To boldly go: Unpacking the NHGRI's bold predictions for human genomics by 2030

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The 2020 strategic vision for human genomics, written by the National Human Genome Research Institute (NHGRI), was punctuated by a set of provocatively audacious "bold predictions for human genomics by 2030." Starting here, these will be unpacked and discussed in an upcoming series in the *American Journal of Human Genetics*.

> Begin, be bold, and venture to be wise.—*Horace*

Since the successful completion of the Human Genome Project in 2003, the promise of genomics is being increasingly realized throughout the entire life sciences ecosystem. Genome sequencing costs continue to shrink, studies of ever-growing sophistication routinely advance our understanding of genome biology in health and disease, and genomic medicine has matured from hypothetical to reality.

To facilitate this maturation and metamorphosis, the National Human Genome Research Institute (NHGRI) has regularly generated strategic visions for human genomics,[1,2] which aim to articulate the state of the science at key inflection points and to provide a blueprint for future advances and appropriate stewardship of the field. The most recent of such efforts began in 2018 and involved collecting input from stakeholders across biomedicine over a two-year period. It was immediately apparent that genomics had become so widely disseminated in biology and biomedical research that it was not practical (or appropriate) for NHGRI to lead strategic planning for all the nooks and crannies in which genomics had seeped. Rather, we used our recently adopted organizational mantra—*The Forefront of Genomics*—to frame and delimit the scope of the strategic planning process, coming to realize that this mantra empowered NHGRI to provide responsible stewardship of those areas of human genomics most relevant for advancing human health.

In the end, the collective ideas and insights received during the strategic planning process could be effectively synthesized into a framework that was organized around four strategic areas[3]: guiding principles and values, a robust foundation for genomics, breaking down barriers, and compelling genomics research projects (https://genome.gov/2020SV). To augment the myriad ideas captured in these four areas, the institute sought to communicate an energetic, optimistic, and audacious spirit that has become part of the DNA of genomics and NHGRI. Toward that end, the 2020 NHGRI strategic vision ended with a set of ten "bold predictions for human genomics by 2030" (Box 1). Crafted to be both inspirational and aspirational, these thought-provoking predictions were intended to spark robust discussions about what might (and might not) be possible in the coming decade as the field strives for goals that at the time seemed out of reach.

The 2020 NHGRI strategic vision was published during the COVID-19 pandemic, which limited opportunities to engage with the genomics community in person. Yet, each of the bold predictions—painfully brief in its text—warranted appropriate unpacking and more extensive discussions, especially as new developments in genomics were being realized. In keeping with NHGRI's passion for communicating all-things genomics, the institute built on the nascent predictions by organizing a virtual ten-part seminar series that explored each prediction in greater detail.

For the seminar series, we sought non-conventional talks that matched the far-reaching nature of the predictions, inviting two experts to discuss each of the ten predictions. The speakers were encouraged to work together, avoid reiterating their "standard" talks, and to embrace the challenging characteristics of each prediction. They were pressed to address whether each prediction was too bold (or not bold enough); what would be needed to realize the prediction; and what the respective roles are for NHGRI and research funders, researchers, policy makers, and others. The seminars provided an opportunity for each prediction to be peeled back like an onion, revealing layers of complexity that might not be obvious from its concise wording.

The ten-part seminar series was broadcast live, routinely attracting hundreds of virtual attendees from an average of 25 countries. The questioning of speakers was vigorous, ranging from 12 to 45 questions in each session. Each session was video-captured and made available on NHGRI's YouTube channel,

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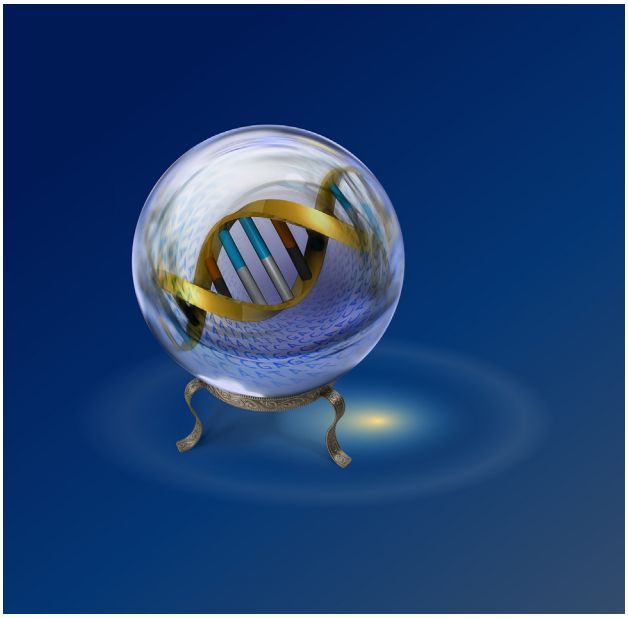
Box 1. Bold predictions for human genomics by 2030

(1) Generating and analyzing a complete human genome sequence will be routine for any research laboratory, becoming as straightforward as carrying out a DNA purification.
(2) The biological function(s) of every human gene will be known; for non-coding elements in the human genome, such knowledge will be the rule rather than the exception.
(3) The general features of the epigenetic landscape and transcriptional output will be routinely incorporated into predictive models of the impact of genotype on phenotype.
(4) Research in human genomics will have moved beyond population descriptors based on historic social constructs such as race.
(5) Studies involving analyses of genome sequences and associated phenotypic information for millions of human participants will be regularly featured at school science fairs.
(6) The regular use of genomic information will have transitioned from boutique to mainstream in all clinical settings, making genomic testing as routine as complete blood counts (CBCs).
(7) The clinical relevance of all encountered genomic variants will be readily predictable, rendering the diagnostic designation "variant of uncertain significance (VUS)" obsolete.
(8) A person's complete genome sequence along with informative annotations can be securely and readily accessible on their smartphone.
(9) Individuals from ancestrally diverse backgrounds will benefit equitably from advances in human genomics.
(10) Genomic discoveries will lead to curative therapies involving genomic modifications for dozens of genetic diseases.



The NHGRI bold predictions crystal ball

GenomeTV (https://www.genome.gov/event-calendar/Bold-Predictions-for-Human-Genomics-by-2030). These videos have since reached thousands of additional viewers and will continue to provide a glimpse into the state of strategic thinking about human genomics in the early part of this decade. We appreciate the willingness of those speakers and the community of viewers to be a part of our audacious goals for the seminars specifically and the future more generally.

Going forward, these predictions will be considered in even greater detail as part of an upcoming series in the *American Journal of Human Genetics*. Inspired by the pithy yet fantastical nature of these statements, the authors will paint a more complete view of the future genomics landscape, thereby illustrating how advances in human genomics are poised to benefit science, medicine, and society. We welcome the insights that have arisen from their questions and conversations with each other, and with you, from the forefront of genomics.

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