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Pattern recognition produces more accurate disease detection

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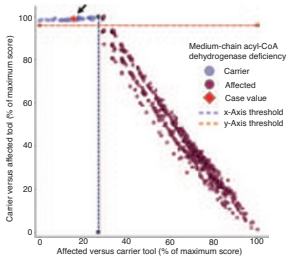

Pattern-recognition software has already proven its worth in the analysis of large data sets, ranging from remote geographic sensing to patterns of brain activation. Now it has been successfully applied to newborn screening. Using data on inborn errors of metabolism collected from newborns at 154 sites worldwide, the Regional Genetics and Newborn Screening Collaborative has developed and tested an analytic tool that reduces false-positive test results. The resulting software (available at http://region4genetics.org/msms_data_project/priority1) converts raw mass spectroscopy data into individual profiles and generates a composite score based on the overlap between values in the normal range versus the disease range. The pattern-recognition software differs from traditional statistical analysis in that an abnormal result is not defined by a deviation from normal but instead by an established analyte disease range set by a worldwide database of more than 12,000 patients affected with 60 metabolic disorders and 644 heterozygote carriers for 12 conditions. Retrospective evaluation of Minnesota cases suggests that use of the method would have halved the number of false-positives caused by carrier status for fatty-acid oxidation disorders and likewise would have prevented 88% of known false-negative events. The developers report that the tool can be applied to any clinical data set with sufficient data defining normal and disease populations.

Calls for comparative-effectiveness research in cancer genomics

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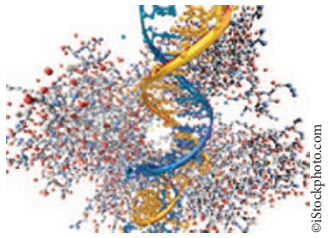
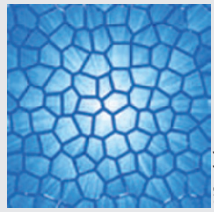


The methods used to generate and review medical evidence are rapidly evolving. Clinical trials structured to meet the requirements of the US Food and Drug Administration are becoming only the first step to ensuring clinical utility. A broad movement is afoot to use comparative-effectiveness research (CER) to contain health-care costs while maintaining (and potentially improving) quality. These patient-centric methods include not only comparative observational and randomized trials but also mathematical and economic modeling and even first-person reports about how medical treatments work in the real world. These methods, structured to extract valuable information from the volumes of raw data generated within the medical research enterprise, are now being applied in cancer genomics, as reported in the review by Goddard et al. The authors describe recent studies that examine issues such as whether single-nucleotide polymorphism testing adds to the predictive value of breast cancer risk screens and whether genotype testing to assist treatment decisions leads to better outcomes for patients. The authors argue that using CER methods in cancer genomics offers the potential for improving the synthesis of evidence from multiple sources and ultimately better informing clinical guidelines.

NEWS BRIEFS

Mosaicism linked to increased cancer risk



The role of chromosomal structural abnormalities in the development of cancer has been at the center of a chicken-or-the-egg controversy for some time. Cancer cells often contain structural abnormalities, but it has been unclear whether (and which) chromosomal defects come first or are part of the oncogenic process. Now, two groups of investigators, led by National Cancer Institute (NCI) and the University of Washington, have independently concluded that older people harboring mosaic cells are at higher risk for some malignancies, including several types of hematologic cancers such as leukemias and lymphomas. The studies, published together online in *Nature Genetics* on 6 May 2012, provide the first large, systematic examination of genetic mosaicism in healthy populations. The authors found mosaic abnormalities most frequently in people with solid tumors (0.97% vs. 0.74% in cancer-free individuals). They studied blood samples from 50,000 participants per study, including more than 30,000 cancer patients in the NCI study. The number of people identified with genetic mosaicism was small (404 of the participants), and most of them were more than 50 years old. These individuals faced a 10 times greater risk of developing a blood cancer than those without genetic mosaicism, according to the retrospective analysis.

Don't like meat? It might be genetic

People who say that pork tastes bad may be more sensitive to androstenone, a hormone produced by boars that is present in some meat. A recent study, conducted in Norway and published in the May issue of *PLoS ONE*, reported that people who have two copies of the human odor receptor gene *OR7D4* said that pork with more androstenone tasted pungent or "urine-like" as compared with heterozygous participants carrying a single-nucleotide polymorphism variant conferring two amino acid substitutions. Although the sample size was small, with 23 participants, the findings have immediate implications because Norway is considering a ban on castrating boars, which would increase the amount of androstenone in meat. More broadly, research on the role of genes in taste is particularly interesting in

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light of the potential impact on nutrition and human health. A larger study comparing African populations recently showed that the gene responsible for conferring a bitter taste to broccoli and other cruciferous vegetables is uniform across Africa and is millions of years old, predating modern humans. That study, published 29 November 2011 in *Molecular Biology and Evolution*, also revealed that differences in local diets across the continent did not seem to have an effect on evolution of the gene, suggesting its importance in other aspects of human health.