Introduction to Pharmacogenetics Competency

Updated on 6/2015

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Pre-test Question # 1

Pharmacogenetics is the study of how genetic variations affect drug response

a) True

b) False

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Pre-test Question # 2

Pharmacogenetic testing can help improve pharmacotherapy by identifying patients

a) At an increased risk of having no response when prescribed conventional drug therapy
b) At an increased risk of experiencing drug-induced toxicities when prescribed conventional drug therapy
c) Both a and b
d) None of the above

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Pre-test Question # 3

When counseling a patient about their pharmacogenetic test results the following statement is most acceptable to use:

a) Your DNA is mutated
b) Your DNA is abnormal
c) You have a genetic variation or polymorphism
d) Both a and c

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Pre-test Question # 4

Which of the following is true regarding re-testing?

a) It is a good idea to have genetic testing repeated, because your genetic tests can change as you age.

b) Pharmacogenetic testing is a lifelong test, so if done correctly, it has implications throughout your lifetime and may only need to be performed once.

c) We can use DNA from the father to predict all of the DNA variation in the child.

d) We can use DNA from the mother to predict all of the DNA variation in the child.

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Pre-test Question # 5

Patients usually inherit ____ copy(ies) of a gene.

a) One
b) Two
c) Three
d) Four

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Objectives

- Upon completion of this module, you will be able to:
  - Define some basic pharmacogenetic terms
  - Describe what pharmacogenetics is and how pharmacogenetics can improve patient care
  - Provide basic explanations to patients and clinicians about pharmacogenetics using appropriate concepts and terminology

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Definitions

- The term **pharmacogenetics** commonly refers to the study of how variations in a single gene affect drug response

- The terms **pharmacogenetics** and **pharmacogenomics** are often used interchangeably

http://ghr.nlm.nih.gov/glossary

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Definitions

Some basic definitions:

- **DNA** (deoxyribonucleic acid) is the chemical name for the molecule that carries genetic instructions for all living things

- **Nucleotides** (also called bases) are the building blocks of DNA. Four nucleotides make up DNA: adenine (A), cytosine (C), guanine (G), and thymine (T)

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Definitions

- A **gene** is the basic physical unit of inheritance
  - Patients usually inherit one version of a gene from the mother (maternally) and one version of a gene from the father (paternally)
- The term **allele** refers to a version of a gene
  - For most genes a patient will have two copies, one maternal allele and one paternal allele

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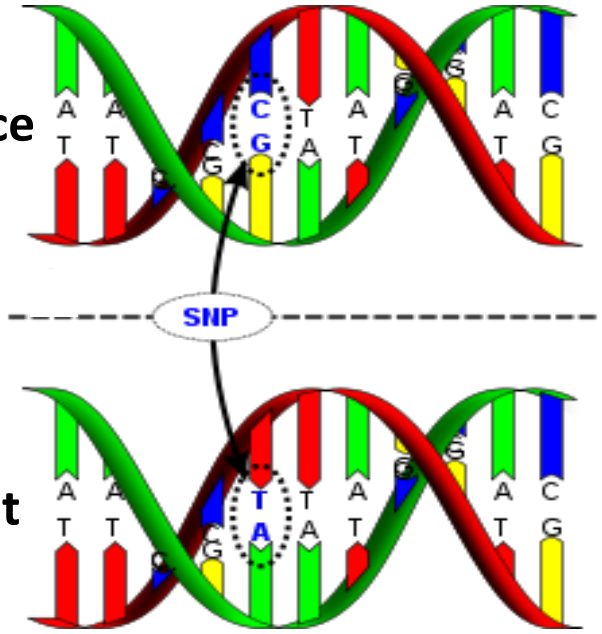
Definitions

- A **polymorphism** may refer to a variation within a gene
  - The most common type of polymorphism involves a variation at a single nucleotide called a single nucleotide polymorphism (SNP)

Wild-type (normal) DNA sequence



Polymorphism, DNA variant

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Definitions

- A **haplotype** is a set of genetic variants that are inherited together
  - A haplotype can be thought of as a collection of genetic variants, such as SNPs, that always travel together (are inherited together) on the same individual allele

- A **diplotype** refers to a haplotype pair where one haplotype is maternally inherited and one haplotype is paternally inherited

