


## PharmGenEd™: Bridging the Gap Between Science & Practice

Overview of PharmGenEd™

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Associate Professor of Clinical Pharmacy  
Associate Adjunct Professor of Family &  
Preventive Medicine



UNIVERSITY of CALIFORNIA, SAN DIEGO  
SKAGGS SCHOOL of PHARMACY  
and PHARMACEUTICAL SCIENCES

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## PharmGenEd™ Program

- Timeline: 2008 - 2011
- Target Audience >100,000 healthcare professionals
  - Pharmacists
  - Physicians
  - Students / trainees
- Will provide
  - Continuing education credits to healthcare professionals
  - Shared curriculum platform
    - Free access to materials for teaching, in-service, grand rounds, or professional meetings

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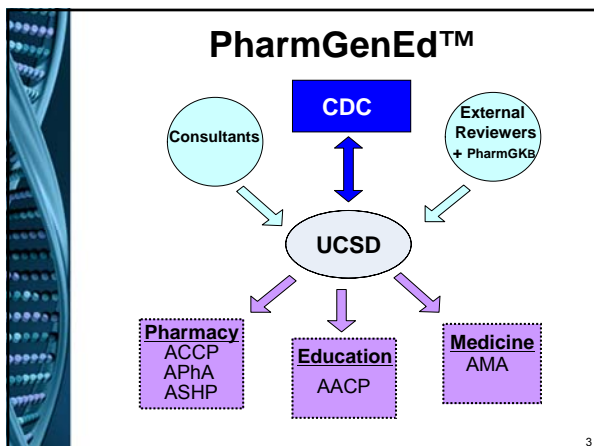
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## PharmGenEd™ Delivery Methods

- Live presentations
  - National, regional, local meetings
- Online presentations
  - Web-based lecture materials
  - Shared curriculum platform
  - Use of SciVee for pubcasts & videocasts
    - The “YouTube™ and Facebook™” for scientists
- Website
  - <http://pharmacogenomics.ucsd.edu>
- To join the virtual community
  - <http://www.scivee.tv/node/7981>

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## PharmGenEd: Bridging the Gap Between Science & Practice

Module I: Principles and Concepts  
Module II: Clinical Applications



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## Presentation Outline (I)

1. Human genome project	8. Ethical, legal, societal issues
2. Pharmacogenetics and pharmacogenomics	9. Resources and role for healthcare professionals
3. Molecular biology 101	10. PharmGenEd™ Program
4. Pharmacogenomic nomenclature	11. Acknowledgements & references
5. SNP types	
6. Other polymorphism types	
7. Translating pharmacogenomics into practice	

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## Presentation Outline (II)

1. Challenges and benefits of pharmacogenomic testing	3. PharmGenEd™ program
2. Therapeutic Areas	4. Information and resource databases
a. Infectious Diseases	5. Acknowledgements
b. Oncology	6. References
c. Anticoagulation	
d. Psychiatry	
e. Neurology	

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## Acknowledgments

- **UCSD**
  - Principal Investigator
    - Grace M. Kuo, PharmD, MPH
  - Co-Investigators:
    - Kelly C. Lee, PharmD, BCPP
    - Joseph D. Ma, PharmD
    - Palmer Taylor, PhD
    - James R. Halpert, PhD
    - Philip E. Bourne, PhD
    - Theodore Ganiats, MD
- **Consultants**
  - Magnus Ingelman-Sundberg, PhD
    - Karolinska Institute
  - Karen S. Hudmon, DrPH, MS, RPh
    - Purdue University
- **Assistants**
  - Trina Huynh
  - Ashley To, BA
  - Jessica Bryan, MPH
  - WeiWei Qin, MS
  - Lilian Wong, PharmD, MBA

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## PharmGenEd™ Contact

- Program Director: Grace M. Kuo, PharmD, MPH
- Phone: 858-822-7754
- Email: [pharmacogenomics@ucsd.edu](mailto:pharmacogenomics@ucsd.edu)
- Website: <http://pharmacogenomics.ucsd.edu>

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## Pharmacogenomics Instruction at Schools of Pharmacy

James S. Green, PharmD, MEd, MBA  
Assistant Professor and Chair,  
Pharmacogenomics Department  
Bernard J. Dunn School of Pharmacy  
Shenandoah University

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## Background

- AACP
  - 2002 Academic Affairs Committee report
  - 2008 policy resolutions
- National Coalition for Health Professional Education in Genetics (NCHPEG)
- Latif and McKay 2004 study\*

\*Latif DA, McKay AB. Pharmacogenetics and pharmacogenomics instruction in colleges and schools of pharmacy in the United States. *Am J Pharm Educ.* 2005;69(2):152-56.

