Genome Medicine

MEETING REPORT

Diverse perspectives on the current state of genomic medicine: has the revolution begun?

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Abstract

A report on the Future of Genomic Medicine IV meeting held in La Jolla, California, USA, 3-4 March 2011.

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Scripps Translational Science Institute (STSI, La Jolla, USA) hosted its 4th 'Future of Genomic Medicine' meeting, to promote the transformation of medicine using genomics. The conference focused on recent advances in whole genome and exome sequencing, gene expression tests for routine medical practice, and consumer genomics. Clinically relevant genomic advances in cancer, diabetes and heart disease were discussed. 'Views from the Outside' sessions featured journalists, entrepreneurs and public figures presenting their perspectives on genomic medicine. The speakers provided evidence that a revolution in genomic medicine is underway and involves not only medical doctors and scientists, but also those outside of the traditional scientific community. Here, we summarize some of the highlights of the medical advances and social implications discussed at this extraordinary meeting.

Advances in genomic medicine are already at the bedside

Genetic diagnostic tests, including whole genome sequencing, are already improving patient care. Gene expression profiling in peripheral blood constitutes the basis for an FDA-approved, cost-effective heart transplant rejection risk test. Matthew Price (Scripps Clinic, USA) described the use of the rapid point of care *CYP2C19* genotyping test to identify patients with cardiac stents who will benefit from clopidogrel, and the use of gene expression signatures such as Corus™ CAD (CardioDX®, Palo Alto, CA, USA) to detect coronary artery disease (CAD). Along the same lines, oncology experts described gene-profiling-based diagnostic and prognostic tests such as MammaPrint® (Agendia, Amsterdam, The Netherlands), Pathwork® Tissue of Origin (Pathwork Diagnostics, Redwood City, CA, USA), and Oncotype DX® (Genomic Health, Inc., Redwood City, CA, USA). Steven Shak (Genomic Health, Inc.), a developer of Oncotype DX®, pointed to a road map for developing similar tests by first identifying a clear clinical dilemma, and then designing a multistep, multistudy approach to develop the assay. Howard Jacob (Children's Hospital of Wisconsin, USA), presented the case of Nicholas Volker, a child with a devastating gastrointestinal disease that was a diagnostic mystery until his physician requested whole exome sequencing, which led to the identification of an unsuspected gene variant associated with inflammation and hematologic malignancies, pointing the way to a life-saving bone marrow transplant.

Tumor sequencing enables better understanding and treatment of cancer

Many cancer-related genes have been identified in large-scale sequencing projects. Some of these, such as *B-RAF* and *K-RAS* mutations, now provide individualized prognostic information. Recent data support the stance that personalized tumor biomarkers can be used to monitor tumor progression, and early genomic changes may be detectable even before cancer develops. Elaine Mardis (Washington University, USA), using next-generation whole genome sequencing of tumors, has identified similarities, yet many differences, between primary tumors and metastases at different sites, suggesting separate clonal evolution. Similarly, Samuel Levy (STSI, USA) talked about the great value of exome sequencing and the importance of accounting for tumor heterogeneity; Levy presented preliminary data from a tumor mapping project in which biopsies were taken from multiple different locations in a single tumor and nearby tissue, and sequences were determined. Daniel

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von Hoff (T-Gen, USA) presented cases of patients treated successfully at his institution with targeted therapies that were selected based on individual tumor sequencing.

Improved risk prediction and management of diabetes and heart disease

Recent advances have been shown to be cost-effective and clinically useful in the treatment of diabetes and heart disease. After identifying 16 new loci contributing to the pathogenesis of type 1 diabetes (T1D), the T1D Genetic Consortium is transitioning from genome-wide association studies to gene discovery, and following strategies such as dense SNP mapping using the ImmunoChip, targeted sequencing studies in regions and exons of interest, and functional evaluation of genes associated with T1D. Advances in the pharmacogenomics of type 2 diabetes include the identification of *TCFL2* variants as predictors of poor response to sulfonylurea treatment. Philippe Froguel (Imperial College, UK) discussed the cost-effectiveness of diagnostic whole genome sequencing and the improvements of quality of life for patients with monogenic forms of diabetes who can stop insulin treatment when correctly diagnosed by genomic testing. Stimulating advances in risk prediction have also been made in the field of cardiology: by adding 9p21 and another seven genetic risk factors to traditional CAD risk factor models, the deCODE MI™ (deCODE Genetics, Iceland) test demonstrated increased sensitivity to predict myocardial infarction.

The public perception of medical genomics reveals promises and pitfalls

The 'Views from the Outside' session provided a variety of perspectives on the impact of genomic medicine. Keynote speaker Juan Enriquez (Excel Venture Management, USA) believes that the genomic medicine biotechnology industry has the potential to foster economic growth, similar to the information technology industry. However, as an investor, he expressed concern about the elevating costs and overly stringent standards for drug development, as these may limit investor participation. In the field of direct-to-consumer testing, Cinnamon Bloss (STSI, USA) presented the results of her study of behavioral consequences of direct-to-consumer genome-wide profiling, where no additional anxiety was detected after learning genetic risk information for multiple diseases. Melanie Swan (DIYGenomics, USA) revealed a truly revolutionary enterprise where consumers, armed with their own genotyping information from commercial platforms, design and conduct their research studies using her web-based DIYGenomics organization. This probably reflects what Eric Topol (Director, STSI, USA) referred to as the 'democratization of American medicine', as the explosion in technologies and social networking result in a transformation in healthcare and medical research. Amy Harmon (The New York Times, USA) presented a cautionary tale about a clinical trial of an agent targeting *B-RAF* mutated melanoma. Despite unprecedented success and evidence of response to this new targeted agent in nearly all patients in initial studies, a randomized clinical trial was initiated, in which half the patients were assigned to the recognized standard treatment, known to have poor efficacy, and were not given the opportunity to try the new treatment option. Harmon made a case for the need for more open conversations about research and its ethical implications with the public and with patients. She encouraged the use of open-access publications.

The bright future of genomic medicine

The current price of sequencing a whole single genome was estimated to be approximately US$30,000, but this figure appears to be dropping rapidly. Several speakers predicted that the cost of analyzing the ever-expanding amount of genomic data and presenting it in a meaningful format to physicians and patients is likely to become greater than the cost of sequencing itself. Clearly, genomic medicine is already benefiting many patients and our evolving tools are rapidly expanding its reach. Clinical applications in cancer, diabetes, heart disease and other conditions are improving patient care and our ongoing discoveries should facilitate further translational advances. At the same time, investigators need to be attentive to the needs of patients and communities, and improve communication with physicians and other individuals outside of our field as we move forward.

Abbreviations

CAD, coronary artery disease; SNP, single nucleotide polymorphism; T1D, type 1 diabetes.

Competing interests

DM and LU-B declare that they have no competing interests.

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