Clinical Pharmacogenetics
From a Nursing Perspective: Personalizing Drug Therapy

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The speaker has nothing to disclose, no conflict of interest or sponsorship

Learning objectives:
1. Describe the promise of pharmacogenetics
2. Identify a major obstacle in implementing pharmacogenetic testing
3. Discuss why personalized medicine is important to patient care
4. Describe nursing considerations related to personalized medicine
Definitions

Pharmacogenomics: the study of the role of the genome in response to medicines

Pharmacogenetics: the study of how DNA variation in a single or few genes influences the response to a single medicine
The Promise of Pharmacogenomics

Patient Outcome
- Mitigate or cure
- No serious adverse drug events

“Personalized Medicine”
A Major Obstacle to Effective Implementation of Pharmacogenomics Testing

The lack of adequate knowledge regarding interpretation of these test results
Patients Respond Differently to Identical Treatments

- Family history
- Drug-Gene interactions (DDIs)
- Drug-Drug interactions (DDIs)
For a growing list of medications, a patient’s pharmacogenotype determines drug response and adverse drug effects.
What is Pharmacogenotyping?

- Simple blood draw or saliva collection
- Results identify variations in human genes
- Variations can alter a person’s ability to metabolize certain drugs
Pharmacogenotyping

Used to characterize mutations in human genes regulating drug disposition

Single nucleotide polymorphisms (SNPs) alter a person’s ability to metabolize certain drugs
Guidelines for interpretation of pharmacogenetic test results,

• The Clinical Pharmacogenetics Implementation Consortium (CPIC®) (https://cpicpgx.org/)

• The Dutch Pharmacogenetics Working Group (DPWG) (https://www.pharmgkb.org/page/dpwg)
Predicted Phenotypes

• The individual’s “metabolizer status”

• Classification system

• The guidelines use an asterisk-based nomenclature, where *1 is often the reference allele and assigned based on an individual lacking the alternative allele
Substrates, Inhibitors, & Inducers

A list of common CYP substrates, inhibitors, and inducers can be accessed here: http://medicine.iupui.edu/clinpharm/ddis/main-table/

**SUBSTRATES**

<table>
<thead>
<tr>
<th>1A2</th>
<th>2B6</th>
<th>2C8</th>
<th>2C9</th>
<th>2C19</th>
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<tbody>
<tr>
<td>amitriptyline</td>
<td>artemisinin</td>
<td>amodiaquine</td>
<td>NSAIDs:</td>
<td>PPIs:</td>
</tr>
<tr>
<td>caffeine²</td>
<td>bupropion¹</td>
<td>cerivastatin</td>
<td>diclofenac¹</td>
<td>esomeprazole</td>
</tr>
<tr>
<td>clomipramine</td>
<td>cyclophosphamide</td>
<td>paclitaxel</td>
<td>ibuprofen</td>
<td>lansoprazole</td>
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<tr>
<td>clozapine</td>
<td>efavirenz¹</td>
<td>repaglinide</td>
<td>lornoxicam</td>
<td>omeprazole2</td>
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<tr>
<td>cyclobenzaprine</td>
<td>ifosfamide</td>
<td>sorafenib</td>
<td>meloxicam</td>
<td>pantoprazole</td>
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</tbody>
</table>
Two Current Pharmacogenetic Studies

1. The Ubiquitous Pharmacogenomics (U-PPGx) Consortium

2. The IGNITE Network
# De-identified Patient Report

## Test Name: Pharmacogenomics Panel

<table>
<thead>
<tr>
<th>Gene</th>
<th>Result</th>
<th>Predicted Metabolizer Status*</th>
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<tbody>
<tr>
<td>TPMT</td>
<td>*1/*1</td>
<td>Normal Metabolizer</td>
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<tr>
<td>CYP2C19</td>
<td>*1/*2</td>
<td>Reduced/Intermediate Metabolizer</td>
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<tr>
<td>SLC01B1</td>
<td>*1/*1</td>
<td>Normal Metabolizer</td>
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<tr>
<td>CYP2C9</td>
<td>*1/*1</td>
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<tr>
<td>VKORC1</td>
<td>G/A</td>
<td>Reduced/Intermediate Metabolizer</td>
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<tr>
<td>CYP2D6</td>
<td>*2/*2</td>
<td>Normal Metabolizer</td>
</tr>
<tr>
<td>CYP3A5</td>
<td>*3/*3</td>
<td>Poor Metabolizer</td>
</tr>
<tr>
<td>CYP3A4</td>
<td>*1/*1</td>
<td>Normal Metabolizer</td>
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<tr>
<td>CYP2B6</td>
<td>*1/*1</td>
<td>Normal Metabolizer</td>
</tr>
<tr>
<td>ITPA</td>
<td>C/A</td>
<td>Reduced/Intermediate Metabolizer</td>
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<tr>
<td>DPYD</td>
<td>*1/*1</td>
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<tr>
<td>CYP4F2</td>
<td>*1/*3</td>
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<tr>
<td>G6PD</td>
<td>No variant detected</td>
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<tr>
<td>IFNL3 (IL28B)</td>
<td>C/T</td>
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<tr>
<td>SV2C</td>
<td>G/G</td>
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<tr>
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<td>C/C</td>
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<tr>
<td>FCAMR</td>
<td>C/T</td>
<td>Increased Risk</td>
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<tr>
<td>rs3125923</td>
<td>A/A</td>
<td>Normal Risk</td>
</tr>
<tr>
<td>rs28714259</td>
<td>A/G</td>
<td>Increased Risk</td>
</tr>
</tbody>
</table>
Nursing Considerations

Consent
If working in an area where pharmacogenotyping studies are being conducted, patients must consent to pharmacogenotyping; Consent and blood draw/saliva sample will be done by trained study personnel

Patient Education
Explain why a dosing adjustment or drug change was made

Medications
Be alert to and verify atypical drug doses; Regularly monitor and report adverse effects;

Documentation
Clarify and verify drug doses; Document patient education efforts; Document response to medications.
Look for pharmacogenetic test results under labs
Advanced Practice Nursing (APN) Considerations

- APNs can do all of the activities mentioned on the previous slide
- Order pharmacogenetic testing for selected patients
- Apply test results within the clinical context
Closing Thoughts

1. Every patient presents a unique challenge to the pharmacogenetic interpretation of his or her case
2. With sufficient knowledge and experience, all nurses will become more confident in applying pharmacogenetic results within the clinical context
References:


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