Future Opportunities for Genome Sequencing and Beyond

Recommendations on Clinical Sequencing at Scale
NHGRI Workshop, July 28-29, 2014

Carolyn M. Hutter, PhD
Integrating Genomic Sequencing into Clinical Care: CSER and Beyond
September 28, 2015
Charting genome sequencing's future: NHGRI workshop offers potential paths to discovery and the clinic

By Steven Benowitz
Associate Director of Communications, Extramural Research Program

On July 28-29, 2014, the National Human Genome Research Institute (NHGRI) convened geneticists, biologists, clinicians, bioinformatics specialists and others to provide expert advice on the future of its flagship Genome Sequencing Program (GSP).

The two-day meeting, titled, Future Opportunities for Genome Sequencing and Beyond: A Planning workshop for the National Human Genome Research Institute, was the third formal review of the GSP, the previous discussions taking place in 2005 and 2009. After the last review, new core programs were added, including efforts to find causes of rare diseases and move genome sequence information into the clinic. In addition to the long-established Large-Scale Sequencing and Analysis Center (LSAC) program, the GSP now includes the Centers for Mendelian Genomics program, the Clinical Sequencing Exploratory Research (CSER) program and the Genome Sequencing Informatics Tools (GS-IT) program.

NHGRI should continue its role as a "genomics trailblazer," said NHGRI Director Eric Green, M.D., Ph.D. This means supporting research into new DNA sequencing methods and data analysis techniques and solving difficult problems in genome sequencing, he said.

The success of NHGRI's efforts in this area will lie in its ability to partner with other institutes and organizations, he

http://www.genome.gov/27558232
July Workshop Topics

I. Genetic architecture of health and disease at scale

II. Integrating genomic variant discovery with function

III. Clinical genome sequencing at scale

IV. Comparative and Evolutionary Genomics
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Clinical Genome Sequencing at Scale

- eMERGE Network
  - electronic medical records & genomics

* >350,000 subjects with DNA samples + EMRs across 10 sites
* electronic phenotyping; GWAS genotyping
  - phenotype → genotype
  - genotype → phenotype

How to ensure that genomic medicine has little or no impact on healthcare:
  - rely on clinicians
  - Reading
  - Remembering
  - clinical reports
  - published literature

Sequencing at Scale

- Current NHGRI efforts:
  - eMERGE
  - CER
  - UNGV
  - INSIGHT (NRG)
  - IGNITE
- What will landscape look like w/o NHGRI?
  - Where is coordinated action necessary?
  - When should market be relied upon?
- Partnership opportunities with others
- ELSI integration
- What types of data?
- Duration of project
- New challenges
Break Out Group Members

- Katrina Armstrong
- David Bentley
- Les Bieseker
- Stephen Chanock
- Rex Chisholm
- Mildred Cho
- Mark DePristo
- James Evans
- Stephen Fodor
- Richard Gibbs
- Robert Green
- Lucia Hindorff
- Carolyn Hutter
- Gail Jarvik
- Hanlee Ji
- Steve Joffe
- Dan Kastner
- Bruce Korf
- David Ledbetter
- Dan Masys
- Amy McGuire
- Patrice Milos
- Cynthia Morton
- Lucila Ohno-Machado
- Sharon Plon
- Heidi Rehm
- Dan Roden
- Pamela Sankar
- Xun Xu
Recommendations for Clinical Genome Sequencing

1. Define clinical contexts in which genome sequencing improves patient outcomes

2. Enable rapid, robust detection of all clinically relevant variation in a single test

3. Leverage clinical sequencing data for research use

4. Improve approaches for determining pathogenicity

5. Identify effective methods for implementing sequencing in medical practice
Define clinical contexts in which genome sequencing improves patient outcomes

- Support catalytic research
- Demonstrate whether/when genome-scale testing improves health
- Develop evidence based paradigms
- Address role of sequencing in public health
Enable rapid, robust detection of all clinically relevant variation in a single test

- Improve accuracy
- Decrease cost and turn-around time
- Expand to RNA/transcriptome variation when merited
- Increase the spectrum of tissues undergoing clinical sequencing
Leverage clinical sequencing data for research use

• Foster a “virtuous cycle”

• Use exemplar studies to influence key areas:
  – clinical utility
  – clinical implementation
  – data sharing
  – tool development
Improve approaches for determining pathogenicity

- Incorporate genetic, functional and computational data
- Expand beyond manual curation
- Facilitate the development of standards
Identify effective methods for implementing sequencing in medical practice

- Develop novel clinical decision support tools
- Broaden the population impact
- Connect with professional societies
July Workshop Resources Online

Future Opportunities for Genome Sequencing and Beyond: A Planning Workshop for the National Human Genome Research Institute

July 28-29, 2014
Bethesda North Marriott & Conference Center
5701 Marinelli Road
North Bethesda, Md. 20852
(301) 822-9200

On July 28-29, 2014, the National Human Genome Research Institute (NHGRI) sponsored the workshop - Future Opportunities for Genome Sequencing and Beyond: A Planning Workshop for the National Human Genome Research Institute - at the Bethesda North Marriott Hotel & Conference Center.

The objectives of the workshop were:

- Discuss the scientific questions and opportunities that can be substantially addressed by large-scale genomics studies, starting with genome sequencing but also considering other genomic technologies.
- Consider options for future NHGRI programs that would address these questions and opportunities.

Submit a Comment: Workshop Report: Future Opportunities for Genome Sequencing and Beyond
The deadline for comments is February 1, 2015

View workshop videos and slides from: July 28 & July 29

Tweets from the Workshop: #GSPFuture

Workshop Agenda

http://www.genome.gov/27558042
Acknowledgements

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Workshop Agenda Committee: Ewan Birney, Eric Boerwinkle, Carlos Bustamante, Joe Ecker, Jim Evans, Bill Gelbart, Len Pennacchio

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Adam Felsenfeld, Shannon Biello, Deborah Colantuoni, Lucia Hindorff, Carolyn Hutter, Lu Wang, Elise Feingold, Mike Pazin, Mike Smith, Heidi Sofia, Chris Wellington, Kris Wetterstrand

Workshop Attendees