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Teaching Assistants: Duluth
Megan Olander (PD3)
olan0051@d.umn.edu

Twin Cities
Lauren Lemke (PD3)
lemke172@umn.edu

Rooms: College of Pharmacy
Twin Cities MT 1450
Duluth 165 LSci

Meeting Time: Tuesdays, 1:25-3:20pm

Course Description: Phar 6224 is a 2 credit elective course directed towards 2rd 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. **Describe** the various biochemical/molecular biology methods used to determine genotype and polymorphic variability.
3. **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.

4. **Describe** the differences between germline and somatic mutations and the therapeutic implications of the presence of somatic mutations in cancer.

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

6. **Critically** evaluate PGx literature.

7. **Discuss** the Clinical Pharmacogenomic Implementation Consortium (CPIC) guidelines, how they are written, how to utilize the information and the limitations.

8. **Recognize** the societal and ethical implications of genetic testing and the resultant individualization of drug therapy.

9. **Apply** pharmacogenomic concepts to a particular drug therapy to solve relevant problems in pharmaceutical care.

10. Critically **evaluate** the current and future literature in the area of pharmacogenomics.

11. **Identify** key resources and genetic data-bases with information relevant to pharmacogenomics.

12. **Evaluate and interpret** commercial pharmacogenomic panels, understand the implications for drug therapy and convey the results to patients and providers.

**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 is based around a situation (problem) that a clinician may
encounter that requires application of the knowledge of genetic variability and drug response.

Exams and assignments: There will be one midterm exam during the semester. This exam will be worth 35 points. The final exam will be worth 35 points. There will also be class assignments/homework (30 points total). Exams will be given in class. Total possible points over the semester are 100.

Field Trip: There will be one optional field trip to a local commercial pharmacogenomic company. Students will learn what services a pharmacogenomic company provides, genetic testing options, the type of people employed and the business model. Students will be responsible for their own transportation to the Minneapolis Headquarters.

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:

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<tr>
<th>Grade</th>
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<tr>
<td>A</td>
<td>93-100</td>
<td>B-</td>
<td>80-82</td>
<td>D</td>
<td>60-69</td>
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<td>A-</td>
<td>90-92</td>
<td>C+</td>
<td>77-79</td>
<td>F</td>
<td>Less than 60</td>
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<td>B+</td>
<td>87-89</td>
<td>C</td>
<td>73-76</td>
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<td>B</td>
<td>83-86</td>
<td>C-</td>
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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: University policy recognizes that there are a variety of legitimate circumstances in which students will miss coursework, and that accommodations for makeup work will be made. This policy applies to all course requirements, including any final examination. Students are responsible for
planning their schedules to avoid excessive conflicts with course requirements. The University policy is located at: https://policy.umn.edu/education/makeupwork

