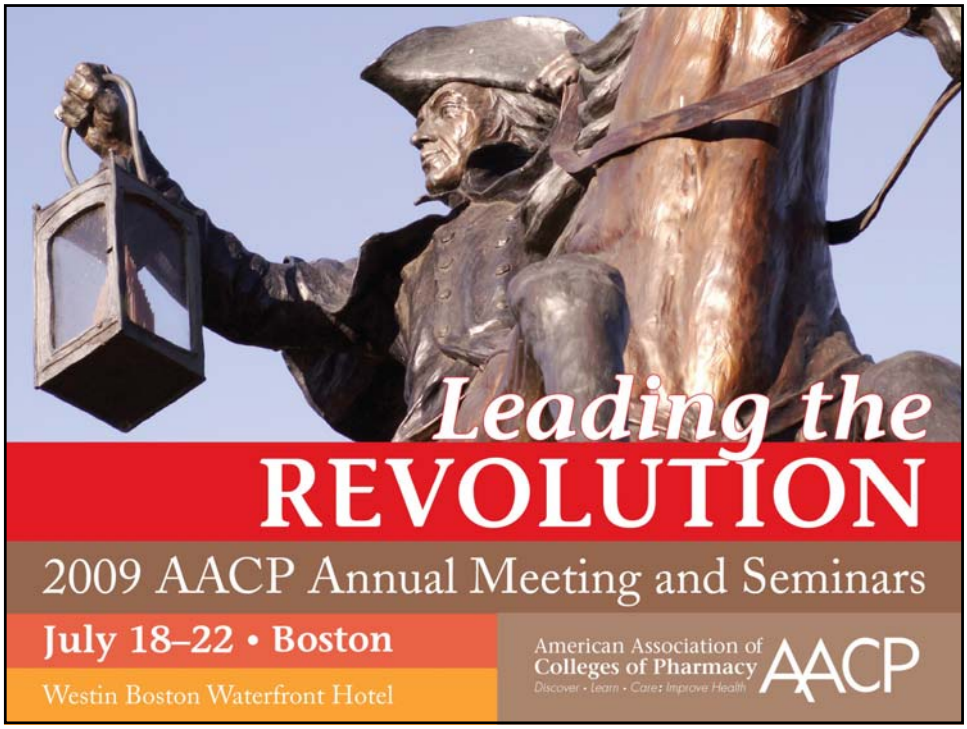

Pharmacogenetics and the PharmD Curriculum: Examples from the UIC College of Pharmacy

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UIC PHARMACOGENOMICS LABORATORY

Goals and Objectives

- To review the integration of pharmacogenetics/genomics (PGx) in UIC PharmD curriculum
- To discuss the type of PGx information included in PharmD courses
  - Required courses/lecture based
  - Electives
  - Lab experiences
- Barriers to integration
  - Challenges
  - Opportunities

Integrating Pharmacogenomics into Patient Care

The Next New Thing

A revolution in genetic research is targeting treatments to patients' unique characteristics. It can mean the difference between life and death. By Sharon Begley

Made-to-Order Medicine

JILL WAS ONLY 2 WHEN the diagnosis came: acute lymphoblastic leukemia (ALL). This rare childhood cancer, the doctors assured her parents, is highly curable with a cocktail of four chemotherapy drugs. But from the very beginning the chemo made Jill acutely ill: her white-cell, red-cell and platelet counts plummeted, and even with biweekly transfusions "her counts kept going lower and lower," says Dr. Mary Relling of St. Jude Children's Research Hospital in Memphis, where Jill was treated. Doctors didn't know whether the leukemia was knocking out her blood production—or whether the chemo itself was. But they had a way to find out. Researchers at St. Jude and at the Mayo Clinic in Rochester, Minn., had recently discovered that patients with a single mistake in a gene called TPMT fail to produce the enzyme that metabolizes the chemo drug, 6-mercaptopurine. As a result, the drug builds up in the body to toxic levels. Jill belonged to the 0.3 percent of the population—one person in 300—that carries two copies of the misspelled TPMT

SPECIAL TREATMENT Herceptin, a drug developed by Dr. Dennis Slamon, targets a receptor found in only 30 percent of breast cancers

