PharmGenEd™ Principles and Concepts of Pharmacogenomics

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Presentation Outline

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Learning Objectives

- **Upon completion of this program, participants will be able to:**
  - Describe and define basic pharmacogenomic nomenclature and principles
  - Describe polymorphism types and their impact on pharmacokinetics (PK) and pharmacodynamics (PD)
  - Understand the ethical, legal, social issues (ELSI) & economic issues related to pharmacogenomic testing
  - Identify resources for obtaining current and updated pharmacogenomic information

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Definitions

- **Pharmacogenetics**
  - "the study of genetic causes of individual variations in drug response" (American Association of Pharmaceutical Scientists (AAPS) Pharmacogenomics Focus Group)
- **Pharmacogenomics**
  - "more broadly involves genome-wide analysis of the genetic determinants of drug efficacy and toxicity" (American Association of Pharmaceutical Scientists (AAPS) Pharmacogenomics Focus Group)
- The terms are used interchangeably. For the purposes of this presentation we will use the term pharmacogenomics (PGx)

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Translating Pharmacogenomics into Practice

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Current Drug Therapy

- **Drug response rate**
  - 30-60% response rate of drug therapies for Alzheimer's, depression, rheumatoid arthritis, hypertension, osteoporosis (Physician's Desk Reference 2007)
- **Adverse drug reactions (ADRs)**
  - ↑ Morbidity and Mortality
    - Up to 100,000 people/year die of ADRs in the U.S. (Lazarou 1998)
  - ↑ Cost

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Pharmacogenomics Impacts Pharmacokinetics and Pharmacodynamics

- Variations in a gene may impact either pharmacokinetics or pharmacodynamics
  - Pharmacokinetics = process by which a drug is absorbed, distributed, metabolized, and eliminated
  - Pharmacodynamics = action or effect of a drug on the body
- These impact efficacy and toxicity

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Value of Pharmacogenomics

- **Personalize medicine using genotyping technologies**
- **Optimize drug therapy**
  - May maximize drug effectiveness
  - May minimize drug toxicity
  - May minimize pharmacokinetic and pharmacodynamic variability of drug therapy
  - May avoid unnecessary treatment
- **Optimize drug development**

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Challenges of Pharmacogenomic Testing

- **Access**
  - Availability of test
  - Providers
  - Insurance coverage
- **Feasibility**
  - Turnaround time
  - Sensitivity/specificity of tests
  - Efficiency
- **Cost**
  - Genetic test
  - Disease management
  - Counseling
- **Limited evidence**
  - Few quality studies
  - Prospective vs retrospective studies
  - Predictive value
  - Analytical and clinical validity
  - Phenotyping of clinical presentation
  - Clinical utility of testing
  - Efficacy
  - Expertise
  - Cost-effectiveness

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Patient/Provider Concerns

- **Patients have high expectations**
  - They expect healthcare providers to explain and interpret pharmacogenomic test results
- **Providers lack evidence-based resources**
  - Reluctant to order pharmacogenomic tests due to limited information about clinical utility
  - There are logistical challenges to testing
  - Health informatics tools (Electronic Medical Records, Computerized Provider Order Entry) do not have pharmacogenomic information at the point of care

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Patient/Provider Concerns

- **Patients and providers have concerns about privacy issues** (Rogausch 2006, Fargher 2007)
  - Genetic testing policies vary from state to state
- **Current healthcare professionals need education** (Frueh 2004)
- **Future healthcare providers need education**
  - Pharmacogenomics curricula have increased in pharmacy schools (Murphy 2010)
  - Pharmacogenomics is not adequately taught in medical schools (Gurwitz 2005)

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Competency in Pharmacogenomics

- **General competency domains include**
  - Genetic basis of disease
  - Impact of genetic variations on drug metabolism
  - Drug discovery
  - Drug disposition and targets
  - Ethical applications, social & economic implications
- **Open-access, comprehensive web-based tutorials are recommended** (Gurwitz 2005)

