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A model for state-based monitoring of inherited hemoglobin disorders

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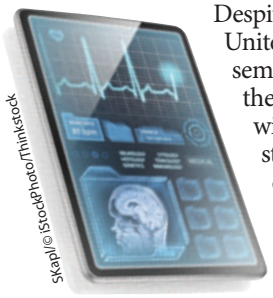

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Despite widespread newborn screening in the United States for sickle cell disease and thalassemia, there is no national system to monitor the health outcomes of individuals diagnosed with these disorders. To gain a better understanding of prevalence and treatment outcomes, the National Institutes of Health and the Centers for Disease Control and Prevention collaborated on a pilot surveillance system in six states, beginning in 2004. The Registry and Surveillance System for Hemoglobinopathies (RuSH) identified individuals using multiple data sources, including newborn screening records, emergency room records, and Medicaid claims. Researchers collected demographic data, clinical characteristics, and health care–utilization records. Although the program was designed to produce a standardized system, difficulties with access to records in some states made a standardized approach untenable. But it did become clear that creating a comprehensive picture required combining data from many sources because information for individuals found through one data source was not present in others. In addition, the various sources contained different types of information. The research team concluded that combining all these data yielded a more comprehensive picture of the number of individuals living with hemoglobinopathies, as well as how and where they receive health care. A follow-up project—the Public Health Research Epidemiology and Surveillance for Hemoglobinopathies (PHRESH), now being conducted in two of the RuSH states (California and Georgia)—is expected to validate and refine the data collected in RuSH. *—Karyn Hede, News Editor*

Detection of copy-number variants and point mutations using only sequence data

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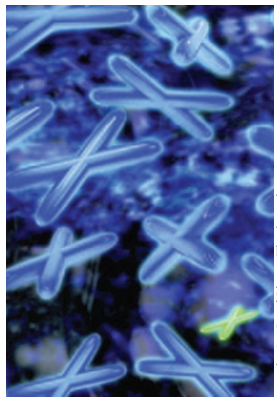

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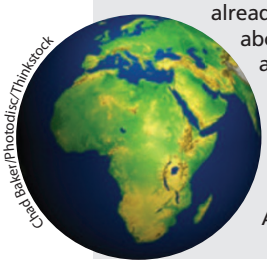
Copy-number variants (CNVs)—structural changes that result in deletion or duplication of chromosomal segments—are a significant contributor to inherited genetic disease. Currently, clinical testing for CNVs involves exon–targeted array comparative genomic hybridization or other methods involving stepwise probing of genomic regions of interest. But molecular diagnosis of human genetic diseases in clinical settings is rapidly moving toward massively parallel sequencing (MPS) technology. The ability to identify both single-nucleotide alterations and larger deletions and duplications using the same technology would greatly simplify and streamline the clinical workflow. Now, a team from Baylor College of Medicine, Houston, Texas, reports that it has taken a step in that direction using a method that analyzes copy number by comparing the number of sequencing reads of each exon of interest. Using previously collected clinical samples, the investigators correctly identified 11 samples with deletions. However, identification of duplications proved more problematic, with high false-positive rates. Similar to previous reports using sequence data, false-positive findings typically arose from areas of highly repetitive GC sequences. The authors concluded that, with further refinements to the methodology, point mutations and exonic deletions can be detected reliably using MPS. *—Karyn Hede, News Editor*

NEWS BRIEFS

African genomics study may aid understanding of disease susceptibility



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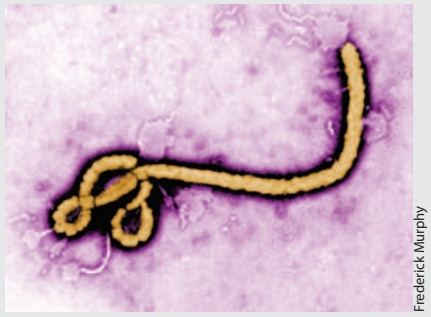
The recently completed genomic mapping of populations in sub-Saharan Africa is already providing information about population expansion and movement among ethnic subgroups. For instance, the study found evidence of reintroduction of Europeans or Middle Easterners into Africa around 9,000 years ago. But understanding population movements was not the primary objective of the study, published in *Nature* in December 2014. The research team, headquartered at the Wellcome Trust Sanger Institute, Hinxton, UK, explored how to determine how genetic variation correlates with susceptibility to a variety of diseases and infectious agents. Researchers from the African Genome Variation Project collected genetic information from more than 1,800 people, including 320 whole-genome sequences from seven populations in sub-Saharan Africa. Doctors and researchers in Ethiopia, The Gambia, Ghana, Kenya, Nigeria, South Africa, and Uganda participated. After analyzing the data, they pinpointed 30 million genetic variants, including many that had not previously been identified. Several loci appeared to be associated with infectious disease susceptibility and severity. For example, the study flagged not only the well-known sickle cell locus related to malaria but new signals for genes potentially under selection in malaria endemic regions. Genes associated with Lassa fever included the already known *LARGE* gene as well as new candidates associated with viral entry and immune response. The results also suggest that existing reference panels are inadequately representing some African populations. The authors note that cur-

NEWS BRIEFS *(continued)*

rent and planned deep sequencing across an even broader swath of populations in Africa will soon provide a comprehensive resource for medical genomic studies in Africa. —*Karyn Hede, News Editor*

Niemann–Pick type C gene may hold key to treating Ebola

An exceedingly rare genetic defect is providing insight into what may be one of the most dreaded infectious diseases: the Ebola virus. It turns out that the virus latches onto the protein that is nonfunctional in patients with Niemann–Pick type C, a neurodegenerative condition affecting about 500 people worldwide. The Niemann–Pick CI (NPC1) protein is involved in transporting cholesterol within



Frederick Murphy

cells. But it is also a target that helps Ebola and HIV enter human cells. Without a functional copy of this protein, patients suffering from the deadly Niemann–Pick type C are, ironically, immune to Ebola and HIV. With the recent Ebola outbreak, more attention has been focused on related research, including the work of Kartik Chandran, of Albert Einstein College of Medicine, Bronx, NY. To better understand how the virus behaves when NPC1 is missing, Chandran is collaborating with families such as the Hempels, of Reno, Nevada, who have twin daughters born with the disease. Chandran and his colleagues have tried without success to infect the girls' cells with Ebola. Studies in mice with only one functioning copy of the gene indicate that heterozygosity may also offer some protection from dying of the disease. In a CBS news report, Chandran speculated that a drug that blocks the virus from binding to the protein may be useful in treating Ebola. The research team is seeking a small-molecule drug that would block the *NPC1* gene temporarily, just long enough to halt the virus in its tracks.
—*Karyn Hede, News Editor*