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Planning for individualized cancer screening programs

see pages 423 and 437

We justify public health screening for cancer by estimating that the benefits of public surveillance outweigh the attendant risks, which include false-positive test results and its associated psychological stress. Public acceptance of and participation in screening programs relies on trust and perceived benefit. Genomically informed screening aims to provide an individualized risk profile that incorporates genomic risk and demographic features to influence how and when each person should be screened. In this issue, Chowdhury et al. examine the ramifications of population-based genomic risk stratification. The authors present the recommendations from a series of workshops convened in 2010 and 2011 by the Foundation for Genomics and Population Health and the University of Cambridge. Genomic information, they explain, could help triage individuals into new risk categories that include genetic risk when determining the appropriate level of cancer screening, including the possibility of earlier screening for those at highest risk and less frequent screening for those at lowest risk. The authors suggest that more personalized communication of risk information may help increase the use of existing screening methods. However, they stress that acquiring and using personal genetic information as part of a population-based screening program will inevitably result in concerns about discrimination and stigmatization.

In an accompanying Special Article, Khoury et al. suggest that our current knowledge of genetic risk for common diseases is insufficient to justify screening in most cases. In the case of colorectal cancer screening, however, they suggest that awareness of genetic risk factors may provide better risk information than family history alone. They also stress that it is unclear whether genetic risk stratification will help distinguish life-threatening cancers from milder manifestations, an ongoing concern with current screening programs. *—Karyn Hede, News Editor*

Karyotyping remains useful in our genomic realm

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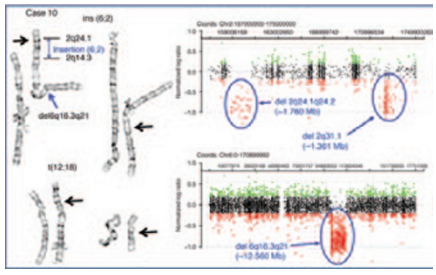
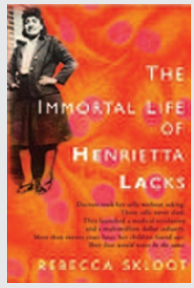


Visual inspection of chromosomes has been a mainstay of genetic diagnosis since the 1960s, when the advent of standardized staining techniques enabled routine identification of chromosomal abnormalities. The ACMG's recommendation of chromosomal microarray analysis (CMA) as a first-tier diagnostic test for congenital developmental disorders has led some to question the continuing value of classic karyotyping procedures. Bi et al.

NEWS BRIEFS

Release of Henrietta Lacks' genome causes uproar



It was only one genome, among the many thousand that have now been sequenced and released publicly. But this wasn't just any sequence; it was the sequence of Henrietta Lacks, a tobacco farmer whose ovarian cancer cells, HeLa, have launched countless research projects. A news release from the European Molecular Biology Laboratory, where the genome was recently sequenced, was greeted mostly with yawns by the media until some realized that the lab had neither sought nor received permission from Lacks' descendants to release the data. A flurry of activity on social media alerted Rebecca Skloot, author of the best-selling book *The Immortal Life of Henrietta Lacks*, who investigated the situation through discussions with researchers and the family. Her opinion piece in the *New York Times* on 23 March 2013 outlined the ethical, legal, and social issues that arise from this case and foreshadow a legal quagmire to come unless our privacy policies and legal protections are updated in parallel with our technology—and in a hurry. Skloot quotes Francis Collins, director of the National Institutes of Health, as saying, "This latest HeLa situation really shows us that our policy is lagging years and maybe decades behind the science. It's time to catch up." Skloot's essay throws out a "new round of ethical questions for science: though their consent is not (yet) required for publishing private genetic information from HeLa, should it be? Should we require consent before anyone's genome is sequenced and published? And what control should gene-sharing family members have?" It's up to the medical genetics community to help answer these pressing questions.
—Karyn Hede, News Editor

Call to "free the data" draws attention: contribute your variants!

Diagnostic molecular genetic testing requires development of databases containing rigorously validated genetic variants that have been assessed and adjudicated for their clinical implications. As large-scale whole-exome or -genome sequencing is increasingly employed, we require open, accessible variant databases that contain this vital information. But access to risk information for two of the

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provide data showing that classic chromosome analysis remains valuable as a second-tier or confirmatory technique for detecting mosaicism and fine mapping of chromosomal structural rearrangements. The authors identified 3,710 cases in which both traditional chromosome analysis and CMA were performed in a clinical setting. Chromosome analysis detected abnormalities in 295 cases (8%); CMA failed to identify the abnormalities in 10 of these cases. Retesting by CMA correctly identified the abnormalities in 4 of the 10 cases. The remaining missed diagnoses involved subtle mosaicism. For patients with normal CMA results, a full chromosome analysis may be warranted if the individual has multiple congenital anomalies that suggest a chromosomal syndrome.—*Karyn Hede, News Editor*

NEWS BRIEFS

most high-profile inherited disease genes, *BRCA1* and *BRCA2*, has been denied by Myriad Genetics, the genes' patent holder. Regardless of the US Supreme Court's ruling on the validity of gene patents, Myriad will be sitting on a potential goldmine of proprietary information. Its database detailing the breast and ovarian cancer risk conferred by variants found in myriad (pun intended) women will remain private. But now an effort to recreate that database in the public domain is drawing media attention. An article appearing in the *New York Times* on 21 April 2013 details the plan by the National Center for Biotechnology Information to launch a publicly available, open-access database called ClinVar to host deidentified genotype and phenotype information for hereditary disease gene variants, including the *BRCA* genes. The article highlights the efforts of Robert Nussbaum, of the University of California, San Francisco, to collect the data from diagnostic reports that were generated by the company and provided to clinicians and thousands of patients who underwent testing. Individuals and physicians can contribute to the effort through its website, http://www.sharingclinicalreports.org. —*Karyn Hede, News Editor*