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## Study Objectives

- Assess the breadth and depth of pgx instruction in US COP/SOP
- Assess the level of pgx faculty development
- Compare results with Latif and McKay study

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## Questionnaire

- Descriptive info related to COP/SOP
- Number of hours of pgx instruction in PharmD curriculum
- Breadth of coverage
  - Genetic basis of disease (16 domains)
  - Ethical, social, and economic (9 domains)
- Interest in having access to and collaborating on a shared curriculum

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### Results

- 75 of 109 (69%) questionnaires returned
- Institutions providing pgx instruction increased from 78% in 2004 to 92%
- The majority incorporate the material in other courses (73%) while 22% have a stand alone course
- Approximately half (47%) plan to increase the number of hours of pgx instruction in the next 3 years

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### Results

- Multiple faculty teach pgx at most institutions (74%) however single faculty members teaching all pgx coursework increased from 7% in 2004 to 25%
- The greatest emphasis in pgx instruction was in the 2<sup>nd</sup> professional year (77%) however 19% taught throughout the first 3 professional years of the curriculum

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### Faculty Resources

- Plans to hire faculty in the next 3 years decreased from 49% in 2004 to 20%
- 44% had a COP/SOP or interprofessional pgx research center
- Only 16% currently have or are developing pgx programs for faculty development

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## Core Competencies

- Domains covered by majority of institutions
  - Genetic basis of disease: 11 of 16 (69%)
  - Ethical, social and economic implications: 2 of 9 (22%)
- Perceived level of importance (>50% of respondents) for PharmD instruction
  - Genetic basis of disease: 9 of 16 (56%)
  - Ethical, social and economic implications: 2 of 9 (22%)

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## Perception of Pgx Instruction

- At most schools of pharmacy
  - 2004: 39% thought poor to very poor
  - 2009: 61% thought poor to very poor
- At their respective institution
  - 2009: 29% thought poor to very poor

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## Shared Pgx Curriculum

- 88% were interested in having access to the curriculum being developed
- 68% were interested in collaborating

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## Conclusions

- Significant increase in the number of COP/SOP teaching pgx
- General consensus among respondents that teaching pgx is becoming increasingly important in the practice of pharmacy
- Limited emphasis on pgx faculty development

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## Acknowledgments

- Dr John Murphy, University of Arizona
- Dr James Green, Shenandoah University
- Dr Laura Adams, University of Arizona
- Dr Robert Squire, University of Arizona
- Dr Grace Kuo, University of California, San Diego
- Dr Alan McKay, Shenandoah University

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## Pharmacogenomics



**There are no such things as applied sciences, only applications of science.**  
Louis Pasteur



Daniel A. Brazeau, Ph.D.  
School of Pharmacy and Pharmaceutical Sciences  
University at Buffalo

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## Pharmacogenomics

□ Cannot be understood much less applied without some basic understanding of the science that underlies the field

**Combination of three sub disciplines of Genetics:**

1. Transmission genetics - Mendelian or classical genetics
2. Population genetics - study of genetic variation within & among populations
3. Quantitative genetics - study of patterns of inheritance where traits are of degree rather than kind

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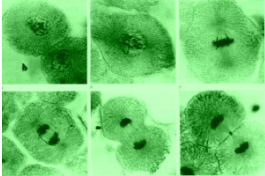
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## Transmission Genetics



Genetic material (DNA) contained within chromosomes are passed from one generation to the next

NOTE: the process is **nearly** perfect

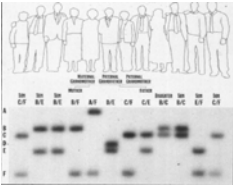
Replication of DNA sometimes results in "copying errors".