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Practice Gap

- The field of pharmacogenomics is growing rapidly, with many new discoveries coming to light
- It is critical for clinicians to…
  – Appropriately interpret emerging data on pharmacogenomic tests
  – Become familiar with resources applicable to their practice

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Molecular Biology 101

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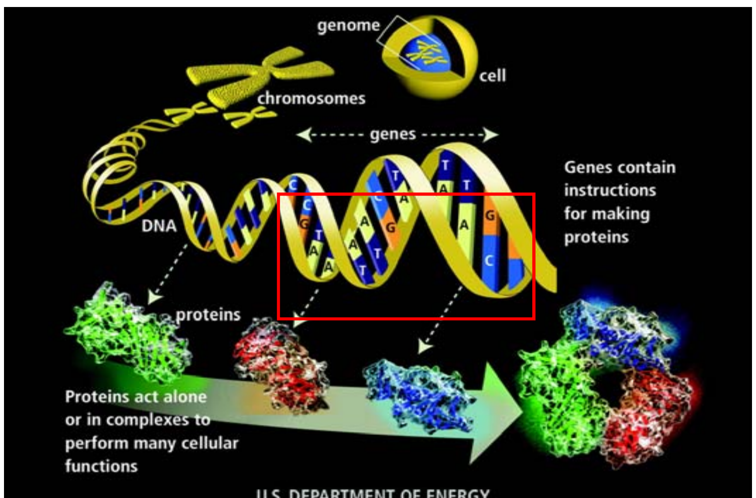

Source: Human Genome Program, U.S. Department of Energy, *Genomics and Its Impact on Science and Society: A 2008 Primer*, 2008. (Original version 1992, revised 2001 and 2008.) https://public.ornl.gov/site/gallery/detail.cfm?id=403&topic=&citation=&general=genomics energy&restsection=all

Molecular Biology 101

- **What are alleles?**
  – Different versions (alternate sequences) of a gene at a particular location on a chromosome
  – Alleles include the wild-type (usual) sequence, mutations, and polymorphisms of a given gene
  – Within a gene, variations of an individual nucleotide can be considered alleles
- **Humans are diploid organisms**
  – Humans normally have 2 copies of every chromosome; thus we have 2 copies of each gene
  – One allele is from your biological mother
  – One allele is from your biological father

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Molecular Biology 101

- **What is a polymorphism?**
  - A variation in DNA sequence
    - If present in >1% of the population, it is known as a polymorphism
    - If present in <1% of the population, it is known as a mutation
  - Types of polymorphisms
    - Single nucleotide polymorphism (SNP, pronounced 'snip')
    - Other types of polymorphisms involve changes in more than one nucleotide

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Molecular Biology 101

- **What is a genotype?**
  - Each person carries 2 alleles of each gene
  - The set of 2 alleles is his/her genotype
- **What is a phenotype?**
  - The characteristics (e.g. clinical presentation) of an individual, that result from his/her particular genotype
  - Examples:
    - ultra-rapid metabolizers (UM)
    - poor metabolizers (PM)

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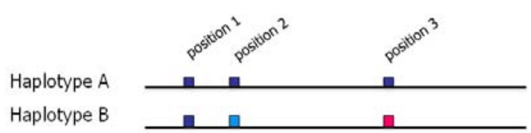
Molecular Biology 101

- **What is a haplotype?**
  - A set of alleles at multiple, neighboring positions that coexist on the same chromosome
  - These alleles may be in separate locations within a single gene or among different genes
  - Neighboring alleles (located near one another) are physically tethered and usually inherited as a set, i.e. their linkage on the chromosome prevents their separation during inheritance
  - One individual inherits two copies of a haplotype



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Pharmacogenomic Nomenclature

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Pre-Test Question:

An example of a SNP is *VKORC1 1173* C>T. Based on the nomenclature of this SNP, what is the gene of interest?

