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Caution urged in interpreting NIPS microdeletion results

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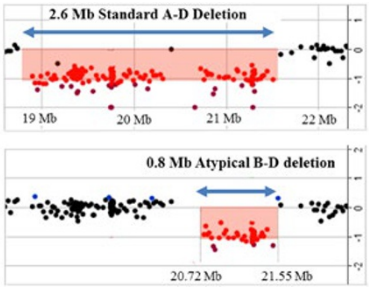

Noninvasive prenatal screening (NIPS) is often seen as a relatively low-risk screening test that can identify chromosomal abnormalities early in pregnancy. Although NIPS has established itself as a useful tool for identifying fetal trisomies, the real-world consequences of adding screening for smaller chromosomal microdeletions have not been rigorously evaluated. In this issue, Yatsenko *et al.* offer a cautionary report involving a false-positive NIPS result in the DiGeorge syndrome region (22q11.2). The report describes the case of a 40-year-old pregnant woman who underwent NIPS due to advanced maternal age. A commercially available NIPS test returned a positive result for a 22q11.2 microdeletion but did not pinpoint its exact chromosomal coordinates. The patient declined further diagnostic testing and delivered a healthy infant at 32 weeks gestation. After the birth, microarray analysis on mother and child revealed a microdeletion of unknown significance that did not include the gene associated with classic DiGeorge syndrome, a genetic defect that affects about one in 4,000 births. Because the accuracy of NIPS microdeletion detection is still unknown, the authors suggest that its commercial use is premature. However, if offered, any positive screening result should trigger further diagnostic testing of the fetus and both parents, if possible. The authors further argue that exact genomic coordinates of any abnormality should be reported. In the case described here, knowing the precise location and extent of the microdeletion would have been valuable to both the patient and the physicians charged with her care. *—Karyn Hede, News Editor*

New model shows genetic risk factors could help personalize prostate cancer screening

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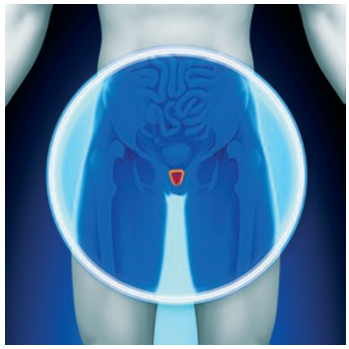

The value of screening men over 50 for prostate-specific antigen (PSA) has been thoroughly refuted in several large epidemiological studies showing that the risks of overdiagnosis and treatment outweigh the test's potential benefits. But some researchers haven't given up on the PSA screening test. In this issue, Pashayan and colleagues describe a mathematical model that combines data from several large United Kingdom–based prostate cancer trials with 66 genetic markers associated with prostate cancer risk in European populations. Dividing the data into quartiles by risk, they calculated that in the lowest-risk group 43% of screening-detected cases were likely to be overdiagnosed, while in the highest-risk group 19% were likely to be overdiagnosed. The proportion of overdiagnosed cases was 56% lower in the highest-risk group than in the lowest-risk group. They conclude that targeting screening to men at higher genetic risk could reduce the number of men likely to be overdiagnosed. However, the research is limited by assumptions made for test sensitivity and tumor behavior, which may be influenced by genetic background in ways that are not yet understood, and more study is clearly warranted before using this type of analysis clinically. Finally, while personalized screening sounds good, public reaction to recommended changes in screening frequency can be volatile, as evidenced by the controversy over proposed changes in mammography screening. *—Karyn Hede, News Editor*

NEWS BRIEFS

Hardcore gamers key to progress in crowd-sourced genomics projects

Move over, Candy Crush. Gamers and bioinformatics experts are harnessing the power of crowdsourcing to solve a genomics puzzle with real-world consequences. Dan MacLean, head of bioinformatics at the Sainsbury Laboratory in Norfolk, UK, and his collaborators devised a Facebook-based game to help align DNA sequence variants generated through a large-scale genomics project aimed at curbing ash dieback, a devastating fungal disease killing off many of Europe's ash trees. The rationale for the project is the well-known observation that human brains are often better at pattern recognition than even the best computational approaches to DNA sequence alignment. Following a media campaign, the game, Fraxinus, began in August 2013 and ran for a year, ultimately receiving over 63,000 visits from more than 25,000 unique addresses in 135 countries. Players competed to score points by producing the best sequence alignment. They matched computational alignments 78% of the time and improved on them 15% of the time, according to a

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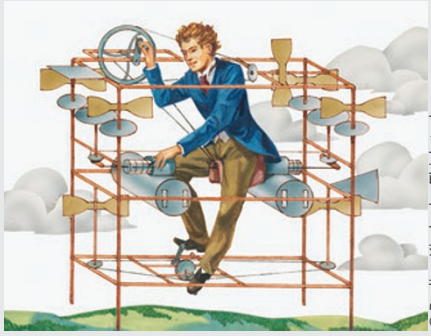
NEWS BRIEFS *(continued)*

report published in eLife in July 2015. The authors observed that while more than 7,000 people completed at least one puzzle, a tiny number—49 players—contributed half the answers. Based on their findings, the research team built a model that can be used to weigh the effort involved in setting up a citizen-science project and to determine whether such a project is plausible and worthwhile. Genomics Ninja, anyone? *—Karyn Hede, News Editor*

Peering into the genomic crystal ball

"It's tough to make predictions, especially about the future"—a great quotation, often attributed to physicist Niels Bohr, but a variant is attributed to the master of inadvertent quips, Yogi Berra. That sage advice hasn't stopped many from trying their hand at forecasting the future, and the rapidly developing field of genomics makes a good target for eager prognosticators. Recently, the journal *PLOS Biology*



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asked eight genomics experts for their thoughts on the field's next 10 years. Predictably, all thought we are in for a tsunami of data that will become more diverse and yet more integrated, thanks to advances in bioinformatics. Most see barriers between the laboratory and clinic dissolving, as genomic data is merged with other forms of clinical data. Of course, the expectation is for genomics to extend its reach into personalized medicine, but what form that will take remains nebulous. Ideas about what constitutes a health risk may change as genomic information suggests recategorizing people into health-risk groups that are now unforeseen. Still, a perhaps overly optimistic thesis that pervades these predictions suggests that more genomic information will lead to better health. A tonic, then, for genomic euphoria is provided in a perspective piece appearing in the 6 August 2015 *New England Journal of Medicine*, where Ronald Bayer and Sandro Galea offer an alternative view. Not mincing words, they suggest that we in the United States, "as a country, are far from recognizing that our collective health is shaped by factors well beyond clinical care or our genes." Indeed, the future of our collective public health may rely, the authors state, on recognizing the inequities in how health care is distributed and addressing the underlying inequities that determine who becomes sick and who dies. Thus—for the time being, and at least for most of us—our health probably depends far more critically on our zip code than our genomic code. *—Karyn Hede, News Editor*