- \* substitutions
- \* insertions/deletions (indels)

resulting in differences (polymorphisms):

- \* individuals
- \* populations
- \* species

□ EVOLUTION



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## Population Genetics

Study of the nature and distribution of polymorphisms within populations

- \* Describe genetic differentiation among population
- \* Assess mechanisms that cause and maintain genetic differences

CYP2C19 allele	Australian Aborigines (n = 227) (%)	Caucasians* (n = 105) (%)	Orientals* (n = 118) (%)
*1	50.2	87	63
*2	35.5	11	32
*3	14.3	0	5

\* (Goldstein et al., 1997)

- Geographic/ancestral origins
- Genetic background

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### Quantitative Genetics

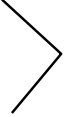
– Study of the inheritance of differences among individuals that are of degree rather than kind, quantitative rather than qualitative.

for example:

- height, intelligence
- disease susceptibility
- drug response

\* traits due to multiple genes including

- interactions among genes
- environmental effects



**variable expression**

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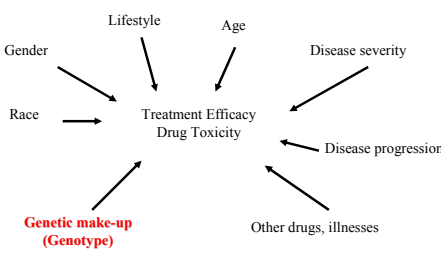
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### Pharmacogenomics



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### After completing a course in Pharmacogenetics students should be able to answer:

One likely characteristic of a compound that would make it more likely to exhibit differences among patients based upon genetics.

1. CYP substrate
2. Low bioavailability
3. **Narrow therapeutic index**
4. Long half-life

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## A Two-Module Educational Curriculum Approach in the Pharmacogenomics of Asthma

Alice J. A. Gardner Ph.D.  
Associate Professor of Pharmacology  
Massachusetts College of Pharmacy & Health Sciences  
School of Pharmacy-Worcester



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## Objectives

- Health care professional as **Scientist**
  - this course will help students **acquire and apply core scientific knowledge**
- Health care professional as **Clinical Problem Solver**
  - this course will help students **understand and apply the scientific method to problem solving and patient care; and will encourage career-long learning**
- Bridging the gap between Science and Practice
  - linkage requires development of a two-module educational curriculum approach

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## β2-adrenergic Receptor Polymorphisms and Clinical Responses in Asthma

Development of the two-module educational curriculum:

- Pharmacogenomics primer
  - Signaling, polymorphisms
- Clinical applications and outcomes

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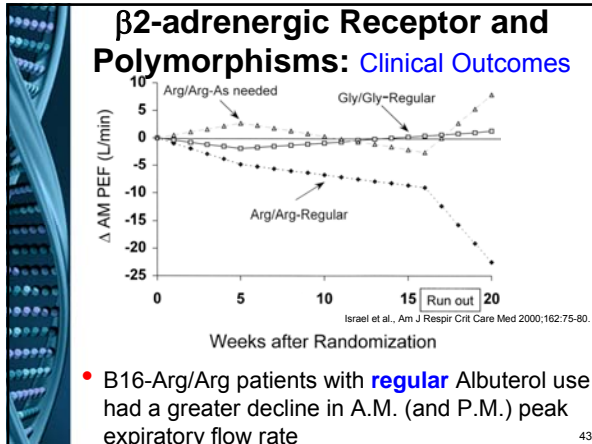
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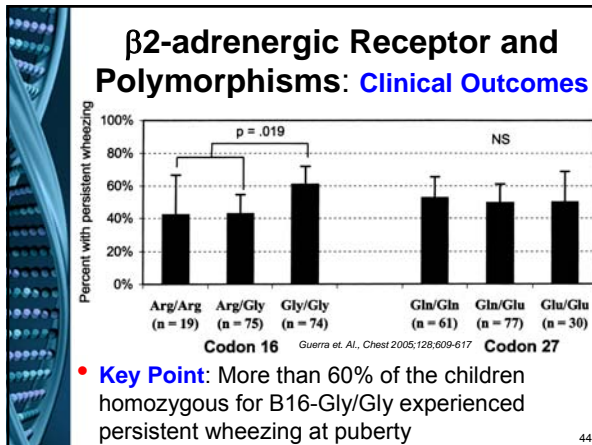
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### Question