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Definitions

- Based upon the reported diplotype a predicted **phenotype** can be assigned to a patient
  - The phenotype refers to an observable physical characteristic such as enzyme activity
  - The predicted phenotype is determined by the functional activity of each inherited allele reported in the diplotype

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Definitions

- A patient may be called **heterozygous** based on either their genotype or predicted function of the alleles inherited
  - Heterozygous may refer to a patient inheriting different alleles for a particular gene from each parent

- A patient may be called **homozygous** based on either their genotype or predicted function of the alleles inherited
  - Homozygous may refer to a patient inheriting the same allele for a particular gene from both parents

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Pharmacogenetics

- Pharmacogenetic testing is the process of analyzing a person's DNA to identify:
  - Genetic variants that may place a patient at a **higher** risk of developing **drug-induced side effects**
  - Genetic variants that may place a patient at a **higher** risk of **failing therapy** due to a lack of response to a drug

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Pharmacogenetics

- Because we are able to study pharmacogenetics, we are better able to determine or predict:
  - An individual's response to a certain drug based on variations in their genes encoding for drug-metabolizing enzymes, drug receptors, drug transporters or drug targets

Meyer UA. *Nature Reviews Genetics.* 2004;5:669-76.
Crews KR, et al. *Clin Pharmacol Ther.* 2012;92:467-75.

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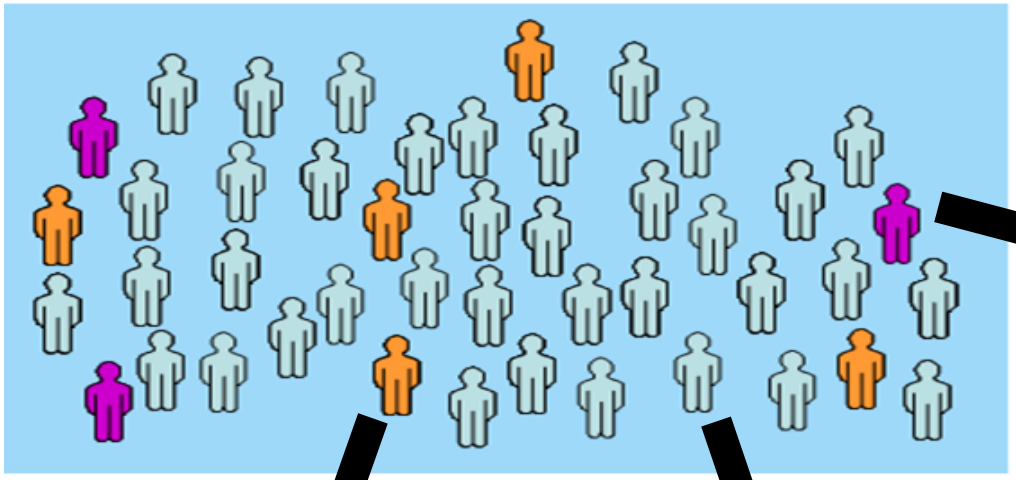
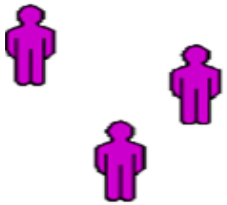
Pharmacogenetic Testing Aids Clinicians to Prescribe Appropriate Drugs at the Appropriate Dose



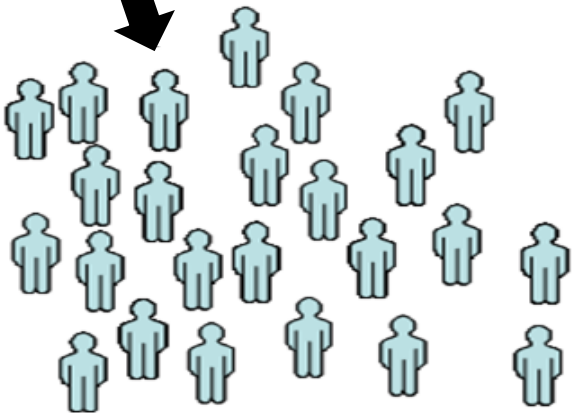
Genetic profile for non-response



Treat with alternative drug

Genetic profile for toxicity

Treat with alternative drug or dose



Genetic profile for favorable response

Treat with conventional drug dosing

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Pharmacogenetics

- Pharmacogenetic test results should not change during a person's lifetime
- Pharmacogenetic test results are lifelong, therefore the results can have implications throughout a person's lifetime
- As genetic testing gets less and less expensive, we are moving from testing a few variants in a few genes to testing for thousands of variants in hundreds of genes

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Pharmacogenetics

Why should **pharmacists** care about pharmacogenetics?

