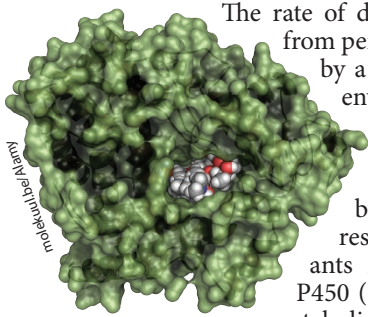


## IN THIS ISSUE

**Personalized antiplatelet therapy not justified by current evidence**

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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**

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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



Khang Ho (iStock/Hemera/Thinkstock)

## 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



Dr. Kristina Narfstrom, University of Missouri

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 domestica-

tion 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