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BabySeq, MedSeq Projects Reveal How Many People Carry Genetic Risk Variants for Rare Diseases

More information on newborn and adult sequencing studies unveiled at American Society for Human Genetics Meeting

Boston, MA — Two projects in which healthy individuals have had their genomes sequenced have revealed that searching for unanticipated genetic results in newborns and adults can unearth far more variants associated with diseases than previously thought, and, importantly, reveal previously unrecognized but related clinical features of genetic conditions. Results from both the BabySeq Project, led by investigators at Brigham and Women's Hospital and Boston Children's Hospital, and the MedSeq Project, led by investigators at the Brigham, are being presented together at the 2018 American Society for Human Genetics meeting.

"These results are unexpected and exciting, suggesting that if we examine enough well-established, disease-associated genes, we will unearth monogenic risk variants in more than 10 percent of purportedly healthy individuals," said Robert Green, MD, MPH, a principal investigator on both projects and a clinical geneticist at BWH. "And if on the basis of these genetic clues, we carefully examine those individuals, we find that a quarter of them have previously unrecognized features of underlying disease – something that we might never have realized had we not performed genetic sequencing."

In the MedSeq and BabySeq Projects, Green and colleagues analyzed approximately 5,000 disease-associated genes to identify monogenic disease risk variants – mutations associated with diseases thought to be caused by variants in a single gene. Examples of such monogenic diseases include hereditary cancer syndromes, hereditary cardiac syndromes and metabolic disorders that can lead to life-threatening complications.

Genome or exome sequencing was performed on a total of 269 individuals. Unanticipated risk variants were found in 16 of 110 adults (14.5 percent) and 18 of 159 infants (11.3 percent).

When individuals were closely examined in the clinic, the team discovered clinical features suggestive of a previously unrecognized genetic condition in four of the adult cases and four of the newborn cases, including three cases with highly effective interventions. An additional newborn case provided an unsuspected molecular diagnosis for an observed clinical condition that had not been previously considered genetic.

The MedSeq and BabySeq Projects, both funded by the National Institutes of Health, explore the ramifications of using genome sequencing in apparently healthy adults and infants. Both are randomized clinical trials designed to explore the medical, behavioral and economic impacts of incorporating genome sequencing into everyday medicine.

In addition to findings related to these unrecognized phenotypes, members of Genomes2People Research Program will also be presenting additional results at the meeting including abstracts on:

- Returning Unanticipated Genomic Results in a Hospital-Based Research Biobank **(embargoed until Oct. 16 at 10 p.m. ET)**
- The Impact of Newborn Genomic Sequencing on Families: Findings from the BabySeq Project **(embargoed until Oct. 17 at 8:15 p.m. ET)**
- Analysis of Actionable Adult-Onset Disease Risk Findings in Newborn Genomic Sequencing (**embargoed until Oct. 19 at 5 p.m. ET)**
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For more details, please visit http://www.ashg.org/2018meeting/ or https://www.genomes2people.org/presentations/american-society-of-human-genetics-ashg-annual-meeting-2018/

Funding for the MedSeq and BabySeq Projects were provided by NIH grants U01-HG006500 and U19-HD077671, respectively. Green has received compensation for advising the following companies: AIA, Applied Therapeutics, Helix, Ohana, OptraHealth, Prudential and Veritas; and is co-founder and advisor to Genome Medical, Inc, a technology and services company providing genetics expertise to patients, providers, employers and care systems.

The Genomes2People Research Program at Brigham and Women's Hospital, the Broad Institute and Harvard Medical School is directed by Robert C. Green, MD, MPH and conducts empirical research in translational genomics and health outcomes. NIH-funded research within G2P seeks to understand the medical, behavioral and economic impact of using genetic risk information to inform future standards for implementing genomic medicine. The BabySeq Project is recruiting families of both healthy and sick newborns into a randomized clinical trial where half will have their baby's genome sequenced. The MilSeq Project is examining sequencing within the military. The PeopleSeq Consortium is tracking the medical, behavioral and economic outcomes of health early adopters who have been sequenced through a number of commercial and research protocols. The MedSeq Project has conducted the first randomized clinical trial to measure the impact of whole genome sequencing on the practice of

medicine. REVEAL and REVEAL-SCAN studies have conducted several randomized clinical trials examining the impact of disclosing genetic risk for a frightening disease. And the Impact of Personal Genomics (PGen) Study examined the impact of direct-to-consumer genetic testing on over 1000 consumers of two different companies. Visit genomes2people.org for more and follow us on Twitter @Genomes2People.

Brigham and Women's Hospital (BWH) is a 793-bed nonprofit teaching affiliate of Harvard Medical School and a founding member of Partners HealthCare. BWH has more than 4.2 million annual patient visits and nearly 46,000 inpatient stays, is the largest birthing center in Massachusetts and employs nearly 16,000 people. The Brigham's medical preeminence dates back to 1832, and today that rich history in clinical care is coupled with its national leadership in patient care, quality improvement and patient safety initiatives, and its dedication to research, innovation, community engagement and educating and training the next generation of health care professionals. Through investigation and discovery conducted at its Brigham Research Institute (BRI), BWH is an international leader in basic, clinical and translational research on human diseases, more than 3,000 researchers, including physician-investigators and renowned biomedical scientists and faculty supported by nearly $666 million in funding. For the last 25 years, BWH ranked second in research funding from the National Institutes of Health (NIH) among independent hospitals. BWH is also home to major landmark epidemiologic population studies, including the Nurses' and Physicians' Health Studies and the Women's Health Initiative as well as the TIMI Study Group, one of the premier cardiovascular clinical trials groups. For more information, resources and to follow us on social media, please visit BWH's online newsroom.

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