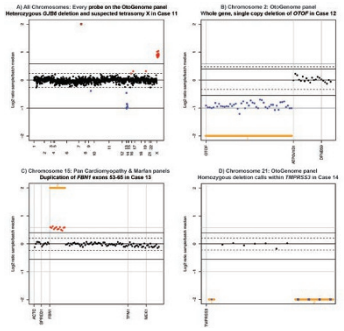
IN THIS ISSUE

Automated assistance with copy-number variant calls

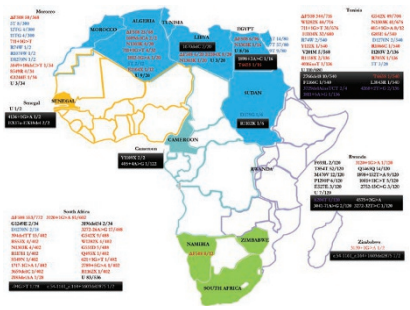
see page 712



Software to assist clinical genomic laboratories in interpretation of complex diagnostic results is becoming essential as the volume and pace of testing continue to accelerate. Here, investigators from the Laboratory for Molecular Medicine, Partners HealthCare Personalized Medicine, Boston, report they have developed a software program to detect and visualize germ-line copy-number variants (CNVs), which can then be confirmed by a trained technician. The open-source software, called VisCap, and accompanying training documents are freely available at http://www.github.com/pughlab/viscap. Designed for use by clinical laboratories, the software allows the setting of laboratory-defined thresholds and standardized procedures. The developers validated the product in their own clinical laboratory by using the tool to conduct CNV analysis on more than 4,000 patients. In addition to data normalization and identification of candidate CNVs, the software provides visualization tools to facilitate quality control through manual review of results. As part of their validation process, trained technicians blinded to results scored VisCap plots for 27 candidate CNVs as either true-positive or false-positive calls. All four technicians correctly identified all 10 verified CNVs. But two of four technicians flagged what were false positives for follow-up, highlighting the need for training and experienced review of data. *—Karyn Hede, News Editor*

Better understanding of cystic fibrosis needed in Africa

see page 653



Cystic fibrosis (CF) is commonly thought of as a disease affecting primarily Caucasians, but of course it also occurs in people of a wide variety of other ethnic heritages. Yet, although mutations leading to CF are distributed globally, in many places a detailed understanding of the disease's incidence and molecular epidemiology is absent. In this issue, Stewart and Pepper, of the University of Pretoria, South Africa, review the literature on molecular analysis of CF in Africa. The disease has been recognized among Africans only since the late 1960s, and the extent of underlying genetic variants, particularly in non-Caucasian populations, remains unknown. Therefore, the use of a standard genetic test for diagnosis of CF would not be practical or realistic in Africa. Developing an effective diagnostic test, the authors point out, would require sequencing the entire *CFTR* gene in people suspected of having CF and using aggregate data to identify the prevalence of each variant. To provide a better understanding of the current state of knowledge about CF in Africa, the team summarizes mutational analysis in patients suspected to have CF reported from 12 of the 54 African states. Of the mutations reported, 39 are known to cause CF, others are of uncertain significance, and 21 are unique to Africa. The authors propose a systematic investigation of the nature and extent of the disease to ensure that "the public health needs of African CF patients—both those in Africa and those of African descent living elsewhere—are met." *—Karyn Hede, News Editor*

NEWS BRIEFS

Woman in famous Wyeth painting suffered from genetic disorder

Its gripping imagery has captivated art lovers for decades, but Andrew Wyeth's almost universally recognizable painting *Christina's World* still has a story to tell. The painting's subject, Wyeth's friend and neighbor Christina Olson, suffered from a progressive neurodegenerative disorder that, although undiagnosed, had been attributed to the effects of polio. Now a modern medical investigation suggests that she actually had a form of Charcot-Marie-Tooth disease (CMT), which would explain the progressive difficulty with movement that eventually made her unable to walk or use her hands. After closely examining the evidence pertaining to her condition—including close scrutiny of the painting itself, which was executed with photorealistic precision—Marc Patterson, a professor of neurology, pediatrics, and medical genetics at the Mayo Clinic in Rochester, Minnesota, made the diagnosis of early-onset CMT. He presented his findings at the 23nd annual Historical Clinicopathological Conference, held May 2016 at the University of Maryland School of Medicine. "This was a fascinating case," Patterson stated in a news release issued by the meeting organizers. "This painting has long been a favorite of mine, and the question of Christina's ailment was an intriguing medical mystery. I think her case best fits the profile of this disease." *—Karyn Hede, News Editor*