"...pharmacogenetics promises to target treatment to a patient's genetic profile..."
Newsweek June 25, 2001

Clinical Applications

- FDA approved drugs with PGx info on labeling
  - N=7 with "recommended" action in the label
  - N=69 labels mentioning human genomic biomarkers
  - N=52 labels mentioning microbial genomic biomarkers

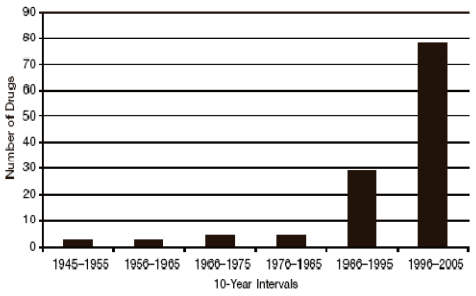
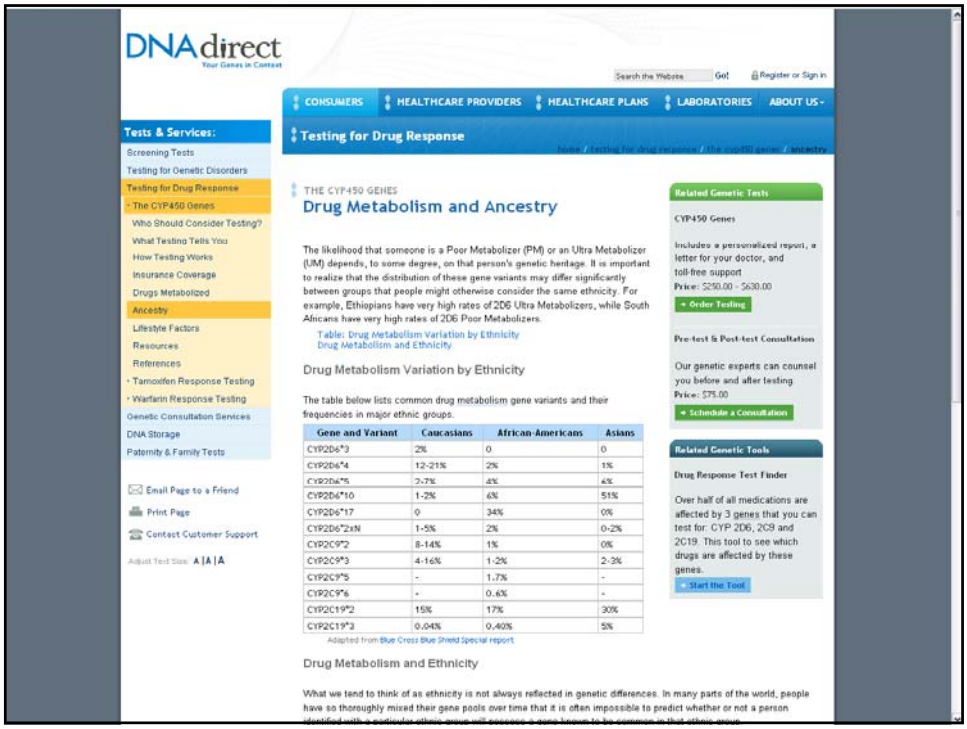


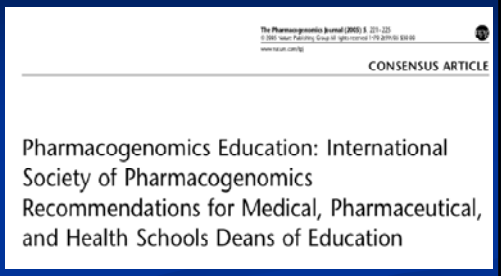
Figure 2. Number of drugs that were approved with pharmacogenomic information in their drug labels during each 10-year period from 1945–2005. During the 60 years covered by this analysis, 121 drugs were approved that have genomic biomarker information in current product labeling.

