Summary of NIH Community Strategic Planning Town Hall – Establishing a 2020 Vision for Genomics
Thursday, June 20, 2019

Overview:
On Thursday, June 20, 2019, NHGRI hosted a strategic planning Town Hall to solicit feedback about genomics issues that should be considered as part of NHGRI's strategic planning process. This Town Hall was held in the Lipsett Amphitheater in Bethesda, Maryland and was open to all members of the NIH community. Attendees were invited to provide comments on all aspects of the strategic planning effort, including scientific opportunities, challenges for the field, and design of the strategic planning process.

NHGRI director, Eric Green, M.D., Ph.D. began explaining the context for this Town Hall and providing information on the plans and timeline for the NHGRI strategic planning process. NHGRI last published a strategic plan in 2011, and the new plan is projected to be published in October 2020. Through Town Halls and other in-person gatherings across the country, NHGRI is collecting input on topics to consider in developing a 2020 Vision for Genomics.

For this Town Hall, NHGRI presented what it has found to be key challenges in the field and asked the community for feedback on those areas. NHGRI wanted to know where its most important contributions to the forefront of genomics might be, and what challenges and bottlenecks other institutes are facing related to genomics.

The Town Hall was broken into 5 thematic areas: Society, Education and Engagement, Genomics of Data Science, Basic Genomics and Technology, Genomics of Disease, and Genomics in Medicine and Health. Each area gave a brief presentation about the key challenges identified and then opened the floor for comments and questions.

Society, Education, & Engagement

Key areas identified:

- Empower people to make well-informed decisions about genomic data access, use, sharing and protection.
- Track and shape genomics' influences on concepts of health and wellness, identity, family and community.
- Promote equitable access to genomic technologies and recognize the enduring effects of societal inequities.
- Develop and use genomic technology in accordance with community needs and values
- Ensure that evidence-based, values-informed policies and governance frameworks guide genomic research and translation.
- Ensure genomics serves individuals, families, communities, and society, recognizing its promise, limitations and social context.
- Meet educational and professional needs of K-16 educators and health care providers.

Discussion:

The conversation started with a comment on the importance of the patient voice in research. Patients should be included in planning and workshopping stages, as well as in RFA's. Just like a statistician, or a

geneticist may be required on an RFA, so too could a patient voice. Patients could also be included on Steering Committees. Following this idea was the proposal that investigators should look more like patients whenever possible. This concept was successfully implemented in the *APOL1* Long-term Kidney Transplantation Outcomes Network (APOLLO), and consequently relationships with patient populations were transformed.

An NCI representative offered the comment that the first key area could be broadened to address empowerment of people to make informed health decisions, specifically through return of results. While an important point, Eric Green noted that the complexities of returning results are often disease-specific and can be more relevant on the agency level. Dave Kaufman pointed out that other institutes also fund ELSI research and that ideally NHGRI's work in this space will influence and encourage that work as well.

Regarding the seventh key area, an NHGRI representative suggested that K-16 education should be expanded to include graduate level education and trainees. Carla Easter, Chief of the Education and Community Involvement branch of NHGRI, commented on the existence of an interactive website associated with the Smithsonian "Genome: Unlocking Life's Code" exhibit. She noted that the institute is constantly looking for innovative ways to connect with K-12 audiences. Young people are worried about germline editing in particular, so this could be addressed.

The conversation then shifted to engaging diverse communities. An NHGRI representative asked if work will be done to address historical wrongdoings related to genetics. In response, Dave Kaufman noted that to gain the trust of diverse communities, those issues will have to be addressed, and the needs of specific communities will have to be understood. NHGRI should have a voice in the public conversation surrounding genetics and identity and a role in educating the public on the values of genomic technology.

NHGRI also must consider the fundamental question of data access equality, especially for institutions with fewer resources.

Genomics of Data Science

Key areas identified:

- Develop computational solutions for the hard problems in genomics.
- Develop genomic data sharing guidelines, policies, and best practices.
- Facilitate storing, sharing, and computing on large-scale genomic data.
- Build sustainable genomic information resources.
- Integrate genomic data science into healthcare.
- Ensure that the next generation of genomicists are trained in data science.

Discussion:
The discussion began with a comment from an NIDCR representative about the great value that NHGRI's genomic resources and databases have had for many of their institute's grantees. The resources are appreciated both for the data that they contain and for the quality of the analytical tools. More expertise and training is needed in this area, which presents an economic challenge as experts tend towards the private sector. This is also an area for potential collaboration between institutes.

The conversation then shifted to key area 1. A representative of the Office of Research on Women's Health asked if sex could be considered an environmental factor and therefore considered one of the hard problems in genomics. Relatedly, the practice of excluding sex chromosomes from genetic association studies could be rectified. More computational power is also needed to address these hard genomic problems, especially because certain phenotypes do not have large numbers of individuals with which to work. This will require tool developers to work with disease-specific researchers.

