National Human Genome Research Institute

NHGRI Strategic Planning Meeting Agenda *January 22-24, 2019*

From Genome to Phenotype:
Genomic Variation Identification, Association, and Function in Human Health and Disease

Hilton Washington DC/Rockville Hotel & Executive Meeting Center, Rockville, MD 20852**.**
Meeting will be recorded and videocast: genome.gov/genometvlive/
Meeting materials: event.capconcorp.com/wp/2019-nhgri/

Workshop Goals:

Participants will help NHGRI develop a strategic approach for the next 5-10 years to significantly advance the state-of-the-art in our ability to find and characterize genomic variants, the genomic elements in which they reside or that they affect and understand the effects of those variants on human health and disease

We seek recommendations for projects, community resources, knowledge, and research directions that NHGRI should pursue, as well as consideration of key ongoing efforts that should be continued or revised.

We also seek recommendations for mid-scale projects that could be initiated in the next year (for example, ideas that build directly on the existing ENCODE Project and the Genome Sequencing Programs) as well as longer-term projects that may require pilot projects, development of technologies or resources and establishment of collaborations, before they could begin.

Workshop Rationale:

Relating genomic variation to human phenotype is a central issue in genomics.

There are several ways to consider this problem, but the elements are: identifying genomic variants; associating them with regulatory elements, genes and phenotypes; and understanding gene, regulatory element and variant function. Within this, or added to it, would be an understanding of epistasis and environmental influences on genotype.

There are now many individual examples (genes/phenotypes) where we have a reasonably detailed understanding of the relationship between variant and disease– these have defined the paradigm. But these so far mostly represent simpler cases: Mendelian (i.e., very strong effect) traits; diseases where the physiology is straightforward (e.g., inborn errors of metabolism); and some cancers.

But the aim of human genomics is to solve this problem at scale for all human traits that have an inherited component, and in so doing, gain biological insight into the nature of inherited disease, insight into mechanisms of variant, regulatory element and gene function, and ultimately to provide a rational foundation for clinical applications. To develop approaches to do this, NHGRI seeks to understand the state-of-the-art, gaps in the field (knowledge, methods, data and resources), find better ways to integrate the information from the separate elements, and identify promising new approaches to address the general problem.

This workshop is one of a series of activities devoted to strategic planning for NHGRI https://www.genome.gov/27570607/strategic-planning-overview/. The recommendations forthcoming from the workshop discussions will inform the NHGRI “2020 Vision for Genomics” Strategic Planning efforts.

Meeting Agenda:

The workshop is divided into four parts:

I. Setting the Stage: "Vision" discussions to imagine what the field can (or must) be a decade from now.

II. Scientific Issues: The current state-of-the-art to identify challenges and opportunities:
- Day 1: variant discovery and association with traits
- Day 2: functional element discovery and characterization, and the interpretation of how variants effect function
- Breakout sessions will extend the discussions, raising specific examples that NHGRI could pursue (e.g., specific projects, methods, knowledge, resources, data, etc.).

III. What should NHGRI do?: Integration of the recommendations from the preceding days; placing them in a wider context; identifying specific things NHGRI should do.

IV. Synthesis and Prioritization: Prioritization among the projects, directions, resources, etc. recommended during the workshop.

Tuesday, January 22, 2019

Location for all sessions excluding Breakout sessions will be in the Plaza Ballroom.
Please note that this meeting will be **live-streamed** and permanently archived.

8:00 – 8:30 a.m.	**Registration**	
8:30 – 8:40 a.m.	**Welcome and Introduction**	Eric Green
8:40 – 9:00 a.m.	**Statement of Meeting Goals**	Elise Feingold Adam Felsenfeld

Part I: Setting the Stage

Visions of the Future

What will the field of genomics look like in 5-10 years? How will it get there?

9:00 – 9:15 a.m.	**Vision Talk 1**	Jay Shendure
9:15 – 9:30 a.m.	**Vision Talk 2**	Judy Cho
9:30 – 9:45 a.m.	**Vision Talk 3**	Emma Farley
9:45 – 10:45 a.m.	**Discussion**	**Moderators**: John Stamatoyannopoulos Heidi Rehm Tuuli Lapplainen
10:45 – 11:00 a.m.	**Break**	

Part II: Scientific Issues

11:00 – 11:05 a.m.	**Deliverables for Part II**	NHGRI Staff Meeting Advisors
11:05 – 11:25 a.m.	**NHGRI's Current Approach to "Variant to Function to Disease"**	NHGRI Staff
11:25 – 12:10 p.m.	**Current State of the Art in Variant Discovery and Association**	Amit Khera Laura Bierut Jonathan Haines
12:10 – 12:55 p.m.	**Moderated Discussion** *How should NHGRI approach these scientific issues in the future? What are the important questions to ask? Where and how will NHGRI get samples/data?*	**Moderator**: Gonçalo Abecasis
12:55 – 2:00 p.m.	**Lunch**	
2:00 – 2:15 p.m.	**Breakout Session Charge** *For more information on breakout sessions, see "Guidance to Breakout Session Participants" document.	NHGRI Staff Meeting Advisors
2:15 – 3:15 p.m.	**Day 1 Breakout Sessions (concurrent)**	
	Breakout 1 (*Roosevelt Room*) *How much more sequencing, if any, is needed to study Mendelian and common disease, and what should NHGRI do in this area? Why?*	**Co-Chairs**: Eric Boerwinkle Nancy Cox
	Breakout 2 (*Madison Room*) *How and why to approach structural variation and other "hard to measure" variation?*	**Co-Chairs**: Charles Lee Karen Miga
	Breakout 3 (*Jefferson Room*) *How and why to approach more complex features- e.g., GxE, epistasis?*	**Co-Chairs**: Andrew Clark Eimear Kenny
3:15 – 3:45 p.m.	**Break**	
3:45 – 5:15 p.m.	**Breakout Summaries and Discussion** *10 minutes each plus one hour discussion*	Breakout Session Co-Chairs **Moderator**: Lon Cardon
5:15 – 5:30 p.m.	**Summation of Day 1 and Prep for Day 2**	NHGRI Staff
5:30 p.m.	**Group Photo**	