Flockhart DA et al. *Clin Pharmacol Ther* 2009

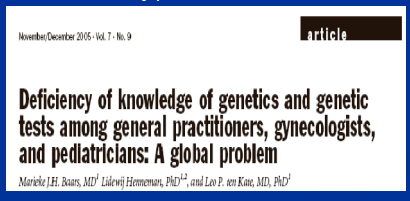


Provider Education is Needed

- Pharmacy
  - ACPE requires PGx education for PharmD students
  - No specific hours
- Medicals Schools
  - Average 1-2hrs (range 1-4hrs) (Higgs 2009 – UK study)


CONSENSUS ARTICLE

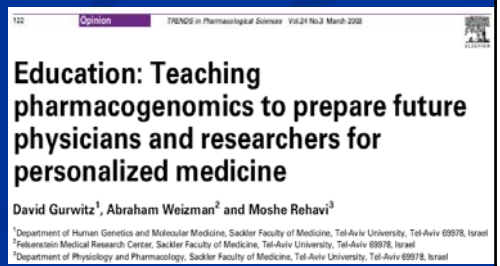
Pharmacogenomics Education: International Society of Pharmacogenomics Recommendations for Medical, Pharmaceutical, and Health Schools Deans of Education


November/December 2005 · Vol. 7 · No. 9

article

Deficiency of knowledge of genetics and genetic tests among general practitioners, gynecologists, and pediatricians: A global problem

Marieke J.H. Baars, MD[1] Lidewij Henneman, PhD[1,2], and Leo P. ten Kate, MD, PhD[1]


122 Opinion TRENDS in Pharmacological Sciences Vol.24 No.3 March 2003

Education: Teaching pharmacogenomics to prepare future physicians and researchers for personalized medicine

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UIC College of Pharmacy

- Professional Students: 650
- Graduate students: 138
- Residents/fellows: 29
- Faculty: 90
- Pharmacy Programs: 6 (5 doctoral)

UIC College of Pharmacy

- PGx in the PharmD curriculum
  - Genetic basis for disease and drug action
  - Genetic basis for alteration of drug metabolism
  - Genome and proteomic principles in relation to disease and drug development
  - Genetic basis for individualizing drug doses
- PGx contact hours (estimate)
  - 6-8 in required coursework
    - 11/30 required courses report *some* PGx-associated content taught
  - Occurs in lectures + selected recitations

PGx in Required Didactic Courses at UIC

Year	Course Name	Content
P1	PHAR400	Clinical PK
P1	PHAR401	Renal, endocrine
P1	PHAR321	Drug Delivery I
P1	PHAR332	Fundamentals of Drug Action II
P2	PHAR402	Cardiology/ Autonomic
P2	PHAR323	Drug Delivery III
P2	PHAR324	Contemporary Pharm Practice
P2	PHAR403	Infectious Disease
P3	PHAR405	Neurology
P3	PHAR406	Psych/pain
P3	PHAR408	Heme/Onc/ rheumatology

PGx Elective Experiences at UIC

Year	Course Name	Content
Misc (PharmD or PhD)	BPS555	Principles of Pharmacogenomics
Misc (PharmD or PhD)	PMMP412	Pharmaceutical Applications of Genomics and Bioinformatics
Misc (PharmD)	PHAR380/390	Psychiatric Pharmacogenomics (independent study)
Misc (PharmD)	PHAR380/390	Cardiovascular Pharmacogenomics (independent study)
Misc (undergraduate honors)	HONORS/BIOS399	Introduction to Laboratory Psychiatric Pharmacogenomics
P4	PHAR388	Advanced Specialty Clerkship (Psych PGx/Cardio PGx)

Integration Example 1

- PHAR400 – P1 year – Pharmacokinetics
  - 1 x 50 min lecture – "Optimizing Pharmacotherapy with Pharmacogenetics"
    - What is PGx?, PGx nomenclature, intro to genetic variability, warfarin and TPMT clinical examples with cases, genetic variability in drug metabolism across race/ethnic groups, PGx labeling for currently approved agents
  - 2 x 50 min lectures – Sources of PK Variability I&II
    - Additional discussion and cases that include PGx variability in drug metabolism