A representative from NICHD then presented the FAIR framework of how data should be Findable, Accessible, Interoperable, and Reusable. She argued that this framework should be applied to even the most basic data sets being generated by all institutes and should be incorporated into basic research. In terms of data access, NHGRI should remember that international policies exist that sometimes present an additional barrier. The summary results policy is great, but one critique is that NHGRI should consider defining what counts as sensitive data.

NHGRI should also be focusing on developing tools for data interpretation in the clinic. Genomic data is already starting to come into the clinic, so support is needed for research into how this information can be made useful for physicians. Relatedly, privacy and security of this information is essential, and NHGRI could look to the private sector for ideas on how to protect data.

Basic Genomics & Technology

Key areas identified:

- Enable facile, routine generation of whole-genome sequences and characterization of epigenomes.
- Establish the role(s) of all genes and regulatory elements in pathways, networks, and phenotypes.
- Use evolutionary and comparative genomic data to markedly advance understanding of human genome function.
- Enable facile, routine generation and use of synthetic nucleic acids in genomics research studies.
- Understand and leverage population structure and diversity to facilitate human genetics studies.

Discussion:
The discussion started on the topic of how NHGRI can distinguish its work from the work of other institutes, especially with just 1.5% of the NIH budget. NHGRI wants to focus on breaking down barriers that disease-specific researchers are facing through development of technology, methods, and standardized pipelines. These common barriers are what NHGRI regards as the forefront of genomics.

The second key area will require interaction between institutes and could be made more specific. Additional publicity of training sessions and conferences is needed, and extramural staff could be invited to disease-specific meetings to help facilitate this interaction.

Participants were particularly interested in the development of a human reference genome and how it will be integrated into NIH intramural research. While funding is currently being dedicated to development, the internal implementation will require a cross-institutional team.

Genomics of Disease

Key areas identified:

- Establish the functional consequences of any genomic variant affecting human health and disease.
- Determine the genomic architecture of all human diseases and traits.
- Develop the methods and analyses to support use of non-sequence genomic data for characterizing human health and disease.
- Transform how we assemble sample sets for genomic studies of human disease.
- Commit to systematic inclusion of appropriate ancestral diversity into all large-scale genomic studies and analyses.

Discussion:
NHGRI could consider the constituents of a "healthy" person's genome. Although there is no totally well person because everyone is aging and exposed to environmental exposures, NHGRI could look at protective variants.

Participants largely agreed that the language in these key areas was too aspirational. The moderators agreed that the areas present lofty goals but need suggestions from other institutes to narrow them down. There was also agreement that computational horsepower will be essential as technologies such as artificial intelligence and machine learning are further deployed.

In terms of the second key area, a participant suggested emphasizing orphan diseases, a space in which NHGRI already has experience. Another participant disagreed saying that it is time to take a deeper dive into polygenic common diseases. There was consensus that both rare and common diseases could have a place in the future of NHGRI.

The discovery of new disease-gene associations is essential and could be promoted through transparency of methods and filters. Relatedly, current technology will need to be improved to address polygenic diseases with thousands of genes that each contribute minorly to the phenotype. Relatedly, phenotypic and genetic data harmonization is critical.

There could also be more of an emphasis on therapeutics and development of a pipeline for intervention. The NIH Clinical Center is a valuable resource in terms of building these tools.

<u>Genomics in Medicine and Health</u>

Key areas identified:

- Create systems to integrate genomics into everyday clinical and public health practice.
- Develop processes for routine, high value clinical genomic evaluation.
- Build knowledgebases for predictive genomic medicine in diverse populations.
- Develop and evaluate genomic prevention and therapeutic strategies in diverse populations.
- Ensure that genomic health information has maximum utility for all members of the public.
- Train providers to integrate genomics into the clinical workflow.

Discussion:
Participants emphasized the importance of the sixth key area and that it should include not just medical students but current physicians as well.

NHGRI should also think about how genomics in medicine will work in the current regulatory framework. Evidence for medical relevance will need to be established. This may involve relationships with sister agencies like the FDA or CMS. In terms of the second key area, NHGRI is thinking about what information is needed to add a variant to a specific test, and there will be a day-long meeting with the FDA in November.

The utility of mobile health data should also be considered – the type of data to collect and standards around its collection. Mobile health data can be thought about in the context of the FAIR framework. Relatedly, access to innovative technology for genetic counseling and how results are best returned is a broad systematic question that can be classified under both the first and sixth key area.

In terms of proteomics and other -omics, NHGRI tries to be open-minded but realistic, keeping in mind the limitations of budget and expertise. Triangulating between DNA, transcriptomics, and subclinical

phenotypes has been identified as an area for potential progress. Institutes should continue to think specifically about the types of data pipelines they would find useful in this context.

Especially considering the NIH HEAL (Helping to End Addiction Long-term) Initiative, the opioid crisis and other maladaptive behaviors could be important focus areas. The success of pharmacogenomics could also be addressed.