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DNA *Today*

ADDRESSING THE DNA TESTING NEEDS OF MEDICAL PROFESSIONALS AND PATIENTS SINCE 1987.

Plavix May be Relabeled to Recommend DNA Testing

The Plavix label was updated by the FDA in May 2009 to explain the importance of cytochrome P-450 2C19 (CYP2C19) genetics. This was in response to two landmark studies indicating that the one-third of patients on Plavix with CYP2C19 variations have a 3.58 times greater risk for major adverse cardiovascular events such as stroke, heart attack, and death.

It now appears that the drug may be relabeled again to recommend DNA testing for all Plavix patients. On January 16th, *Seeking Alpha*, a popular investment blog, stated, "Larry Lesko, Ph.D., director of the FDA's office of clinical pharmacology, said the agency is in discussions with Plavix's maker, Bristol-Myers Squibb Co., about updating the label. Dr. Lesko said the agency is considering adding a recommendation that patients get a genetic test to screen

them for the gene mutation." This news came out not long after a study published in *Cardiovascular Interventions* demonstrated that doubling the dose of clopidogrel (Plavix) in intermediate metabolizers, who represent the majority of patients with CYP2C19 variations, leads to improved outcomes. Learn more about Plavitest™ at www.Plavitest.com.



Gladding P et al, Pharmacogenetic Testing for Clopidogrel Using the Rapid INFINIT Analyzer – A Dose Escalation Study. *J Am Coll Cardiol Intv*, 2009; 2:1095-1101, doi:10.1016/j.jcin.2009.08.018

<http://seekingalpha.com/article/115125-plavix-winners-and-losers>

DNA in the News



Even though approximately 1 in 8 rape kits collected can lead to a match in a criminal DNA database, most are sitting untested in storage facilities. A report compiled by Human Rights Watch puts the number at more than 400,000. The Justice for Survivors of Sexual Assault Act of 2009 would help remedy this situation, but it is still sitting in committee. For your safety, and the justice of others, please contact your congressional representatives to urge the passage of this important bill.

What You Need to Know About Adverse Drug Reactions



Adverse drug reactions are not medical errors; they are reactions to medications prescribed following recommended dosing guidelines. Medication errors are also a big issue. Medication errors account for approximately one out of 131 outpatient deaths and one out of 854 inpatient deaths.

Most people are aware of the leading causes of death—heart disease, cancer, and stroke—but few are aware that adverse drug reactions are the 5th leading cause of death, killing more than 100,000 Americans each year—twice as many as are killed in car accidents. Adverse drug reactions are not medical errors; they are reactions to drugs given following recommended dosing guidelines. Medication errors are also a big issue. Medication errors account for approximately one out of 131 outpatient deaths and one out of 854 inpatient deaths. Despite these staggering statistics, and the fact that many Americans take drugs daily, few people know much about medication safety or how drugs are processed.

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How do we process medicine?

Drugs are metabolized by the body in much the same way as food and chemicals; they are broken down by liver and gut enzymes so they can be absorbed and eliminated. Most medications are taken in an active form which is then converted by enzymes to a form that the body can then eliminate. Some medications, called prodrugs, are taken in an inactive form and then converted to the active form by enzymes. For example, codeine is a prodrug that is converted to morphine by a liver enzyme called CYP2D6. Only after this conversion occurs does a patient get pain relief.

Each drug goes down one or more specific paths. Picture a roadmap: while some drugs take the highway, others take side roads to get to the final destination.

How does genetics play a part in this?

To continue with the road analogy, a person normally has two active lanes—one from mom and one from dad. These individuals, who represent about 50% of the population, can take drugs following normal dosing guidelines. If a person inherits a closed lane from one parent, that person is called an intermediate metabolizer. This may require the individ-

ual to lower the doses of current medications as well as be careful about taking other drugs, herbals, or foods that add more “traffic to the lane.” Intermediate metabolizers represent about one third of the population. If a person inherits a closed lane from both parents, that person is a poor metabolizer. This is the most dangerous class of metabolizer, and can lead to dangerous reactions to standard doses or, in the case of prodrugs, failed treatment. This category accounts for about 10% of the population.

The lanes in the above analogy are representative of a group of three enzymes, called cytochromes, which are responsible for processing about half of the most commonly prescribed medications. About two-thirds of the population has one or more variation in at least one of these three key enzymes. Gene variations have a large impact on drug safety. According to the Journal of the American Medical Association, fifty-nine percent of the drugs most commonly cited in adverse drug reaction studies are processed by enzymes with genes known to have poor metabolizer variants. For more information, visit www.GeneMedRx.com/explainreport.ppt.

The United States Pharmacopeia. *Summary of Information Submitted to MEDMARX in the Year 2002: The Quest for Quality*. 2002.

Three Tips For Impro

1. Use only one pharmacist. If you do use more the-counter medicines you are taking. You may cause grapefruit juice reduces the availability fairly common for herbals and over-the-counter.
2. Keep a list of all of your medications and doses. Adverse drug reactions during your treatment. In
3. Finally, if you or a loved one has a history of insurance in diagnostic situations. Since half relatives informed. Visit www.HealthandDNA



DID YOU KNOW?



