IN THIS ISSUE

Phenotype analysis software helps narrow possible genetic diagnoses

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While exome sequencing has shown its value in the clinic relative to candidate gene panel sequencing, yields remain stubbornly low, at slightly less than half of evaluated cases. Overlap of clinical signs, such as in intellectual disability, as well as the sheer volume of disorders, contribute to the diagnostic complexity. The analytic challenge lends itself well to the development of bioinformatics tools, and several software programs that aim to assist diagnostic accuracy and overall yield are now in use. In this issue, Thuriot et al. report their experience with PhenoVar, a software tool they developed to compare gene–phenotype and phenotype–disease correlations and to prioritize potential disease variants. The results include cases accrued from one Canadian health center over three years, from 2013 to 2016. The research team did not perform a systematic comparison of available tools, but compared their tool with conventional manual analysis of variants. Patients with suspected genetic disorders of unknown origin underwent exome analysis in addition to conventional analysis. Among 51 patients studied, 18 diagnoses were obtained using conventional methods. Use of PhenoVar independently identified 17 of the 18 diagnoses. The software proved most valuable in narrowing the list of potential diagnoses that needed to be individually reviewed by a clinical geneticist. The team reports that the number of potential diagnoses per patient fell to a mean of 15 (range 1–26) from 34 (range 26–45). The time spent per patient dropped to roughly 15 minutes compared with 90 minutes per patient for variant analysis and review of candidate conditions. Given the time efficiencies gained, such tools may soon gain routine use in clinical practice. *—Karyn Hede, News Editor*

Cost-effective exome sequencing can impact clinical practice in China

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A model program to increase access to genetic testing in China has demonstrated a large impact on patient management. The finding offers a potential model for increasing access while expanding physician awareness of genetic testing in patient management. Currently, China lacks trained medical genetics professionals and the high cost of testing has created a wide disparity in access. The few medical geneticists practicing in China were mainly trained abroad. Genetic counseling as a profession does not exist in China, and follow-up genetic testing for suspected inherited disorders does not exist in routine medical practice. In a report detailed in this issue, a group of academic medical geneticists practicing in urban settings evaluated the clinical utility of a lower-cost solution to expensive exome sequencing. The research team offered proband-only medical exome sequencing to ordering physicians who lacked the resources and training for the diagnostic task. Over a year and a half, from April 2015 to December 2016, the geneticists took 1323 referrals at Shanghai Children's Medical Center. The overall diagnostic rate for this unselected patient population was 28.8%. Skin, kidney, skeletal, gastroenteric, and endocrine diseases, as well as metabolic disorders and multiple malformation, comprised the range of diagnoses. As a result of these diagnoses, patients received genetic counseling, referral for systemic evaluation, and new treatment or change of treatment. After receiving a molecular diagnosis, 28% (46/164) of the patients had physical examinations focusing on various organs or systems, and 45.1% (74) of patients' clinical management changed based on the molecular findings. The study shows that nations underresourced in clinical genetics professionals can offer genetic testing to larger numbers of patients through innovative use of existing technology. *—Karyn Hede, News Editor*

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