A 16 y/o male Caucasian diagnosed with mild asthma is managed on a SABA, prn. Since joining the soccer team he has begun to overuse his SABA because of exercise-induced shortness of breath. Subsequently, his peak flow meter readings are in the yellow zone every morning. Given this scenario you would predict that he carries which of the following polymorphisms:

- Arg16/Arg16
- Arg 16/Gly16
- Gly16/Gly16
- Thr164/Ile164
- Ile164/Ile164

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## PharmGenEd™: Bridging the Gap Between Science & Practice

Development of an Educational Curriculum

Joseph D. Ma, PharmD  
Assistant Professor of Clinical Pharmacy



UNIVERSITY of CALIFORNIA, SAN DIEGO  
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and PHARMACEUTICAL SCIENCES

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### When you hear “pharmacogenomics curriculum...”

- Students: Exam Questions?
- Faculty: Topic areas?
- Administrators: Who will teach?
- Practicing pharmacists: Which drugs?
- Physicians: Clinical evidence?
- Other health care professionals: CE credit?
- Patients: How much will it cost me?
- “My Mom”: “Your school does genetic testing on students!?”
- **A matter of perspective!**

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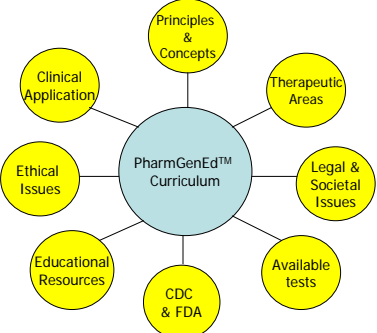
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## PharmGenEd™ Curriculum



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### Premature Stop Codon SNP CYP2C19

- Nomenclature: CYP2C19\*3
  - Nucleotide change occurs (G > A), the reference amino acid (Trp) is no longer coded, and results in termination of protein synthesis (Demorais et al 1994)
  - Functional Effect: CYP2C19\*3 results in no enzyme activity
  - Affected drugs: PPIs (omeprazole, lansoprazole)

Reference or 'wild type' nucleotide sequence  
 ACC | CCC | **TGG** | ATC | CAG  
 Subsequent amino acid sequence  
 Thr | Pro | **Trp** | Ile | Gln

CYP2C19\*3 polymorphism – nucleotide sequence  
 ACC | CCC | **TAG** | ATC | CAG  
 Subsequent amino acid sequence  
 Thr | Pro | **STOP** | - | -

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### Therapeutic Areas

- Infectious Diseases
- Oncology
- Anticoagulation
- Psychiatry
- Neurology

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### What other therapeutic area should be considered?

- Asthma
- Diabetes
- Pain Management
- Cystic Fibrosis
- Other

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### What other therapeutic area should be considered?

- A. Asthma
- B. Diabetes
- C. Pain Management
- D. Cystic Fibrosis
- E. Other

Therapeutic Area	Percentage
Asthma	20%
Diabetes	20%
Pain Management	20%
Cystic Fibrosis	20%
Other	20%

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### General approach to each therapeutic area

- Functional effect
- Population variance
- Clinical Relevance
  - Dose
  - Efficacy
  - Toxicity
- Genomic test
- Testing recommendation by EGAPP and/or FDA
- Case presentation and case summary

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### Psychiatry: Selective Serotonin Reuptake Inhibitors (SSRI)

- Gene: Cytochrome P450 (CYP) enzymes
- Functional Effects
  - Null or ↓ CYP activity confers poor metabolizer phenotype
  - ↑ enzyme activity confers extensive metabolizer phenotype

CYP2D6 Genotypes	Phenotype (Metabolizer Status)	Expected SSRI Effects from Usual Doses
>2 copies of wild-type alleles	Ultra-rapid Metabolizer (UM)	Sub-therapeutic drug concentrations <input type="checkbox"/> non-response
2 copies of wild-type alleles	Extensive Metabolizer (EM)	Expected drug concentrations and response
2 copies of inactive alleles	Poor Metabolizer (PM)	Higher than expected drug concentrations <input type="checkbox"/> adverse reactions