A. *1173*
B. *VKORC1*
C. Thymine (*T*)
D. Cytosine (*C*)

Pharmacogenomic Nomenclature

The following slides will describe:

- SNP nomenclature
- Reference SNP (rs) nomenclature
- "Star" nomenclature
- Genotype nomenclature
- Haplotype nomenclature

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SNP Nomenclature

- **Examples**
  - ***VKORC1 1173* C >*T***
  - ***ABCB1 3435* C >*T***
- **Explanation**
  - The **first few letters/numbers** (e.g. ***VKORC1***, ***ABCB1***) identify the gene
  - The **numbers** following the gene (e.g. ***1173***, ***3435***) indicate the nucleotide position in the gene
  - The **first letter** (e.g. **C**) represents the original (or wild-type) nucleotide
  - The **second letter** (e.g. **T**) represents the change in the nucleotide sequence (i.e. the SNP)

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Reference SNP (rs) Nomenclature

- The "rs" naming system is used by the SNP database (dbSNP)
  - dbSNP is the central database for all genetic variation information
  - Recommended by Human Genome Variation Society as the standard nomenclature for SNPs
  - As each new polymorphism is identified, the information is submitted by researchers to the SNP database. The sequence data are curated and an "rs" number is created

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"Star" Nomenclature

- **Example 1:** ***CYP2C19*1*** and ***CYP2C19*2***
- *CYP2C19* function varies based on the allele
  - **1* allele → normal (wild-type) enzyme activity
  - **2* allele → no enzyme activity
- **Example 2:** ***CYP2C9*1*** and ***CYP2C9*2***
- *CYP2C9* function varies based on the allele
  - **1* allele → normal (wild-type) enzyme activity
  - **2* allele → decreased enzyme activity
- Key point: Identical allele names may indicate different functional outcomes, depending on the specific gene/protein

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Genotype Nomenclature

- Genotype refers to the two alleles inherited for a specific gene
- **Example:**
  - A person may carry two copies of the *2 allele for *CYP2C19*
  - Genotype = ***CYP2C19 *2/*2***
- **Genotypes may impact drug metabolism**
  - ***CYP2C19 *1/*1*** → normal (wild-type) enzyme activity
  - ***CYP2C19 *1/*2*** or ****1/*3*** → reduced enzyme activity
  - ***CYP2C19 *2/*2, *2/*3, or *3/*3*** → no enzyme activity

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Haplotype Nomenclature

- Haplotype refers to a combination of alleles or a set of SNPs found on the same chromosome
- **Example: *VKORC1* gene**
  - There are SNPs in at least 10 separate positions throughout the gene that may have functional effects
  - A haplotype name is used to simultaneously describe each set of linked SNPs in an individual
    - **Haplotype A** = a set of SNPs at 10 different positions along one chromosome
    - **Haplotype B** = a different set of SNPs at the same 10 positions on another chromosome

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Post-Test Question:

An example of a SNP is *VKORC1 1173 C>T*. Based on the nomenclature of this SNP, what is the gene of interest?

A. *1173*
B. *VKORC1*
C. Thymine (*T*)
D. Cytosine (*C*)

Polymorphism Types

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Polymorphism Types

- Single nucleotide polymorphism (SNP)
- Variable number tandem repeat
- Gene deletion
- Copy number variant

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Single Nucleotide Polymorphism (SNP)

- A single base substitution
- Several million SNPs have been identified, and novel SNPs continue to be discovered
- Some SNPs lie outside the protein-coding regions of genes
- Other SNPs lie within coding regions of genes
  - These may or may not alter protein synthesis
    - Synonymous polymorphism
    - Non-synonymous polymorphism
    - Premature stop codon

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Pre-Test Question:

A polymorphism has been found in the gene for a drug-metabolizing enzyme. A nucleotide change occurs, yet the encoded amino acid is unchanged. What type of SNP is this?

