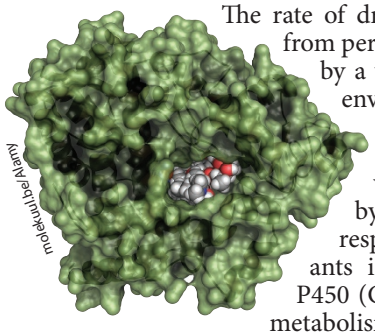
IN THIS ISSUE

Personalized antiplatelet therapy not justified by current evidence

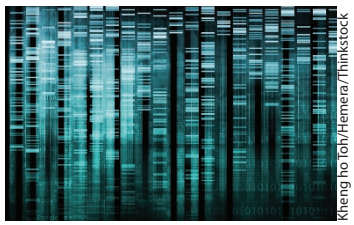
see page 3



The rate of drug metabolism by the liver varies from person to person and can be influenced by a variety of factors, both genetic and environmental. Ideally, medication dosage should be calibrated for each patient, taking into account variation in metabolic rate caused by functional differences in enzymes responsible for these processes. Variants in the gene encoding cytochrome P450 (CYP) are well known to affect drug metabolism and have been the target of efforts to personalize medications in the context of several ailments. However, clinical outcomes of such personalization have often been difficult to document. Osnabrugge et al. reviewed several meta-analyses, and the primary literature cited therein, examining the association between loss-of-function variants in *CYP* and clinical efficacy of the popular antiplatelet drug clopidogrel, commonly used to treat acute coronary syndrome. All the meta-analyses within the scope of the review found substantial differences in the characteristics of study populations and primary outcome measures. However, they differed greatly in how they handled these heterogeneous study characteristics. Some ignored studies considered to introduce heterogeneity, a practice that Osnabrugge and colleagues believe is unjustified. The authors also uncovered evidence of bias in publication of small studies that showed relatively large effects. They therefore argue that the 2010 recommendation by the US Food and Drug Administration that *CYP2C19* genotyping be considered for individualized antiplatelet management is currently not sufficiently evidence-based and should be abandoned. To support their case, they point to recent large clinical assessments, such as the ARCTIC trial, that showed no benefits of *CYP2C19* genotyping. —*Karyn Hede, News Editor*

ACMG updates policy statement on release of secondary findings

see page 68



The results of a member survey conducted by the American College of Medical Genetics and Genomics (ACMG) revealed mixed opinions about what should be considered best practices for release of secondary findings (genetic variants that might be relevant for purposes of management but were not the primary targets of testing). However, contrary to ACMG recommendations released in 2013, most survey participants said they believe patients should be informed of the possibility of secondary findings during the consent process and be able to opt out of such analysis. In addition, members agreed that the ACMG should continue to maintain and update a list of medically actionable genes as a reference point for those offering clinical exome or genome sequencing. With this input from members in hand, the ACMG has published an update to its policy statement, which is available both in print and online (http://www.nature.com/gim/journal/v17/n1/full/gim2014151a.html). The update underlines the importance of obtaining written informed consent via a qualified genetics health-care professional detailing the nature of clinical genome-scale sequencing, addressing interpretive uncertainty, and explaining the inevitable generation of data not immediately medically relevant, among other issues. The guidelines suggest that patients be able to opt out of receiving the information but stress that they should be made aware of the ramifications of doing so. The ACMG is also recommending that, in the absence of clear consensus on how secondary findings should be handled when the patient is a child, parents be given the option to opt out of receiving secondary findings when such analysis is performed in their children. —*Karyn Hede, News Editor*

NEWS BRIEFS

Cat genome confirms that pet cats maintain wild streak

The first complete report of the domestic cat genome reveals that, although our pet cats harbor genetic variations that allow them to tolerate their human companions, they are still wild at heart. After comparing the genome of Cinnamon, a female Abyssinian, with others, including tiger, dog, cow, and human genomes, researchers recently reported in the *Proceedings of the National Academy of Sciences* that cats maintain much of the genomic traits of their wild counterparts, owing to lack of selective pressure to eliminate such traits after their initial domestication. The researchers did find changes in genes hypothesized to be linked to domestication syndrome, that is, behavioral changes brought on by mild neural crest cell deficits during gestation. These changes probably occurred as a result of humans having selected companion animals for docility. Indeed, investigators found changes in genes implicated in neural crest cell migration, in agreement with analyses of the genomes of other domesticated animals, including dogs. But our furry friends differ in the extent of genomic change, with dogs having many more genetic changes, probably due to their longer association with people and more human selection for physical and

NEWS BRIEFS *(continued)*

behavioral traits. Another major difference the team noted between cats and dogs was an apparent trade-off between acute scent perception in dogs and chemosensory acuity in cats, which rely on pheromone detection for social communications. The presence of white spotting provided the only clear phenotypic hallmark of domestication, with genes inducing all-white fur, white spotting, and white "gloves" showing up in the analysis. The cat reference genome is now available in the GenBank database. *—Karyn Hede, News Editor*

Canadians challenge US gene patents

A Canadian hospital, fed up with being forced to pay thousands to United States–based companies to test patients for rare genetic diseases, is challenging

ronniechua/© iStockphoto/Thinkstock

the legality of these gene patents. Court papers filed in late 2014 in the Federal Court of Canada claim that gene patents are constraining the ability of Canadian doctors to provide care to patients. The argument is that physicians should be able to test for genetic diseases without the threat of a lawsuit from patent holders. The Children's Hospital of Eastern Ontario started the legal process to force the issue of whether human genes can be patented in Canada. The legal case is based on patents for genes associated with long QT syndrome, an inherited heart-rhythm disorder that can result in sudden death. In its court filing, the hospital named as defendants the University of Utah Research Foundation, Yale University, Genzyme Genetics, and other US patent holders, in addition to the US lab that provides the pertinent test (LabCorp, in Burlington, North Carolina). The lab charges about $4,500 per test, according to the Canadian hospital, which claims that, if permitted, it could do the equivalent test in house for about half that price. The Canadian legal case seeks to create an opening to allow expanded testing for thousands of genes linked to human disease.
—Karyn Hede, News Editor

Genetics in Medicine | Mission Statement

Genetics in Medicine is a monthly journal committed to the timely publication of:

- Original reports which enhance the knowledge and practice of medical genetics
- Strategies and innovative approaches to the education of medical providers at all levels in the realm of genetics

As the official journal of the American College of Medical Genetics and Genomics (ACMG), the journal will:

- Provide a forum for discussion, debate and innovation concerning the changing and expanding role of medical genetics within the broader context of medicine
- Fulfill our responsibility to the College membership through the publication of guidelines, policy statements and other information that enhances the practice and understanding of medical genetics

Finally, as genetics becomes increasingly important in the wider medical arena, we will be an accessible and authoritative resource for the dissemination of medical genetic knowledge to providers outside of the genetics community through appropriate reviews, discussions, recommendations and guidelines.