End of Day 1

Wednesday, January 23, 2019

Location for all sessions excluding Breakout sessions will be in the Plaza Ballroom.
Please note that this meeting will be **live-streamed** and permanently archived.

8:00 – 8:15 a.m.	**Introduction: Variant and Genome Function**	NHGRI Staff
8:15 – 9:00 a.m.	**Current State of the Art: Functional Data, Analysis and Interpretation**	Hugo Bellen Lea Starita Timothy Reddy
9:00 – 10:00 a.m.	**Moderated Discussion** *How should we be doing this into the future? What resources, new technologies and computational capabilities do we need to generate and make use of functional data? What is needed to overcome barriers to performing functional studies at scale?*	**Moderator**: Brenton Graveley
10:00 – 10:15 a.m.	**Break**	
10:15 – 10:30 a.m.	**Breakout Session Charge**	NHGRI Staff Meeting Advisors
10:30 – 11:30 a.m.	**Day 2 Breakout Sessions (concurrent)**	
	Breakout 4 (*Roosevelt Room*) Identification and characterization of all genes and regulatory elements	**Co-Chairs**: Ross Hardison Bing Ren
	Breakout 5 (*Madison Room*) Determining the functional consequences of variants acting individually and in combination	**Co-Chairs**: Kelly Frazer Wendy Chung
	Breakout 6 (*Jefferson Room*) Accurate prediction of the regulatory consequences of variants, and modeling gene regulation	**Co-Chairs**: Trey Ideker Christina Leslie
11:30 – 12:30 p.m.	**Lunch**	
12:30 – 2:00 p.m.	**Breakout Reports and Discussion** *10 minutes each plus one hour discussion*	Breakout Session Co-Chairs **Moderator**: Joseph Ecker
2:00 – 2:15 p.m.	**Break**	
2:15 – 3:00 p.m.	**Focus Discussion 1** *What can NHGRI do to facilitate bridging molecular and organismal phenotype?*	**Moderators**: Len Pennacchio Barbara Wold Andrea Califano
3:00 – 3:45 p.m.	**Focus Discussion 2** *Bridging Day 1 and Day 2: Connecting discussions about variation, function and phenotype*	**Moderators**: Richard Myers Katherine Pollard Daniele Fallin

Part III: What should NHGRI do?

3:45 – 4:00 p.m.	**Brief recap of Part III deliverables: Brainstorming for NHGRI-supported Activities** **How to Achieve the Science – Four Topics (below)** *What can NHGRI do to address the major recommendations? What insights, capabilities, policies, initiatives, collaborations, alliances, etc. should we pursue?*	NHGRI Staff Meeting Advisors
4:00 – 4:45 p.m.	**Topic 1: Discovery and Interpretation of Variation Associated with Human Health and Disease**	**Panel**: Barbara Stranger Anshul Kundaje David Valle **Moderator**: Michael Boehnke
4:45 – 5:30 p.m.	**Topic 3: Predicting and Characterizing Functional Consequences of Genome Variation, Including Beyond Single Variant/Gene**	**Panel**: Nadav Ahituv Dana Crawford Neville Sanjana **Moderator**: Jonathan Pritchard

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End of Day 2

Thursday, January 24, 2019

Location for all sessions excluding Breakout sessions will be in the Plaza Ballroom.
Please note that this meeting will be **live-streamed** and permanently archived.

8:00 – 8:15 a.m.	**Day 3: Introduction**	NHGRI Staff
8:15 – 9:00 a.m.	**Topic 4: Data Resources, Methods, Technologies and Computational Capabilities**	**Panel**: Christina Leslie Marylyn Ritchie Jason Buenrostro **Moderator**: Aviv Regev
9:00 – 9:45 a.m.	**Topic 2: Addressing Basic Research Questions that Anticipate Clinical Needs**	**Panel**: Howard Chang Stephen Chanock Howard Jacob **Moderator**: Sharon Plon
9:45 – 10:15 a.m.	**Break**	
Part IV: Synthesis and Prioritization		
10:15 – 12:15 p.m.	**Recommendations for NHGRI Priorities** *Moderated discussion on future NHGRI priorities for specific initiatives, data sets, knowledge, capabilities*	**Meeting Co-chairs & Meeting Advisors**: Jay Shendure Joseph Ecker Sharon Plon Katherine Pollard
12:15 – 1:00 p.m.	**Summation of the Meeting**	NHGRI Staff
1:00 p.m.	**Main Meeting Adjourns**	

End of main meeting

1:00 – 3:00 p.m.	**Working Lunch/NHGRI and Advisors** *Meeting summary with ad-hoc advisors to the NHGRI Basic Genomics and Genomics of Disease Strategic Planning Focus Groups*	NHGRI Staff Meeting Advisors