK ASSIGNMENT</strong></td>
<td>Jeff Bishop/Jacob Brown</td>
<td>15</td>
<td>1/1</td>
</tr>
<tr>
<td></td>
<td><strong>Spring Break March 13-17, 2017 (No Classes)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3/21/17</td>
<td><strong>In Class Midterm Exam</strong> <strong>Covers lectures 1-16</strong></td>
<td>Pamala Jacobson</td>
<td>17-18</td>
<td>1/6</td>
</tr>
<tr>
<td>3/28/17</td>
<td>Oncology Part 2. Genetic variation in tumors and how they affect response or toxicity to anticancer and targeted cancer agents.</td>
<td>Brian VanNess</td>
<td>20</td>
<td>1/1</td>
</tr>
<tr>
<td>3/28/17</td>
<td>Ethical, social and legal issues. Equity of access cost of treatments and genetics, possible adverse consequences of knowledge of risk alleles, duties to warn, returning genetic results to patients.</td>
<td>Brian Van Ness</td>
<td>21</td>
<td>1/1</td>
</tr>
<tr>
<td>Date</td>
<td>Activity</td>
<td>Instructor</td>
<td>Time</td>
<td>Date</td>
</tr>
<tr>
<td>----------</td>
<td>-------------------------------------------------------------------------------------------</td>
<td>-------------------</td>
<td>-------</td>
<td>------------</td>
</tr>
<tr>
<td>4/4/17</td>
<td>Commercial genotyping, 23 and me case, and interpretation of genotypes.</td>
<td>Pamala Jacobson</td>
<td>22</td>
<td>1/1</td>
</tr>
<tr>
<td>4/4/17</td>
<td>Specific use cases of genetic variants (germline) or expression (tumor, Oncotype) to select therapy or assess toxicity for drugs such as warfarin, immunesuppressant, tamoxifen.</td>
<td>Pamala Jacobson</td>
<td>23</td>
<td>1/1</td>
</tr>
</tbody>
</table>
| 4/11/17  | **In class quiz (15 minutes)**  
**Covers lectures 20-23**  | Pamala Jacobson  |       | 1/1        |
| 4/11/17   | Ethical, social and legal issues. Equity of access, cost of treatments and genetics, possible adverse consequences of knowledge of risk alleles, duties to warn, returning genetic results to patients.  | Brian Van Ness    | 24    | 1/1        |
| 4/18/17  | Student group presentations on pharmacogenomics topic in class on a drug or class of drugs not covered in class. | Pamala Jacobson, Jeff Bishop, others | 25    | 1/3        |
| 4/18/17  | Student group presentations on pharmacogenomics topic in class on a drug or class of drugs not covered in class. | Pamala Jacobson, Jeff Bishop, others | 26    | 1/3        |
| 4/25/17  | Student group presentations on pharmacogenomics topic in class on a drug or class of drugs not covered in class. | Pamala Jacobson, others | 27    | 1/3        |
| 4/25/17  | Student group presentations on pharmacogenomics topic in class on a drug or class of drugs not covered in class. | Pamala Jacobson, others | 28    | 1/3        |
| 5/2/17   | **Final exam in class (comprehensive)**                                                   | All available faculty | 29-30 | 1/8        |
|          | Finals week May 8-12, 2017                                                                |                   |       |            |

Updated: December 1st, 2016
Updated: January 3rd, 2017
Updated: January 31st, 2017
Updated: February 13th, 2017