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Warranted confusion

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Many consumers realize they don't really understand genetics after receiving direct-to-consumer test results from companies, according to a study of 23andMe and Pathway Genomics customers. Faced with detailed reports that highlight the complexity of interpreting genomic test results, consumers became less confident in their own understanding of genetics. The study results, reported in this issue, highlight the gap between what even highly educated and informed consumers think they know about genetics versus its inherent complexities. The Impact of Personal Genomics study, conducted by the PGen Study Group based at the University of Michigan, surveyed 998 customers before they purchased kits from two companies selling direct-to-consumer genetic tests and then followed up six months later. The surveys revealed that people who purchase these tests tend to be wealthy, college-educated, and overwhelmingly of non-Hispanic white ethnicity. They scored highly on baseline genetic knowledge, with the exception of one true–false question, "Most genetic disorders are caused by only a single gene," which most participants thought was true. The research team suggests that the follow-up survey revealed a reevaluation of self-knowledge and a consequent better understanding of both the customers' own limitations and the inherent complexities of the genomic tests currently being offered to the public. Few participants (20) consulted with a health-care provider before ordering the test, but those who did reported a better understanding of results, suggesting that greater involvement by health-care providers in the testing process may help consumers' confidence in interpreting results.
—Karyn Hede, News Editor

Variant interpretations inconsistent among genetic testing laboratories

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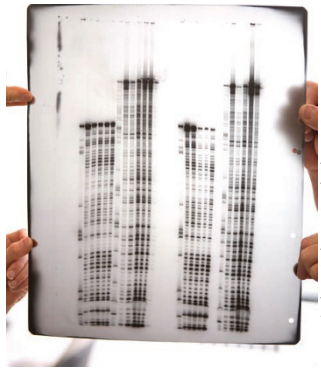

Jason Lindsey / Alamy Stock Photo

A comparison among a small sample of variant interpretations conducted by a variety of testing laboratories reveals that inconsistencies among reported results are alarmingly common. The Collagen Diagnostic Laboratory (CDL) at the University of Washington, a university-based clinical and research laboratory specializing in heritable connective-tissue disorders, studied reported results of 38 cases in which they were called in to offer a second opinion. These cases involved situations in which variant results identified a gene among those studied in the CDL. Data came from five private commercial laboratories (20 cases) and six academic laboratories (12 cases); the remaining 6 cases were from unidentified laboratories. The research team found 27 discrepant results, one-third of which were attributed to lack of access to private CDL data. However, half of the discrepant results could be attributed to lack of reference to current understanding of the biology of the investigated gene, and 19% could be attributed to lack of reference to publicly available data. The investigators concluded that laboratories are not making use of readily available public information that could improve the quality and consistency of variant interpretation and point out that data sharing among laboratories could also help minimize discrepant variant interpretations. To minimize inconsistent results, variant interpreters at different clinical genetics laboratories should be using the same interpretative tools, data sources, and variant-classification guidelines. The ACMG's recent promulgation of interpretive standards may help this situation.
—Karyn Hede, News Editor

NEWS BRIEFS

NIPT extended to small deletions and duplications—but many false positives

A research team based in China and California has used a rapid semiconductor sequencing platform to identify small chromosomal deletions and duplications in fetal DNA from a noninvasive prenatal test (NIPT) blood draw. Analyzing plasma from 1,476 pregnant women who had been identified by ultrasound as having potential fetal structural abnormalities, the new method detected 69 of 73 (94.5%) of abnormalities greater than 1 Mb in size. The women also had conventional invasive fetal DNA analysis. The report, published November 2015 in *Proceedings of the National Academy of Sciences*, also noted that the NIPT test generated 55 false positives, of which 35 were attributed to maternal chromosomal abnormalities. According to the researchers, as the cost of NIPT with semiconductor sequencing goes down, it has the potential to be less expensive (in addition to being, of course, safer) than conventional, invasive prenatal testing methods. However, implementing the

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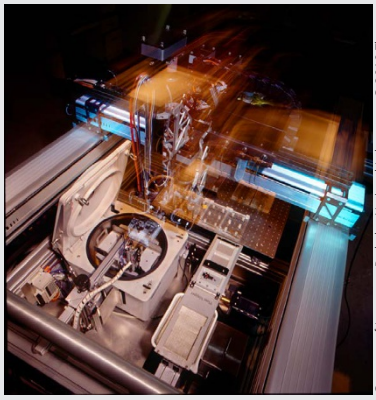
NEWS BRIEFS *(continued)*

technology could introduce a whole raft of complications, not the least of which is that, as more variations are detected, they are likely to flag chromosomal deletions or duplications of unknown clinical significance. "If our NIPT extension is put into clinical practice, great care must be taken in presenting results and providing appropriate counseling to patients," said principal investigator Kang Zhang, professor of ophthalmology and chief of ophthalmic genetics at UC San Diego School of Medicine and founding director of the school's Institute for Genomic Medicine in a statement accompanying the research article. *—Karyn Hede, News Editor*

Extreme-scale analysis produces the 8.4-minute human genome

Supercomputers at Lawrence Berkeley National Laboratories can now churn out a completely assembled human genome sequence in 8.4 minutes, raising expectations that real-time whole-genome



Courtesy of Lawrence Berkeley National Laboratory. © 2010 The Regents of the University of California, Lawrence Berkeley National Laboratory.

testing may be coming sooner than we thought. The announcement was made in November 2015 at the SC15 conference, where supercomputing insiders gather to show off their latest achievements. A research team from Berkeley Labs' Joint Genome Institute and UC–Berkeley presented HipMer, which they characterized as "the first high-quality end-to-end de novo assembler designed for extreme scale analysis." For those not well versed in high-end computing, the research team explained that the speed and efficiency of the algorithm exceed the capability of all the world's current sequencers combined. The HipMer technology, they say, could usher in a new era of genome analysis. It could, for instance, be used to rapidly identify all the species in a microbial community or to compare genetic variants in hundreds of tumor cells from a single biopsy. For now, the technology will be used by researchers interested in testing hypotheses that involve rapidly assembling multiple genomes. Because current genome-assembly programs are unable to keep pace with the flood of genomic data, the new technology may help speed analysis and break up logjams of data. The researchers note that HipMer is "adaptable and scalable," allowing it to be used in a variety of computing environments. After additional testing, the team plans to release it as publicly available open-source code. *—Karyn Hede, News Editor*