SORS: Interpreting newborn genomes

Objectives

Abstract:

This presentation will cover three projects in interpretation of human genomic variation.

We have developed an analysis protocol whose distinctive features enabled solving clinical cases. Applied to exomes from newborn patients with undiagnosed primary immune disorders, it helped guide appropriate treatment, family genetic counseling, and avoidance of diagnostic odyssey.

This inspired a project that explores the feasibility of sequencing to augment or supersede mass spectrometry for pervasive public health newborn screening. We sequenced exomes from de-identified dried blood spots of nearly all newborns affected with any metabolic disorder screened by tandem mass-spectroscopy (MS/MS) in California from 2006 to 2013 (around 1300 out of around 4.45 million screened). Our preliminary analysis indicates that several affected individuals lack any obviously damaging mutations in genes responsible for their metabolic disorders. We also found some cases where exomes confidently implicated a disorder different from the original diagnosis by the metabolic center clinician, suggesting that sequencing information would have been valuable for proper clinical diagnoses in some cases. While still not sufficiently specific to used alone for screening of all inborn errors of metabolism, exomes could facilitate timely and more precise clinical resolution for some disorders.

To conclude, I will briefly present results from The Critical Assessment of Genome Interpretation (CAGI, \'k?-j?\), a community experiment to objectively assess computational methods for predicting the phenotypic impacts of genomic variation.

Short bio:

California, San Francisco. As an undergraduate he studied in Walter Gilbert's laboratory at Harvard College. He received his M.Phil from the Department of Biochemistry at Cambridge University, and obtained a Ph.D. from the MRC Laboratory of Molecular Biology and Cambridge where he studied with Cyrus Chothia. After graduation Brenner had a brief fellowship at the Japan National Institute of Bioscience, followed by postdoctoral research supervised by Michael Levitt at Stanford University School of Medicine.

Brenner's research is primarily in the area of computational genomics, covering topics in protein structure, RNA regulation, function prediction, metagenomics, and individual genome interpretation. He is founding chair of the Computational Biology graduate program at Berkeley. He is currently a director of the Human Genome Variation Society, and is a founding editor of PLoS Computational Biology. He has served two terms as a director of the ISCB and was a founding director of the Open Bioinformatics Foundation. His recognitions including being a Miller Professor, a Sloan Research Fellow, a Searle Scholar, an AAAS Fellow, and named the recipient of ISCB's Overton Prize.

Speakers

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