Integration Example 2

- PHAR402 – P2 year – Cardiology
  - Warfarin PGx
    - Included in antithrombosis section
    - Discussion and case study of using VKORC1/CYP2C9 genotypes + race + weight + etc to select dosing
    - Done alongside "traditional" dosing titration and monitoring recommendations
    - "Bridge" between traditional dosing and dosing guidelines recently incorporated into PI

Integration Example 3

- PHAR406 – P3 year – Psychiatry
  - Carbamazepine PGx
  - Included in Mood Stabilizers II lecture
    - Description of HLA-B*1502 allele
    - Review of racial diversity (more common in SE Asians
    - Review of testing recommendations
    - Recitation – case study
      - To test or not to test
      - Review of informed consent for genetic testing and how to "counsel" on the test form and potential results

Integration Example 4

- PHAR408 – P3 year – Heme/Onc/Rheumatology
  - Various lectures
    - PGx included as ancillary information – not generally specifically tested
  - Challenge
    - Course material challenging
    - Incorporating PGx details above and beyond general concepts may have diminishing returns

Example 4 Cont'd

- Hematology /Oncology Examples:
  - Trastuzumab – HER2+ status
  - Chronic myleogenous leukemia – BCR-ABL translocation
  - 6-MP - Thiopurinemethyltransferase (*TPMT*)
  - Cetuxumab, panitumumab, erlotinib – EGFR/KRAS status

Applied Elective Experiences

- UIC Pharmacogenomics Lab
  - Undergraduate honors
    - E.g. targeting guaranteed admission students
  - PHAR380/390 Independent Study/Research
  - Advanced Specialty Clerkships
  - Summer PharmD Fellowship Experience
  - ~2 independent study students/semester
  - ~6 rotation students/year
  - ~1-2 summer PharmD student fellows

Applied Elective Experiences: Consistency with flexibility

- All students
  - Lab skills
    - Lab safety, lab etiquette, pipetting, principles of PCR, gel electrophoresis, DNA extraction/quantification/banking, genotyping (Pyrosequencing/TaqMan techniques), etc.
  - Introduction to PGx
    - PGx Tutorials, one-on-one discussion, journal club
  - Paper (lab-report, manuscript style, or review article format)

Applied Elective Experiences: Consistency with flexibility

- Some students
  - Clinical Research
    - HIPAA training, informed consent
    - Subject enrollment
    - Data collection/entry
- Summer Fellows
  - Complete lab based research project, analyze data, write research manuscript

PharmD/PhD Didactic Electives

- BPS555 – Principles of Pharmacogenomics
  - 2 Credit Hours – lecture format
  - Team taught – mix of Biopharmaceutical Sciences and Pharmacy Practice faculty
  - Progression from more "molecular/basic science" to clinical applications
  - In class exam, term paper, 20 min oral presentation