A. Gene deletion
B. Synonymous
C. Non-synonymous
D. Premature stop codon

Synonymous SNP: *ABCB1* and P-glycoprotein

- **The gene *ABCB1* encodes P-glycoprotein**
- ***ABCB1 3435C >T* allele** (rs1045642)
  - Nucleotide change occurs (C > T), yet the resultant amino acid (isoleucine) is unchanged

Reference or 'wild type' nucleotide sequence					
GTG	TCA	CAG	GAA	GAG	AT**C**
Corresponding amino acid sequence					
Val	Ser	Gln	Glu	Glu	**Ile**
ABCB1 3435C >T polymorphism – nucleotide sequence					
GTG	TCA	CAG	GAA	GAG	AT**T**
Corresponding amino acid sequence					
Val	Ser	Gln	Glu	Glu	**Ile**

  - Function effect: Conflicting data on whether there is an effect on P-glycoprotein expression or function (Kimchi-Sarfaty 2007, Leschziner 2007, Fung 2009, PharmGKB)
  - Affected drugs: efavirenz, cyclosporine

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Non-Synonymous SNP: *TPMT*

- **The gene *TPMT* encodes thiopurine methyltransferase**
- ***TPMT*3A* haplotype** (Tai 1996, Weinshilboum 2001)
  - *TPMT 615 G > A* results in an amino acid change (alanine > threonine)
  - *TPMT 874 A > G* results in an amino acid change (tyrosine > cysteine)

Reference or 'wild type' nucleotide sequence					
GCA	TTA	AAG	TTA	T**A**T	CTA
Corresponding amino acid sequence					
Ala	Leu	Lys	Leu	**Tyr**	Leu
TPMT*3A polymorphism – nucleotide sequence					
ACA	TTA	AAG	TTA	T**G**T	CTA
Corresponding amino acid sequence					
Thr	Leu	Lys	Leu	**Cys**	Leu

- Functional effect: Decreased TPMT enzyme activity
- Affected drugs: azathioprine, 6-mercaptopurine

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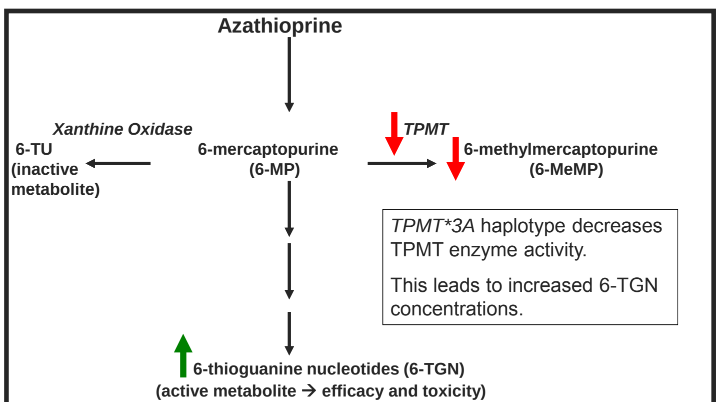
Non-Synonymous SNP: *TPMT*



Adapted from Weinshilboum 2001

Post-Test Question:

A polymorphism has been found in the gene for a drug-metabolizing enzyme. A nucleotide change occurs, yet the encoded amino acid is unchanged. What type of SNP is this?

A. Gene deletion
B. Synonymous
C. Non-synonymous
D. Premature stop codon

Patient Case #1

- 7-year old Caucasian child diagnosed with acute lymphoblastic leukemia. Patient has finished remission induction and will begin intensification chemotherapy that will include 6-mercaptopurine (6-MP)
- Allergies: no known drug allergies
- Questions:
  - Should a genetic screening test be done before starting 6-MP?
  - What will be the empiric 6-MP starting dose?