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## SSRI: Clinical Relevance

- Dose
  - Single dose SSRI studies showed that CYP genotype/phenotype status correlates with circulating SSRI levels (Matchar et al 2007)
  - No evidence that results of CYP testing influenced SSRI choice or dose
- Efficacy
  - No association between metabolizer status and clinical response in adults treated with SSRIs (Matchar et al 2007)
  - Decreased SSRI efficacy in ultra-rapid metabolizers of CYP enzymes
- Toxicity
  - Conflicting evidence for CYP genotypes and SSRI adverse effects
  - Potential increased toxicity in poor metabolizers

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## SSRI: Clinical Applications

- Genomic Test
  - AmPliChip™ CYP450 (Roche Diagnostics)
    - Approved by the FDA; tests for polymorphisms in CYP2D6 and CYP2C19 enzymes
- Pharmacogenomic Test Recommendations
  - Insufficient evidence to support recommendation *for or against* testing in non-psychotic depression prior to initiating treatment with SSRIs (EGAPP)
  - Information only (FDA)
    - [http://www.fda.gov/cder/genomics/genomic\\_biomarkers\\_table.htm](http://www.fda.gov/cder/genomics/genomic_biomarkers_table.htm)

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## PharmGenEd™: Bridging the Gap Between Science & Practice

### Implementation of an Educational Curriculum

Kelly C. Lee, Pharm.D., BCPP  
Assistant Professor of Clinical Pharmacy



UNIVERSITY of CALIFORNIA, SAN DIEGO  
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## Current Recommendations for Implementation

- 2008: AACP House of Delegates recommended
  - 1) increased education in biotechnology with competencies in:
    - Bioengineering
    - Genetics/genomics
    - Proteomics
    - Nanotechnology
    - Informational technologies
  - 2) faculty development in biotechnology areas

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## How Do We Implement?

- Identification of teachers/trainers
- Mode of teaching
- Mode of learning
- Selection of topics
- Incorporation into curriculum
- Faculty development
- Development of assessment tools
- Identification of resources for maintaining current knowledge

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## How Do We Implement?

- Question:
  - If you were given the opportunity to **train others** in pharmacogenomics, which mode of teaching would be most desirable to you?



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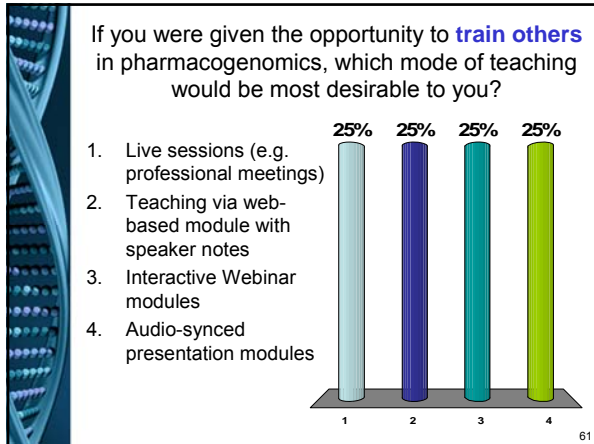
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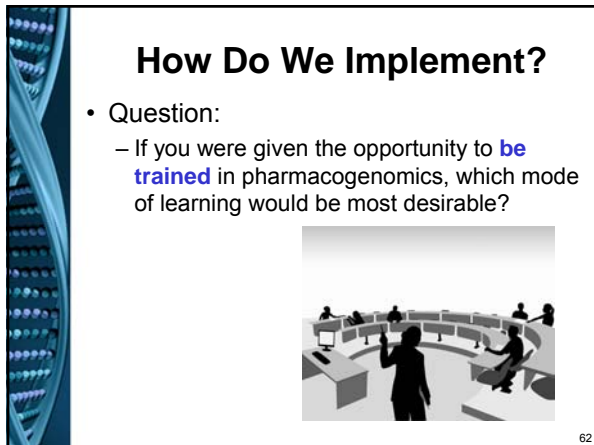
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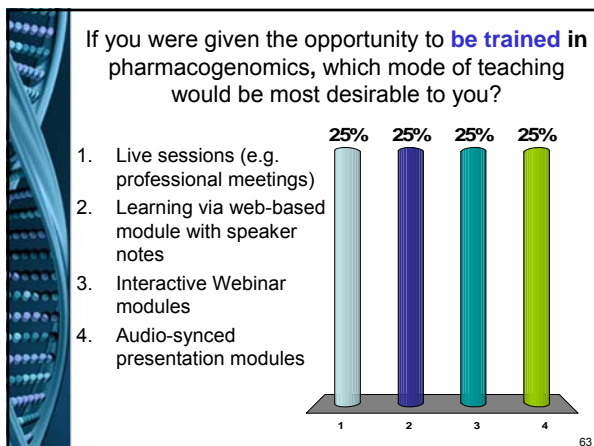
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**Pharmacogenomics Education Program**

