Welcome to Pharmacogenomics and Personalized Medicine

Statement of Objectives, Financial Disclosure Statements, and Accreditation Statement

Learning Objectives

1. Users will be able to describe basic DNA and gene structure, transcription, and translation.
2. Users will be able to discuss the basic findings of the human genome project.
3. Users will be able to describe how the CYP450 genes influence drug metabolism.
4. Users will be able to discuss the clinical implications of poor, as well as, ultra-rapid metabolizer phenotypes.
5. Users will be able to interpret the various ways that pharmacogenomic information is supplied in prescription drug labeling.
6. Users will be able to discuss clinical examples of drugs whose metabolism and/or cellular response is genetically controlled.

Financial Disclosure Statements:
In order to assure the highest quality of CME programming, and to comply with the ACCME Standards for Commercial Support, the AMA requires that all faculty and planning committee members disclose relevant financial relationships with any commercial or proprietary entity producing health care goods or services relevant to the content being planned or presented. The following disclosures are provided:

Barry Dickinson, PhD  Nothing to Disclose (Planning Committee/Faculty)
Katherine Johansen, PhD  Nothing to Disclose (Planning Committee/Faculty)
Lijen Tan, PhD  Nothing to Disclose (Planning Committee/Faculty)
Federico Goodsaid, PhD  Nothing to Disclose (Planning Committee/Faculty)
John F. Schneider, MD, PhD, FACP  Nothing to Disclose (Planning Committee)
William E. Evans, PharmD  Discloses Scientific Advisor relationship with Genticis Corporation (Faculty)
David A. Flockhart, MD, PhD  Discloses Consultant relationships with Roche Diagnostics and Tm Biosciences (Faculty)
Howard L. McLeod, PharmD  Nothing to Disclose (Faculty)

Accreditation Statement
The American Medical Association is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The American Medical Association designates this educational activity for a maximum of 3.0 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

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Pharmacokinetics is concerned with the relationship between drug dosage and the time and course of drug concentration in the body, usually as reflected in plasma drug concentrations.

Pharmacodynamics is the study of the biochemical and physiological effects of drugs and their mechanism of action, including the relationship between the dose or concentration of a drug and the effect that it produces.
Drug Transformations
Drugs Metabolized by Major Cytochrome P450 CYP Families
Metabolizer Classifications

Poor, Intermediate, Extensive or Ultra-rapid Metabolizers
### Polymorphic P-450s

<table>
<thead>
<tr>
<th>CYP2B6</th>
<th>CYP2C9</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Selected Substrates</strong></td>
<td><strong>Location</strong></td>
</tr>
<tr>
<td>bupropion, cyclophosphamide, efavirenz, methadone, ifosfamide</td>
<td>Chromosome 19</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CYP2C19</th>
<th>CYP2D6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Selected Substrates</strong></td>
<td><strong>Location</strong></td>
</tr>
<tr>
<td>Proton pump (-), amitriptyline, cyclophosphamide, diazepam, indomethacin, phenytoin, phenobarbital, progesterone, voriconazole</td>
<td>Chromosome 10</td>
</tr>
<tr>
<td>NSAIDs, celecoxib, diclofenac, ibuprofen, naproxen, piroxicam, Oral Hypoglycemic Agents, tolbutamide, glipizide, ARBs, irbesartan, losartan, fluvastatin, warfarin, phenytoin</td>
<td></td>
</tr>
</tbody>
</table>
### Effect of Metabolic Rate on Drug Dosage

<table>
<thead>
<tr>
<th>Drug</th>
<th>Poor Metabolizer Phenotype</th>
</tr>
</thead>
</table>
| Prodrug, needs metabolism to work (e.g. codeine is metabolized by CYP 2D6 to morphine) | Poor efficacy  
Possible accumulation of prodrug |
| Active drug, inactivated by metabolism (example is omeprazole) | Good efficacy  
Accumulation of active drug can produce adverse reactions  
May need lower dose |

<table>
<thead>
<tr>
<th>Drug</th>
<th>Ultra-rapid Metabolizer Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prodrug, needs metabolism to work (e.g. codeine is metabolized by CYP 2D6 to morphine)</td>
<td>Good efficacy, rapid effect</td>
</tr>
</tbody>
</table>
| Active drug, inactivated by metabolism (example is omeprazole) | Poor efficacy  
Need greater dose or slow release formulation |