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Systematic Approach to Understanding Polymorphisms

- **Identify the polymorphism and what it may affect**
  - Enzyme, transporter, receptor
  - It may or may not have functional effect
- **Who is impacted?**
  - Individual and population variation may exist
- **Relevance to a drug?**
  - May affect drug PK or PD, influencing dosing, efficacy, or toxicity
  - May have no effect on a drug
- **Relevance to a disease?**
  - May increase or decrease disease susceptibility or disease condition
  - May be useful as a screening or diagnostic tool

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Systematic Approach to Understanding Polymorphisms

- **Identify the polymorphism and what it may affect**
  - *TPMT*3A* → decreased TPMT enzyme activity
- **Who is impacted?**
  - 1-10% in Caucasian populations
- **Relevance to a drug?**
  - Increased 6-mercaptopurine (6-MP) concentrations
  - Increased toxicity risk (myelosuppression)
  - 6-MP dose reduction is needed
- **Relevance to a disease?**
  - No difference in overall survival in individuals who have the *TPMT*3A* polymorphism

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Patient Case #1 Summary

- Patient was screened for the *TPMT* polymorphism before starting intensification chemotherapy
  - Patient's genotype was *TPMT*3A/*3A*
- Patient's genotype increases risk of myelosuppression upon starting 6-MP
- To decrease this risk, 6-MP starting dose reductions are recommended (Purinethol® Prescribing Information)

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Pre-Test Question:

If drug X is predominantly metabolized by the CYP2C19 enzyme, which *CYP2C19* genotype may result in the lowest amount of metabolite Y in the blood?

A. *CYP2C19 *1/*1*
B. *CYP2C19 *1/*2*
C. *CYP2C19 *1/*3*
D. *CYP2C19 *3/*3*

Premature Stop Codon SNP: *CYP2C19*

- ***CYP2C19* encodes a cytochrome P450 enzyme**
- ***CYP2C19*3* allele** (Demorais 1994)
  - The nucleotide change (G >A), replaces reference sequence (encoding the amino acid tryptophan) with a stop codon, resulting in termination of protein synthesis

Reference or 'wild type' nucleotide sequence				
ACC	CCC	TGG	ATC	CAG
Corresponding amino acid sequence				
Thr	Pro	**Trp**	Ile	Gln
*CYP2C19*3* polymorphism – nucleotide sequence				
ACC	CCC	TAG	ATC	CAG
Corresponding amino acid sequence				
Thr	Pro	**STOP**	-	-

  - Functional effect: *CYP2C19*3* abolishes enzyme activity
  - Affected drugs: proton pump inhibitors (omeprazole, lansoprazole)

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CYP2C19 Genotype and Omeprazole Pharmacokinetics

Genotype	*CYP2C19* activity	Omeprazole Exposure (Mean + SD)
*CYP2C19 *1/*1*	normal	384 ± 64
*CYP2C19 *1/*2* *CYP2C19 *1/*3*	reduced	1002 ± 532
*CYP2C19 *2/*2* *CYP2C19 *2/*3* *CYP2C19 *3/*3*	absent	5590 ± 294

Drug X (omeprazole) —*CYP2C19*→ *Metabolite Y*

(Furuta 1999)

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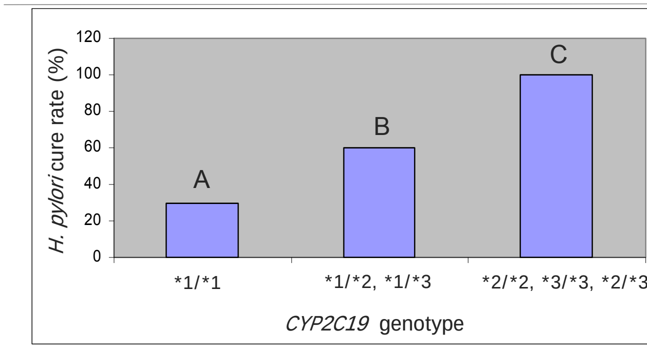
CYP2C19 Genotype, Omeprazole Therapy, & *H. pylori* Cure Rates



p < 0.05 for A vs B, and A vs C (Adapted from Furuta 1998)

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Patient Case #2

- 35 year old Asian female complains of dyspepsia & epigastric pain. Denies nausea and vomiting and blood in stools. Urea breath test is positive. She is diagnosed with *H. pylori* peptic ulcer disease
- **Past Medical History:**
  - No other significant past medical history
  - No known drug allergies
- **Medications:** Begins 10-day course of omeprazole, amoxicillin, and clarithromycin
- **Questions:**
  - What is the primary enzyme responsible for omeprazole metabolism?
  - Does a polymorphism exist for this enzyme?
    - What is the anticipated effect on omeprazole pharmacokinetics and the *H. pylori* cure rate?