Why the Mother's Sample Matters in Paternity Testing

Although the mother's sample is not required for paternity testing, it is always highly recommended if the sample is available. Before we explain why this is the case, let's explore the basics of paternity testing.

The DNA, and hence the genetic code of humans, is almost the same for all individuals. It is the very small amount that differs from person to person that DNA scientists analyze to identify people. These differences are called polymorphisms (from the Greek word for "many forms") and are the key to DNA typing.

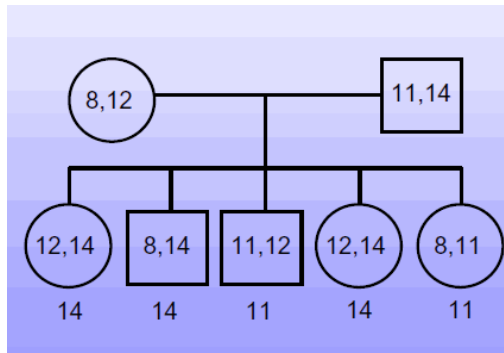
In paternity testing, we examine variations in the length of the DNA at specific locations (loci) known

as STRs (short tandem repeats). These STR regions consist of stretches of DNA made up of short repeating DNA sequences. The number of times the short DNA

known as alleles.

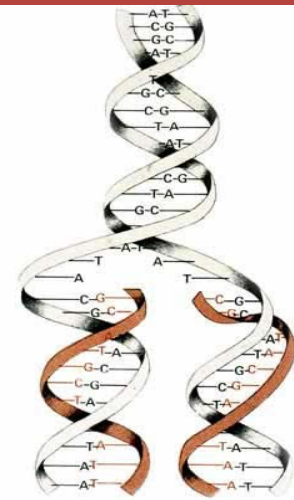
A child inherits one allele from his mother and the other from his father. An examination of the mother's DNA enables the lab to know exactly what half of the DNA was contributed to the child by the mother. This means that the remaining half, called the "obligate paternal allele," had to come from the father.

Having this information increases the certainty of paternity testing. At Genelex, results including the mother often exceed 99.9999% vs 99.9% without.



In the example above, the mother (circles are female, squares are male) had to contribute an 8 or 12 to each child. The number underneath each child is the obligate paternal allele, and must come from the father.

sequence is repeated determines the physical length of the DNA molecule at these specific loci. Each of the many versions that may be found in the population are



Many people think that when it comes to genes, what you get is what you get. In some cases, that is true. If you have the genes for brown eyes, you will have brown eyes. However, there are a number of genes that only express themselves in response to environmental factors. For example, a person may have a genetic predisposition to a certain disease, but it will only be the person if it is triggered. Triggers vary widely—stress, obesity, deficiency in vitamins, or a combination of these and many other factors. Think of it as an on/off switch. Research in this area of genetics is not yet well understood, but research is rapidly expanding. In the meantime, exercise and eat your vegetables; it may be more important than you think.

Medication Safety

than one, be sure that one is aware of all prescription drugs, herbal preparations, and over-the-counter medications. You may have been warned at some point not to take a medication with grapefruit juice. This is because of a liver enzyme called cytochrome 3A4 that processes a number of medicines. It is actually a common enzyme, as well as foods, to interfere with metabolism—so check with your pharmacist.

Keep a list of medications in your wallet. In case of an emergency, this information can be vital in avoiding adverse reactions. If you have had bad reactions to certain medicines, keep these on the same list.

If you have had adverse drug reactions or treatment failures, consider genetic testing. It is often covered by insurance. Some of your DNA come from each parent, drug metabolism issues run in families. Be sure to keep a list of medications in your wallet. For more information on testing, visit www.genelex.com.





Help Prevent Breast Cancer Recurrence for 30,000 Women!

Half a million women in the U.S. are taking tamoxifen to prevent breast cancer recurrence. Almost half have a genetic variation that reduces the effectiveness of the drug. For patients with these gene variations, alternative treatments with higher success rates are available! If all of the women taking tamoxifen had a DNA test and had their treatment adjusted accordingly, 30,000 breast cancer recurrences would be avoided!

The majority of an FDA advisory panel recommended updating the tamoxifen label in 2006 to reflect this important information, but the change has still not occurred. Since that time, three additional studies have been published, further confirming the importance of genetic testing, yet **most women taking tamoxifen still do not know about the test!** To make

matters worse, according to a poster presented at the San Antonio Breast Cancer Symposium in December, less than 20% of oncologists currently recommend testing for their patients, and another 50% only if the patient asks.

Spread the word at www.tamoxitest.com/get_involved.html.

To help raise awareness, Genelex has launched a social media

campaign to make sure that every one of the women taking tamoxifen learns about testing. For every member joining our Facebook cause, and every \$1 they donate to breastcancer.org, we donate \$1 to the Tamoxitest™ Patient Assistance Fund to provide free testing to patients with financial need. We have also posted a YouTube video, a petition, and created a Twitter account. Spread the word at www.tamoxitest.com/get_involved.html.

Questions? Comments?

Call a Genelex DNA Testing Consultant
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www.HealthandDNA.com



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