

For Immediate Release

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Antidepressants and DNA testing Science fuels controversy with prejudicial misquote

There is a policy comment due out in Science today in which Genelex's website is prejudicially quoted out of context.

The quote in the article is:

"Some Web sites make explicit claims about the utility of CYP450 testing for particular drugs, such as the claim by Genelex that pharmacogenetic testing is "required to effectively prescribe Paxil" (10).

The actual statement is:

Paxil (paroxetine) is metabolized through CYP2D6. Pharmacogenetic testing of this pathway serves as an anchor for the intense personalization required to effectively prescribe Paxil and other antidepressant medicines. <http://www.healthanddna.com/professional/paxil.html>

We are narrowing the focus of our response to the focus of the policy comment – SSRIs. However, this focus also points out the continuing problem in healthcare of putting patient information in silos. The fact is just three P450 enzymes – 2D6, 2C9, and 2C19 are responsible for the metabolism of over half of commonly prescribed medications and over half of the population has a variation in one of these key processing enzymes. This information can be used for a lifetime to help caregivers provide more effective and safe treatment regimens. Considering that adverse drug reactions currently kill twice as many as people as vehicle accidents and cost billions of healthcare dollars, a panel that costs less than installing an airbag will certainly prove to be cost-effective when taken in the context of overall medication management not one medication or class at a time.

Relevant facts and quotes:

- "The cytochrome P-450 test represents a major advance in the ability to provide the best care possible for depression" Access April 2, 2008 Mayo Clinic Web site <http://www.mayoclinic.org/depression/cytochrome.html>
- Hospitalized psychiatric patients who are poor metabolizers cost \$4,000 - \$6,000 more in medical care compared to patients with an average metabolizer genotype. Virtually, all antidepressants and antipsychotic medicines are processed by enzymes with a high incidence of poor metabolizers. Journal of Clinical Psychopharmacology 20:246 2000
- Fifty-nine percent of drugs most commonly cited in ADR studies are processed by enzymes with genes known to have poor metabolizer variants. This is compared to 7% of a random selection of the top selling drugs. (JAMA 286:2270 2001).

- Multiple studies have found that people with CYP variants require lower doses of the affected medications. *Molecular Psychiatry* 9:442-473, 2004
- Hundreds of studies stretching back to the 1960s of the genetics of CYP2D6, 2C9, and 2C19 have led the FDA to consider DNA testing of the genes for these enzymes as valid biomarkers of in vivo drug levels. *Tox Mech Meth* 16:89-99, 2006
- “Putting what we know into practice would prevent more disease than worshipping at the altar of randomized trials.”
John Concato, MD (Director, VA Clinical Epidemiology Research Center, Yale University)

Genelex’s Position:

- Individuals have a right to learn their genotype and control that information. If patients are denied direct access to this testing they may be reluctant to be tested because they are not confident that the confidentiality of the test results will be adequately protected.
- Excessive regulation, such as is advocated by the Genetics and Public Policy Center, will impede the already excessively slow rate of adoption of DNA testing for use in medication management. Were this testing adopted at a faster pace there are likely tens of thousands of adverse medical events that would have been prevented.
- There needs to be symmetry between the level of proof required for the adoption of a technology and the potential risk and cost benefit ratios.
- A peer developed rating system that describes where a given test lies on the continuum of scientific knowledge about the utility, acceptance and proof of that test. In this way individuals would be provided with the tools needed to help them make informed decisions.

Randomized trials are in progress that will add to our knowledge. In the meantime clinicians and patients who find this information useful should have access to it. Physicians don’t prescribe without knowing the patient’s age, sex, and medical history. In many instances CYP genetics are more important than all these other factors combined. The trend in psychiatry is to utilize polypharmacy and many of these patients have co-morbid conditions for which they are also receiving drugs. The complexity of these medication regimens heightens the need for DNA testing and the use of interpretive software as a step toward comprehensive personalized medication management.

For further information and comment including patients and physicians and patients willing to be interviewed please contact:

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