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Systematic Approach to Understanding Polymorphisms

- **Identify the polymorphism and what it may affect**
  - *CYP2C19*3* allele → no CYP2C19 enzyme activity
- **Who is impacted?**
  - Frequency of the *CYP2C19*3* allele higher in Asian populations
- **Relevance to a drug?**
  - The *CYP2C19*3* allele leads to higher omeprazole plasma concentrations, compared to the wild-type *CYP2C19*1* allele
- **Relevance to a disease?**
  - H. pylori cure rates in patients taking omeprazole vary based on *CYP2C19* genotype

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Patient Case #2 Summary

- Patient purchased a commercially available genotyping kit
  - Patient's genotype was *CYP2C19*3/*3*
- *H. pylori* cure rate is anticipated to be 100% in patients with the *CYP2C19*3/*3* genotype (Furuta 1998)
- Patient completed 10 day course of omeprazole, amoxicillin, and clarithromycin
  - Symptoms of dyspepsia and epigastric pain resolved
  - Patient was *H. pylori* negative and considered cured

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Post-Test Question:

If drug X is predominantly metabolized by the CYP2C19 enzyme, which *CYP2C19* genotype would be predicted to result in the lowest amount of metabolite Y in the blood?

A. *CYP2C19 *1/*1*
B. *CYP2C19 *1/*2*
C. *CYP2C19 *1/*3*
D. *CYP2C19 *3/*3*

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Variable Number Tandem Repeat: *UGT1A1*

- ***UGT1A1* encodes UDP-glucuronyl transferase 1A1**
- ***UGT1A1*28* allele**
  - Insertion of one additional T, followed by one additional A
  - Copies of the "T-A" dinucleotide repeat increase from 6 to 7, in the promoter region of the gene (not the coding region) (Hall 1999)

Reference or 'wild type' nucleotide sequence
G T A T A T A T A T A T A G T A A

*UGT1A1*28* polymorphism – nucleotide sequence
G T A T A T A T A T A T A T A G T A A

- Functional effect: decreased *UGT1A1* transcription & enzyme (glucuronidation) activity
- Affected drug: irinotecan (metabolized by UGT1A1)

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Gene Deletions and Copy Number Variants - *CYP2D6*

- *CYP2D6* encodes a cytochrome P450 enzyme
- Deletions and duplications of *CYP2D6* alter the number of copies of the gene, and the resulting activity of the CYP2D6 enzyme
- *CYP2D6* polymorphisms have as much as a 200-fold effect on drug metabolism
- *CYP2D6* polymorphisms affect pharmacokinetic variability among patients:
  - Ultra-rapid metabolizers
  - Extensive metabolizers
  - Intermediate metabolizers
  - Poor metabolizers

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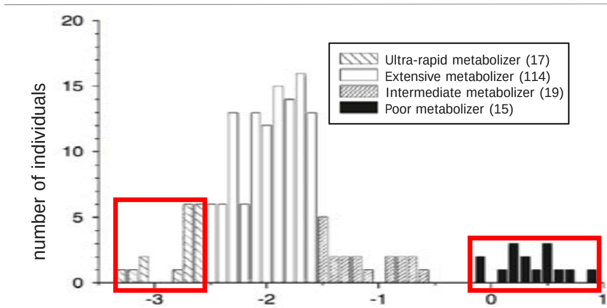
Metabolizer Variability, Resulting from *CYPD6* Genotypes



log[urinary ratio of dextromethorphan:dextrorphan]
(a measure of dextromethorphan metabolism)

(Rebsamen MC, et al. *Pharmacogenomics Journal* 9:34-41, 2009. Permission from Macmillan Publishers Ltd.)