HOME ABOUT US CE/CME SHARED CURRICULUM RESOURCES PODCASTS VIRTUAL COMMUNITY

**Topics**

- Principles and Concepts
- Evidence-Based Recommendations for Clinical Practice: an Overview
- Oncology I
- Oncology II
- Psychiatry
- Cardiology
- Anticoagulation
- Neurology
- Infectious Diseases
- Other Diseases/Conditions
- Laboratory Basis of Tests
- Clinical Applications
- Ethical, Social, & Legal Issues
- Economic Perspectives

**Shared Curriculum**

Because the field of pharmacogenomics is developing rapidly, it is critical that clinicians and students learn to appropriately interpret emerging data on pharmacogenomic tests and become familiar with resources applicable to their practice.

PharmGenEd prepares shared curriculum, open-access educational materials to train future healthcare providers about the various pharmacogenomic tests and their applications to clinical practice. PharmGenEd collaborates with the American Association of Colleges of Pharmacy (AACP) and uses a "Train-the-Trainer" approach to disseminate educational materials to faculty from all colleges of pharmacy in the U.S. The content materials will also be available to schools of medicine faculty members.

The PharmGenEd materials can be used in the classroom, for students in the health professions, or as training for licensed clinicians. Modules related to specific therapeutic areas will be developed in the coming months. We openly share our materials with others at no cost; however, all persons who receive any component of the PharmGenEd Program must complete an online registration process which includes acceptance of our [End-User Licensing Agreement](#).

PharmGenEd materials can be used only for non-commercial teaching and research purposes and cannot be used for profit.

To gain access to downloadable program materials from the PharmGenEd Internet site, please [register here](#).

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## Faculty Development

- Question:
  - What are the barriers to implementing a faculty development program to facilitate implementation of a pharmacogenomics curriculum in your institution?

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What are the barriers to implementing a faculty development program to facilitate implementation of a pharmacogenomics curriculum in your institution?

1. Financial
2. Time
3. No need for faculty development

33% 33% 33%

1 2 3

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## Resources

- Question:
  - What type of resources would be most beneficial to you as the trainer to improve the quality of your existing curriculum?



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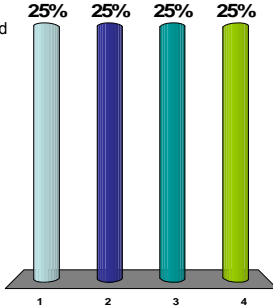
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### What type of resources would be most beneficial to you as the trainer to improve the quality of your existing curriculum?



Resource Type	Percentage
1. Updated evidence-based summaries of primary literature	25%
2. List of publicly available databases	25%
3. Updated regulatory and consensus recommendations	25%
4. Practice protocols translating pharmacogenomics evidence into practice	25%

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## Future Plans for Implementation

- Lack of faculty with expertise
  - Recruitment of new faculty
  - **Development of existing faculty**
  - Basic science vs clinical faculty
- Rigidity of curriculum
  - Number of hours for course (hours and selection of topics)
  - Place in curriculum (PY1, PY2, PY3)
  - Pre-requisites
  - Physical space
  - Student workload
- Faculty workload
  - Redistribution of workload
  - Type of faculty
  - Team teaching
- Optimal method for teaching
  - **Didactic**
  - **Laboratory component**
  - **Practice-based**
- Rapidly evolving and expanding field
  - **Limited clinical utilization**
  - **Uncertain role for pharmacists**
  - **Access to resources**

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# Discussions

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