PharmD/PhD Didactic Electives

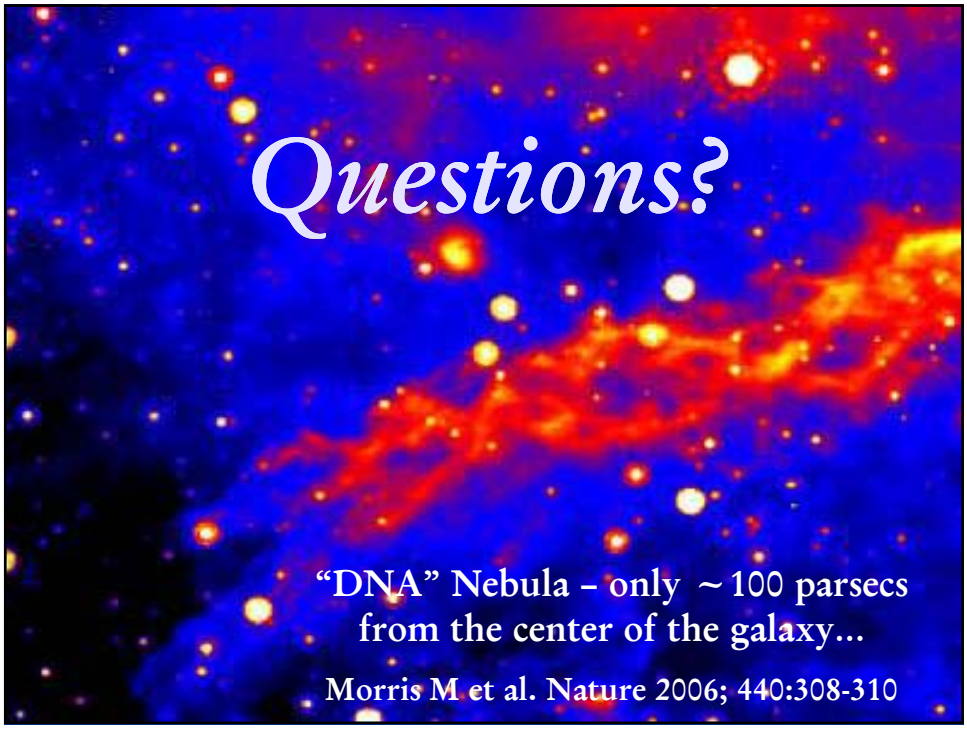
- BPS555 Cont'd – Principles of Pharmacogenomics
  - **Objectives**
    - Introduce genetic concepts
    - Explain the molecular basis for genetic variability in humans
    - Identify methods to determine genetic variability
    - Identify clinical applications of PGx
    - Demonstrate the power and challenge of applying PGx in new drug research and development
    - Develop skills to be able to understand, evaluate and design PGx studies
    - Identify potential ethical issues relating to PGx

Challenges

- Incorporating new and innovative technologies to an already packed PharmD curriculum
- Difficult to quantify PGx integration
  - Some "stand alone" lectures needed for foundation
  - Genetic variability treated like another "monitoring" parameter or marker of response
- Integration into therapeutics courses dependent on expertise and/or interest of faculty
- Applied experiences dependent on lab-based faculty with resources and existing/ongoing

Opportunities for Growth

- Ethical issues
  - Informed consent issues surrounding testing
  - Patient counseling
  - Implications of genetic testing for self, family, employment, insurance, etc.
- Standardization of integration
- "Real life" application
  - Will increase as more drugs have PGx labeling requirements



University of Connecticut

Pharmacogenomics Education

Megan J. Ehret, PharmD, BCPP

Integrated Curriculum-Pharmacogenomics

- Didactic Coursework in P1, P2, and P3
  - 11-30 hours
  - Multiple faculty involved
- APPE Rotation

The Basics of Genomics

- Cell Biology
  - DNA Structure and Replication
  - Consequences of drugs and mitochondrial genome replication
  - DNA biotechnology
    - Consequences of SNPs for drug metabolism
    - Response vs. nonresponse
  - Gene Regulation

Clinical Pharmacokinetics

- Kinetics vs. Dynamics
- CYP450 Metabolism
  - Ultrarapid, Extensive, Intermediate, Poor
- Pgp
- N-Aceetyltransferase type 2
- UGT1A1
- TPMT
- Risk vs. Benefits

Therapeutics

- Nutrition
- Autonomic and Neurologic System
- Immunology
- Dermatology
- Endocrine
- Gastro-Intestinal
- Psychiatry
- Cardiac
- Renal
- Respiratory
- Infectious Disease
- Hematology-Oncology

Ethics

- Ethical, legal, and social issues related to genomic testing
- Storage of genetic information
- Public policy issues- regulatory statements

Uncovered Areas

- Informed consent process for pharmacogenomic testing
- Specific methods of genotyping and phenotyping
- Important issues in pharmacogenomic study design
- Regulatory issues that may result from testing being incorporated into Phase II and II testing

APPE Rotation

- Psychiatry Rotation
  - Ongoing research studies involving CYP450 enzyme genotyping
  - Ordering labs
  - Interpreting results
  - Discussing results with treatment team and patients

Integrated Pharmacogenomics Vs. One Course

- Pros
  - Discussion throughout the curriculum
  - Each faculty discusses the use/need in their area of expertise
  - Frequent assessment of students
- Cons
  - Time in each course
  - Faculty may not be familiar with the use of pharmacogenomics
  - Consistency of terminology and interpretation of results