Group 3: Clinical Genome Sequencing at Scale

Facilitators:
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Survey

Interpretation support	1	1	1	1	1	1	1	1	1	1	2	2	2	3	3	4	4
Functional genomics	1	1	1	1	1	2	2	2	2	2	2	2	2	3	3	4	4
Sequence data analysis	1	1	2	2	2	2	2	3	3	3	3	3	3	3	4	4	4
Technology development	1	1	1	2	2	3	3	3	3	3	4	4	4	4	4	4	4

Goal #1: Improve technical sequencing platforms

- Improve accuracy and decrease cost and turn-around time
- Define interoperable sequencing and analysis standards
- Harmonize technical aspects of research and clinical sequencing
- Detect all types of clinically relevant variation in a single genome scale test
- Increase the spectrum of tissues undergoing clinical sequencing including analysis of circulating and single cells

Goal #2

Improve our understanding of variant and gene disease relationships

- Gather data from multi-ethnic populations with geographic diversity
- Leverage a variety of approaches that span other omics
- Leverage the large amount of accumulating clinical sequencing data for research use
- Requires laboratory, physician and patient participation in all aspects of the clinical genomics enterprise

Tactics for Goal #2

1. Develop robust approaches to determine the pathogenicity of genomic variants using genetic, functional, and computational data in a statistically valid framework
2. Develop distributable platforms for clinical laboratories and physicians to submit genotypes, phenotypes and clinically interpreted variants
   - Make sharing as easy as possible for busy labs and doctors
3. Improve patient engagement in clinical genomics
   - Improve education of the public in genomics of health
   - Develop a multi-use longitudinal cohort of all patients undergoing clinical genome-scale sequencing
   - Targeted rephenotyping based on sequence results

Goal #3: Determine clinical utility, value and cost-effectiveness of genomic sequencing in a variety of medical settings

Goal #4: Ensure equitable access to genome medicine across populations and healthcare settings

- This is a critical role for NHGRI

Tactics for Goals 3 and 4

1. **Encourage randomized trials of genome scale sequencing in a variety of medical settings**
   - Define the evidence development paradigm for demonstrating the clinical utility of testing
   - Develop cost-effectiveness and value trials of genomic sequencing
   - Ensure that participation in studies reflects the US patient population
2. **Partner/cost share with other NIH institutes in selecting the most appropriate clinical setting and designing these large-scale clinical trials**

Goal #5: Identify efficient and effective methods for implementation of sequencing into routine medical practice. Tactic examples include:

1. Develop clinical decision support tools for ordering and applying genomic information
2. Develop improved methods for education of physicians (point of care education)
3. Implement our experience with return of results into wider clinical settings

Goal #6: Further refine an NHGRI agenda for implementation research in genomic medicine

Overarching Strategy

Creating a learning health system for clinical genomics for patients, physicians, and insurers

Consider development of a national cooperative group for genomic medicine