- As the drug experts, pharmacists should be familiar with all factors that affect pharmacotherapy
- Pharmacy benefit managers are starting to incorporate pharmacogenetics into the drug approval and reimbursement process
- As more patients are genotyped, the likelihood increases that you will be asked questions about pharmacogenetics

Reiss SM, et al. *J Am Pharm Assoc*. 2011;51:e64-74.
Barlow, JF. *Personalized Medicine*. 2012;9:441-450.

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What is Reported?

- The most commonly reported alleles are usually given a functional status based upon the predicted activity of the protein they encode
  - Some alleles are considered to have normal activity meaning they are **fully functional** and some alleles have little to no activity and are considered **non-functional**

NOTE: It is the functionality **OR** lack of functionality that allows us to predict if a patient will experience more toxicity at conventional doses, less efficacy, **OR** can receive standard therapy with no modifications to drug therapy

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What if You Are Asked About A Pharmacogenetic Result?

- When communicating with patients/parents pharmacogenetic concepts should be explained as simply as possible
  - For example
    - Avoid terms like haplotype and diplotype and instead say test result
    - Say low enzyme activity instead of poor metabolizer phenotype
    - Say genetic variant instead of mutation or abnormal result and point out that all humans carry DNA variations

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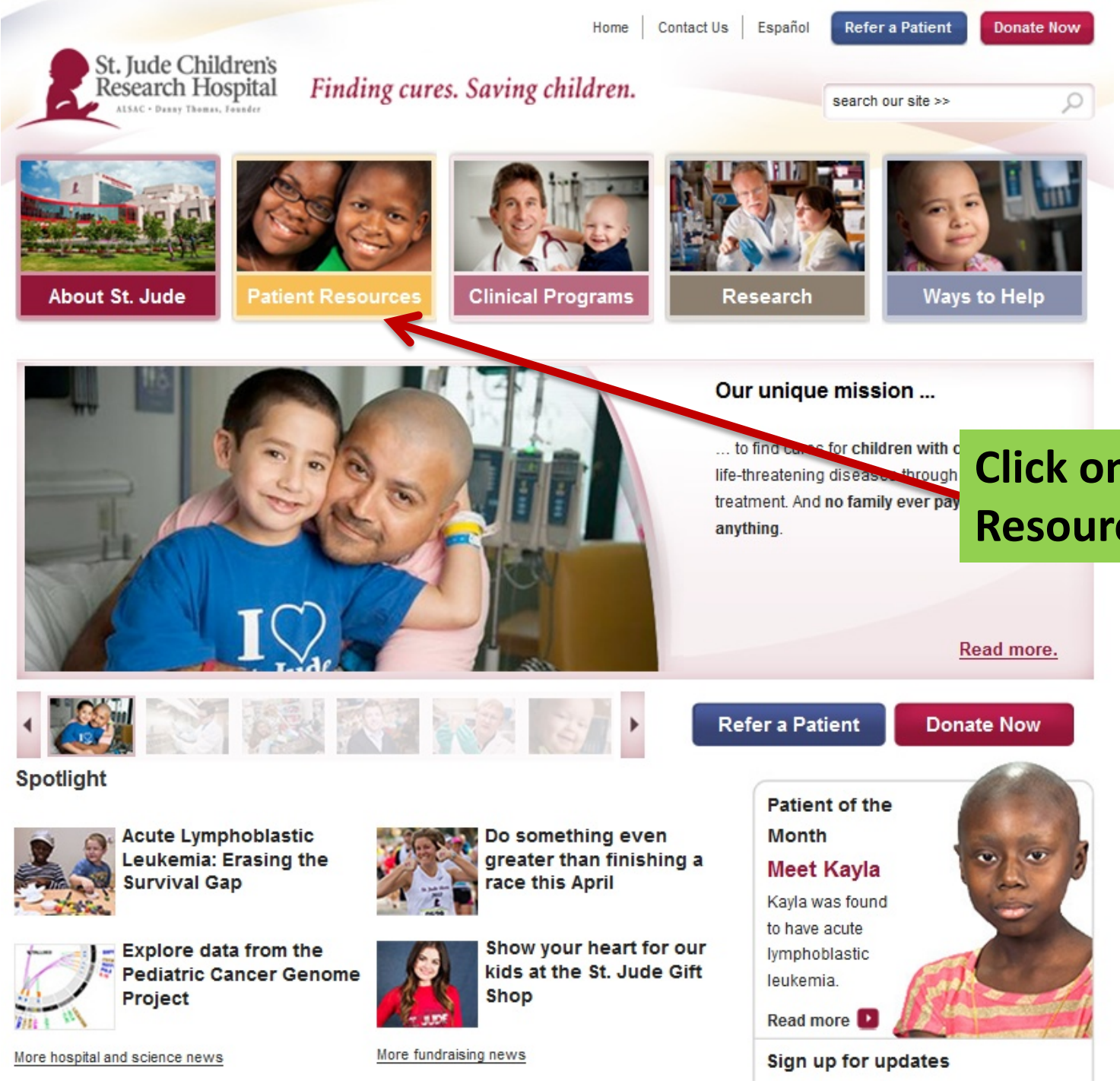
Patient Counseling