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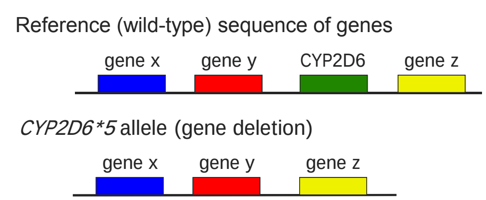
Gene Deletion: *CYP2D6*

- ***CYP2D6*5* allele** (Gaedigk 1991)
  - The entire gene (thousands of nucleotides) is deleted



- Functional effect: Loss of function of CYP2D6 enzyme
  - Contributes to a poor metabolizer phenotype
- Affected drugs: selective serotonin reuptake inhibitors (SSRIs), tamoxifen, codeine, β-blockers

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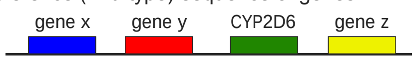
Copy Number Variant: *CYP2D6*

- ***CYP2D6*2XN* allele** (Dahl 1995)
  - Extra copies of the *CYP2D6* gene are present on a single chromosome (N = 2,3,4,5,13)

Reference (wild-type) sequence of genes



*CYP2D6*2X2* allele (copy number variation)

  - Functional effect: increased amount of CYP2D6 enzyme
    - Contributes to an ultra-rapid metabolizer phenotype
  - Affected drugs: SSRIs, tamoxifen, codeine, β-blockers

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Ethical, Legal, Social Issues (ELSI) & Economics

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Ethical Issues

- **Loss of privacy**
- **Whom do we test?**
  - Genetic profiling
  - Discrimination/stigmatization
- **Distributive justice**
  - Equitable distribution of benefits to patient populations
- **Prevention strategies** (public health at large)
  - Genotypic versus phenotypic prevention
- **Clinical decisions**
  - Should the test be ordered?
  - What should be done with test result?

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Legal Issues

- **Case Study**
  - In 2001, the Equal Employment Opportunity Commission (EEOC) filed suit against the Burlington Northern Santa Fe (BNSF) Railroad for secretly testing its employees for predisposition to a rare genetic condition (carpal tunnel syndrome)
  - Genetic testing for other medical predispositions (e.g. diabetes, alcoholism) was also performed
  - BNSF employees were not informed of the genetic testing and were threatened with possible termination if they did not comply
  - EEOC argued that the tests were unlawful under the Americans with Disabilities Act because the tests were not job-related
  - BNSF settled lawsuit with EEOC and stopped testing in 2002

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Legal Issues

- **Legislation**
  - The Genetic Information Nondiscrimination Act (GINA) of 2008 protects Americans from discrimination regarding health insurance and employment, based on genetic information
- **Questions to consider**
  - If testing is recommended, are clinicians liable if they do not offer or order the test?
  - If an adverse an drug reaction occurs, who is responsible?
- **Resources**
  - National Human Genome Research Institute www.genome.gov/24519851
  - University of Michigan Center for Public Health and Community Genomics http://www.sph.umich.edu/genomics/

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Social Issues

- **Health disparities**
  - Access to pharmacogenomic tests
  - Limitation of race-based therapeutics
- **Employment**
- **Insurance**
  - Loss of coverage
  - Increase in premiums
  - Life, disability and long-term care insurance
  - Unfair risk assessment for coverage
- **Societal benefits and burdens**
- **Mandatory versus voluntary screening**

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Economics & Cost Implications for Public Health

- **Implementation of pharmacogenomic (PGx) tests will require**
  - Evidence-based rationales demonstrating cost-effectiveness (Vegter 2008)
  - Payers agreeing to cover costs (Williams 2007)
- **Cost of PGx tests is unlikely to disrupt the current public health system**
  - Gradual and incremental progression
  - Our system has flexibility to adapt (Garrison 2008)

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Roles for Healthcare Professionals

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Potential Roles for Healthcare Professionals