NEWS BRIEFS *(continued)*

New tool for sifting functional genomics data

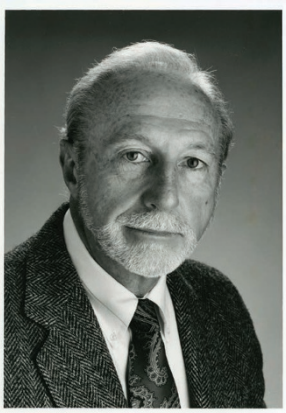
A new publicly available tool is designed to help investigators understand the functional significance of genomic data. University of California San Diego bioengineers created what they are calling the first online search engine for functional genomics data. GeNemo (http://www.genemo.org) allows users to input any complete or partial functional genomic data set, such as a binding intensity file, and the algorithm will search online functional genomic data sets, including the entire collection of ENCODE and mouse ENCODE data sets, for matching pattern in functional genomic regions. GeNemo reports matches ranging from 100 bases

Colin Cuthbert/©Getty Images

to 100,000 bases that share patterns such as binding, modification, and accessibility, according to Xiaoyi Cao, one of the developers. The tool addresses the problem of matching functional outcomes, which are stored as genome-wide intensities (WIG/bigWig files) or functional genomic regions (peak/BED files), with the results of high-throughput DNA sequencing. It can search genome-wide distributions of transcription factor binding, epigenetic modifications, regulatory regions, and other functional outcomes. "I am excited to see how different research teams from around the world use this powerful new tool to make better use of the massive amounts of functional genomic data that is being generated every day," said Sheng Zhong, the lead author of the *Nucleic Acids Research* article that announced the new search engine.
—Karyn Hede, News Editor

IN MEMORIAM

R. Neil Schimke, MD (1935–2016)



Robert Neil Schimke was a professor of internal medicine and pediatrics at the University of Kansas Medical Center. His dual expertise in clinical genetics and endocrinology provided unique insights in more than 180 publications on hereditary cancer, birth defects, endocrinology, heart disease, kidney disease, connective-tissue conditions, and developmental delay. An early disciple of Victor McKusick, Neil excelled in the art of clinical delineation and sorting out genetic heterogeneity long before the relevant genes were discovered, for example, delineating MEN 2B and distinguishing Marfan syndrome from homocystinuria in the late 1960s.

Dr. Neil Schimke wrote some of the earliest books on clinical genetics, endocrinology, and genetic disorders of human sexual development, including *Genetic Disorders of the Endocrine Glands* (coauthored with David Rimoin, 1971), and served as editor of the endocrinology section of the *Birth Defects Compendium*. He also wrote book chapters on thyroid diseases, metabolic genetic conditions, and kidney disorders.

Demonstrating early recognition of the role of genetics in cancer, *Genetics and Cancer in Man* was written during his 1977 sabbatical in the Department of Human Genetics, University of Edinburgh, under Alan Emery. This book highlighted individual and family characteristics that identify hereditary cancer syndromes. Another book, *Clinical Genetics* (1979), coauthored with Laird Jackson, was among the core texts used by geneticists, genetic counselors, and laboratory geneticists hoping to pass the first American Board of Medical Genetics exam.

An early leader in the field, Neil was elected to the board of directors of the American Society of Human Genetics and the American Board of Medical Genetics. He was also an editor of internal medicine, endocrinology, and genetics journals and a member of the review committee of the National Cancer Institute.

His longstanding expertise and von Hippel-Lindau profile in GeneReviews.org grew out of early collaborations with colleagues, all contributing to mapping the VHL gene.

Dr. Schimke's long, distinguished career was, and will continue to be, an inspiration to those of us who spend their lives in the field of Medical Genetics.—*Debra Collins and William Horton*