- Patients may be more sensitive about pharmacogenetic test results when compared to other test results
  - A patient or parent **MAY NOT** take offense if you tell them a sodium or glucose level is abnormal
  - However, a patient or parent **MAY BE OFFENDED** if you tell them a "DNA result is abnormal"; a patient may think you are calling him/her abnormal
- When counseling patients about their genetic test results use terms such as **genetic variant, variation** or **polymorphism** instead of the words mutation or abnormal

St. Jude Website Resources for Pharmacogenetic Information



www.stjude.org

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Patient Resources

A to Z Disease Info

Treatment Programs

My St. Jude

St. Jude is not a typical children's hospital. St. Jude is first and foremost a hospital that provides unsurpassed care to children, but it is also a research center that specializes in finding cures for childhood catastrophic diseases. It is the largest childhood cancer research center in the world in terms of the number of patients enrolled and successfully treated on research protocols.

We know that you and your child are unique individuals. Our social workers, psychologists, child life specialists and chaplains help patients and their families cope with facing a life-threatening illness. At St. Jude, we believe that families are essential in psychosocial care for their children. And, we know that the family is a child's primary source of strength and

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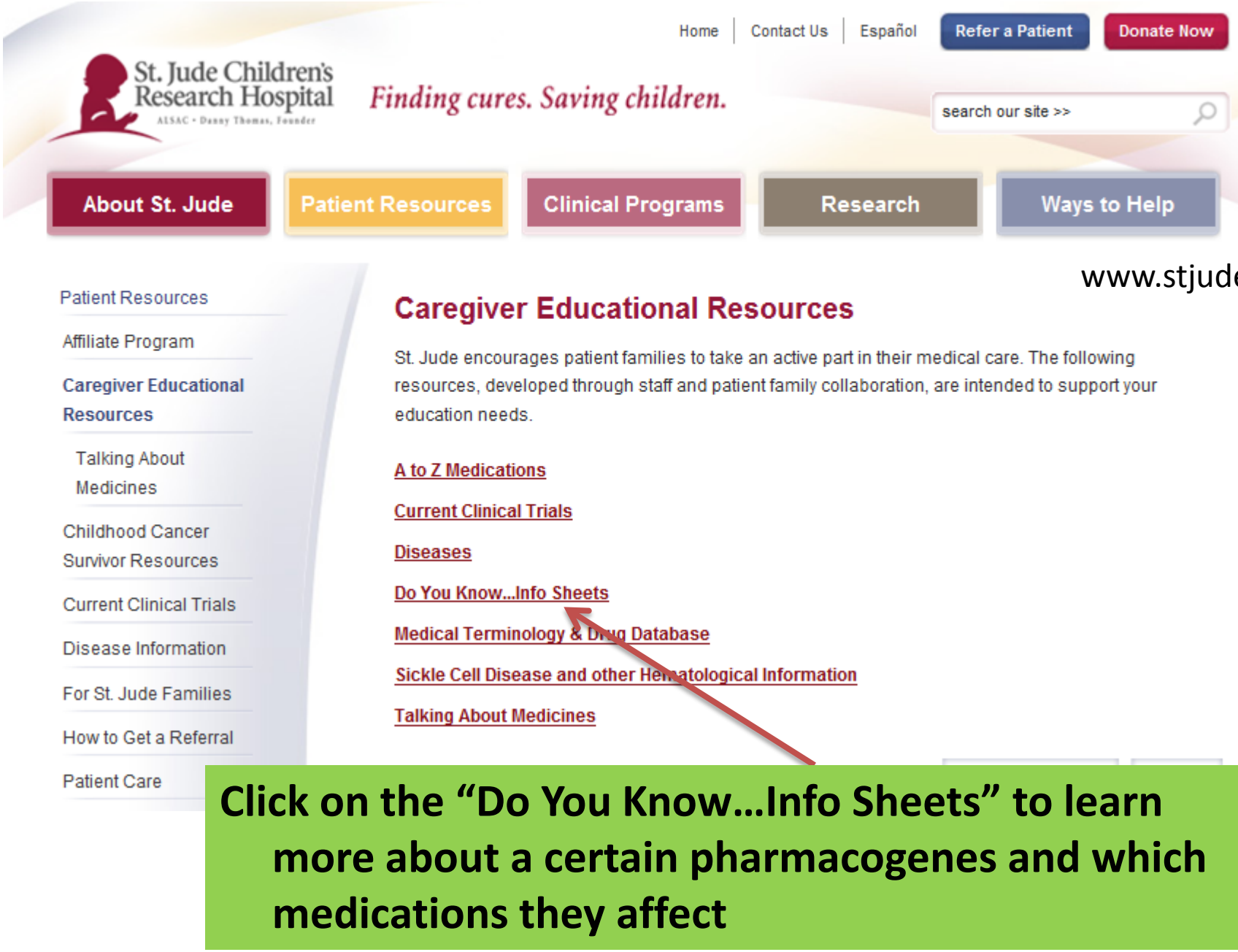
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Patient Care
Caregiver Educational Resources
St. Jude encourages patient families to take an active part in their medical care. The following resources, developed through staff and patient family collaboration, are intended to support your education needs.
A to Z Medications
Current Clinical Trials
Diseases
Do You Know...Info Sheets
Medical Terminology & Drug Database
Sickle Cell Disease and other Hematological Information
Talking About Medicines
Click on the "Do You Know…Info Sheets" to learn more about a certain pharmacogenes and which medications they affect