- **Become an informational resource by:**
  - Identifying published literature and online resources
  - Maintaining up-to-date knowledge
  - Interpreting test results (potential outcomes and adverse reactions)
- **Educate:**
  - Healthcare professionals
  - Patients (genetic counseling)
- **Collaborate with:**
  - Researchers
  - Clinicians
  - Educators

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Patient Counseling

- Information about pharmacogenomics tests
- Assessment of risk in absence of genetic testing
- Cost associated with testing and counseling
- Technical accuracy of test
- Interpretation of positive, negative and inconclusive results
- Psychological impact of test results
- Confidentiality issues and risks of potential discrimination
- Sharing genetic test results with at-risk relatives

(Pharmacogenomics: Applications to Patient Care. 2004)

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Implications for Clinical Practice

- It is unclear how standard of care will be developed
  - Mandate testing
  - Restrict testing
  - Offer testing & let the patient decide
- Role of epigenomics should be considered
  - Influence of environment on gene expression
- Cost and coverage
- Informed consent and patient counseling
- Confidentiality and privacy

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Pharmacogenomic Resources

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Centers for Disease Control and Prevention (CDC)

- **Evaluation of Genomic Applications in Practice and Prevention** (EGAPP) launched in 2004
  - EGAPP Working Group (2005)
  - Independent, multi-disciplinary panel reviews available evidence on genetic tests, highlights critical knowledge gaps, and provides guidance on appropriate use of genetic tests in specific clinical scenarios (http://www.egappreviews.org/about.htm)
- **GAPP Translation Programs**
  - Currently there are 5 translation programs (Michigan Department of Community Health, Oregon Department of Human Resources, Sepulveda Research Corporation, University of California at San Diego, University of Washington)

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Food and Drug Administration (FDA)

- **Examples of topic areas for required or voluntary submissions to FDA**
  (Attachment to Guidance on Pharmacogenomic Data Submissions 2005)
  - Metabolizing Enzymes, Transporters, Receptors, Clinical Outcomes: Efficacy and Safety, Nonclinical Safety
- **Of 1,200 drug labels reviewed from 1945-2005**
  - 121 labels contained pharmacogenomic information (Frueh 2008)
  - 69 of these referred to human genomic biomarkers
- **Currently, FDA lists 155 approved drugs with valid genomic biomarkers described their labels** (Table of valid genomic biomarkers in the context of approved drug labels 2014)

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Information and Resource Databases

- **Definitions, Terminology, Nomenclature**
  - National Human Genome Research Institute (NHGRI) http://www.genome.gov/10002096
  - Genetics Home Reference by the U.S. National Library of Medicine http://ghr.nlm.nih.gov/glossary
- **Molecular Biology and SNP concepts**
  - National Center for Biotechnology Information (NCBI): A Science Primer http://www.ncbi.nlm.nih.gov/About/primer/index.html
  - Court MH. A Pharmacogenomics Primer. J Clin Pharmacol 2007; 47:1087-1103 http://jcp.sagepub.com/cgi/reprint/47/9/1087.pdf

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Information and Resource Databases

- **Information for Health Care Professionals**
  - NIH G2C2: Genetics/Genomics Competency Center for Education http://www.g-2-c-2.org/index.php
  - CDC National Office of Public Health Genomics http://www.cdc.gov/genomics/links.htm
  - PharmGKB http://www.pharmgkb.org/
  - FDA: Valid Pharmacogenomic Biomarkers http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm
  - National Coalition for Health Professional Education in Genetics http://www.nchpeg.org

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Information and Resource Databases (cont.)

- **Information for Patients** (Public policy, Ethical issues, Genetic testing)
  - CDC National Office of Public Health Genomics http://www.cdc.gov/genomics/resources/e.htm#Ethical
  - University of Michigan Center for Public Health and Community Genomics http://www.sph.umich.edu/genomics
  - National Human Genome Research Institute http://www.genome.gov/policyethics
  - Genetic Alliance http://www.geneticalliance.org

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References

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Disclaimer

The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Patients should seek the advice of their physicians, pharmacists, or other qualified health providers with any questions they may have regarding a medical condition or a medication.

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