**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 Disability Services</th>
<th>Duluth Campus Disability Services</th>
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<tbody>
<tr>
<td>McNamara Alumni Center</td>
<td>256 Kirby Student Center</td>
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<tr>
<td>200 Oak St SE Suite</td>
<td>180 1120 Kirby Drive</td>
</tr>
<tr>
<td>Minneapolis, MN 55455</td>
<td>Duluth, MN 55812</td>
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<tr>
<td>612-626-1333</td>
<td>218-726-8217</td>
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<tr>
<td><a href="http://www.ds.umn.edu/students/">www.ds.umn.edu/students/</a></td>
<td><a href="http://www.d.umn.edu/access/">www.d.umn.edu/access/</a></td>
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</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>
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</table>
| 1/22/19| Course Introduction  
Course expectations, sequencing of material, course schedule.  
Introduction to the human genome. Introduction to genetic variation, types of variants, SNPs, coding and cis/trans regulatory variants, insertion/deletions, copy number variants. Star allele nomenclature and SNPs vs haplotypes. DNA markers vs RNA expression from tissue | Pamala Jacobson & R. Stephanie Huang | 1           | 1/1              |
|        | From DNA to a clinical result. Description of candidate SNP panels, GWAS panels, whole genome, whole exome sequencing and how each are used in PGx. The bioinformatics behind PGx testing and the creation of a clinical interpretable report will be covered. | R. Stephanie Huang           | 2           | 1/1              |
|        | Pharmacogenomics in Psychiatry Part 1.  
Variants affecting drugs used for psychiatric indications such as the SSRIs and TCA will be presented. The controversies and difficulty in using PGx in this field will be discussed. | Jeff Bishop                 | 4           | 1/1              |
| 2/5/19 | Pharmacogenomics in Psychiatry Part 2. Continued                     | Jeff Bishop                 | 5           | 1/1              |
|        | Pharmacogenomics in Cardiology Part 1.  
The effect of genomic determinants on warfarin INR and outcomes, and the effect of genomic markers on statin related outcomes and mylagias will be covered. The importance of using clinical factors with PGx markers for determining warfarin dose through the use of online dosing equations will be presented. | Robert Straka               | 6           | 1/1              |
| 2/12/19| Pharmacogenomics in Cardiology Part 2.  
Clinical consequences of pharmacogenomic based drug interactions. The impact of how genetic variants modify the severity of a drug interaction.  
**HOMEWORK ASSIGNMENT 1** | Robert Straka               | 7           | 1/2              |
| 2/12/19| Drug development in the post-genomic era.  
Use of genetics in the discovery and development of new therapies in the pharmaceutical industry e.g. imatinib, ivacaftor, maraviroc, CNS drugs of the future. | Michael Walters             | 8           | 1/1              |
<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Instructor</th>
<th>Page</th>
<th>Homework Assignment</th>
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</thead>
<tbody>
<tr>
<td>2/19/19</td>
<td>Adult Neuropsychiatric PGx cases and interpretation of genetic results</td>
<td>Jeff Bishop &amp; Jacob Brown</td>
<td>9</td>
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<td><strong>HOMEWORK ASSIGNMENT 2</strong></td>
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<tr>
<td>2/26/19</td>
<td>Pediatric Pharmacogenomics Part 1.</td>
<td>Jacob Brown</td>
<td>10</td>
<td>1/2</td>
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<td>Variants affecting common drugs used in children and special considerations of genetics in this population (e.g. ADHD, PPIs, codeine, asthma)</td>
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<td>2/26/19</td>
<td><strong>Pediatric Pharmacogenomics Part 2.</strong></td>
<td>Jacob Brown</td>
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<td>1/1</td>
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<td><strong>Pediatric Neuropsychiatric PGx cases and interpretation of genetic results</strong></td>
<td>Jacob Brown</td>
<td>12</td>
<td>1/2</td>
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<tr>
<td>3/5/19</td>
<td><strong>In Class Midterm Exam (2 hours covers lectures 1-12)</strong></td>
<td>Available faculty Pamala Jacobson</td>
<td>13-14</td>
<td>1/6</td>
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<tr>
<td>3/12/19</td>
<td>Oncology Part 1.</td>
<td>Sophia Yohe</td>
<td>15</td>
<td>1/1</td>
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<td>Genetic variation in tumors. Mutations vs expression testing. Technology to test for mutations, companion diagnostics vs laboratory developed testing</td>
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<tr>
<td>3/12/19</td>
<td><strong>Oncology Part 2.</strong></td>
<td>David Stenehjem</td>
<td>16</td>
<td>1/1</td>
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<td>Pharmacogenomics in Phase I/II metabolism and drug transport of common anticancer therapies: germline genetic variants impacting pharmacokinetics</td>
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<td>3/19/19</td>
<td><strong>Spring Break March 18-22, 2019 (No Classes)</strong></td>
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<td>3/26/19</td>
<td>Oncology Part 3. Precision Oncology – somatic alterations in the tumor impacting pharmacodynamics of anticancer therapies.</td>
<td>David Stenehjem</td>
<td>17</td>
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<tr>
<td></td>
<td><strong>Oncology Part 4.</strong></td>
<td>Pamala Jacobson &amp; David Stenehjem</td>
<td>18</td>
<td>1/2</td>
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<td>Specific use cases of germline genetic variants for toxicity, somatic variants predicting response, and expression panels to select therapy (e.g. Oncotype, Mammmaprint).</td>
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<tr>
<td>4/2/19</td>
<td><strong>PGx tools to create phenotypes from genotypes. Part 1.</strong></td>
<td>Zach Rivers</td>
<td>19</td>
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<tr>
<td></td>
<td>Case examples of creation of phenotypes from genotypes and alleles. Examination of different PGx panels and the differing phenotype calls.</td>
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<tr>
<td>4/2/19</td>
<td><strong>PGx tools and databases; hands on exercises and cases part 2:</strong></td>
<td>Zach Rivers</td>
<td>20</td>
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<td>Solving a PGx case without a CPIC guideline. Complex cases.</td>
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<td><strong>HOMEWORK ASSIGNMENT 5</strong></td>
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<td>Date</td>
<td>Assignment</td>
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<td>Start/End</td>
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<td>4/9/19</td>
<td>Field Trip to OneOme Company. OneOme was established by Invenshure and the Mayo Clinic, and provides a comprehensive, cost-effective pharmacogenomic testing panel. OneOme’s key product offering is the RightMed® comprehensive test.</td>
<td>Pamala Jacobson, Brian Van Ness &amp; any available faculty</td>
<td>21-22</td>
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<tr>
<td>4/16/19</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>23/1/1</td>
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<td>Ethics Debate – in class</td>
<td>Brian Van Ness</td>
<td>24/1/2</td>
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<td><strong>ETHICS REFLECTION ASSIGNMENT 6</strong></td>
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<tr>
<td>4/23/19</td>
<td>Pros and Cons of Direct to Consumer PGx testing e.g. 23andMee, Color Genomics. Assessment of an actual 23andMee panel.</td>
<td>Pamala Jacobson</td>
<td>25/1/2</td>
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<td><strong>HOMEWORK ASSIGNMENT 7</strong></td>
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<td>Implementation of PGx in a health care system. Creation and description of a PGx inpatient service and a pharmacist run PGx clinic. Barriers in implementation and how to overcome.</td>
<td>David Gregornik</td>
<td>26/1/1</td>
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<tr>
<td>4/30/19</td>
<td>Genetic Counseling Counseling on genetic findings, tools to assist in counseling, how to explain genetic and genetic variation to patients, relative risk, disease risk vs pharmacogenomic genes, case example on how to explain risk</td>
<td>Heather Zierhut</td>
<td>27/1/1</td>
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<td>Emerging areas in Genomics. gene editing, CRISPR, emerging gene expression profiling, epigenetic shifts, tumor heterogeneity and plasticity, immunotherapy biomarker</td>
<td>Brian VanNess</td>
<td>28/1/1</td>
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<tr>
<td>5/7/19</td>
<td>In Class Final Exam (2 hours covers lectures 15-28)</td>
<td>Available faculty Pamala Jacobson</td>
<td>29-30/1/6</td>
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Finals week May 13-17, 2019

No Class

Updated 12-10-18