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Do you know...

An educational series for patients and their families

Cytochrome P450 2D6 (CYP2D6) and medicines

When you take a medicine (drug), your body has to have a way to handle the medicine. One way is for enzymes to metabolize (break down) the medicine. A family of enzymes called cytochrome P450s have the ability to break down certain medicines. By metabolizing a medicine, cytochrome P450 enzymes make the medicine either more or less active, depending upon the medicine. Cytochrome P450 2D6 (CYP2D6) is part of the cytochrome P450 family of proteins in the body. It is responsible for breaking down many medicines that are commonly used.

Pharmacogenetic testing

DNA is like a set of instructions for your body that can help decide how well your enzymes will work. Each person differs from another at the DNA (gene) level. This means that each person has small differences in the genes that code for enzymes. The part of DNA that instructs how well the CYP2D6 enzyme will work is

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For More Information…

- **For more information about pharmacogenetics visit the following website: www.pharmgkb.org**
- **For more pharmacogenetic service implementation resources visit the following website: www.stjude.org/pg4kds/implement**

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Question # 1

Pharmacogenetics is the study of how genetic variations affect drug response

a) True
b) False

Correct answer: a

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Question # 2

Pharmacogenetic testing can help improve pharmacotherapy by identifying patients

a) At an increased risk of having no response when prescribed conventional drug therapy
b) At an increased risk of experiencing drug-induced toxicities when prescribed conventional drug therapy
c) Both a and b
d) None of the above

Correct answer: c

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Question # 3

When counseling a patient about their pharmacogenetic test results the following statement is most acceptable to use:

a) Your DNA is mutated
b) Your DNA is abnormal
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d) Both a and c

Correct answer: c

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Question # 4

Which of the following is true regarding re-testing?

a) It is a good idea to have genetic testing repeated, because your genetic tests can change as you age.

b) Pharmacogenetic testing is a lifelong test, so if done correctly, it has implications throughout your lifetime and may only need to be performed once.

c) We can use DNA from the father to predict all of the DNA variation in the child.

d) We can use DNA from the mother to predict all of the DNA variation in the child.

Correct answer: b

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Question # 5

Patients usually inherit ____ copy(ies) of a gene.

a) One
b) Two
c) Three
d) Four

Correct answer: b

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