Even with carefully validated biomarkers with overwhelming clinical utility, commercial assays are often deployed for clinical use before rigorous assay validation has been performed and before consensus is reached on how to interpret results. The motto of precision medicine, the right treatment for the right patient given at the right time, fails to emphasize the importance of careful validation of the diagnostic testing that is essential for successful implementation of precision medicine.

The key to effectively implementing precision medicine lies in recognizing the underlying root causes of its current underperformance, which are intertwined into an ancient system that dictates how both basic and applied research is funded, judged, and reported. The solution to these problems, as Hey and Kesselheim point out, may be a reformulation of how research institutions, funding agencies, and regulatory groups interact. A more focused collaborative effort is needed with a common goal of overseeing and assessing the discovery and subsequent delivery of scientific knowledge into the clinical space, with the goal of supporting precision medicine initiatives. Research funding could be tied to completing designated tasks, with transparency provided by publically sharing directives and ensuring data are publically available to the greater scientific community. The goal would be to produce a more concerted effort toward precision medicine initiatives and eliminate the disorganized and sporadic nature of current public research funding. Although this may be a utopic vision, it remains clear that the current system has underperformed and that changing our trajectory to a more efficient, collaborative, and valid approach will require a profound shift in how we approach precision medicine.

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Writing the Genome: Are We Ready?

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Since the completion of the Human Genome Project (HGP-read), improvements of sequencing technology, dramatic reductions in sequencing cost, and importantly, progress in understanding of the function of the human genome have been continual. Recent advances in sequencing-based technologies and DNA-editing methods [e.g., CRISPR (clustered regularly interspaced short palindromic repeat)] present the possibility of synthesizing and editing DNA on a large scale. With these possibilities, a question is raised: would construction of large scale (0.1–1 billion bp) genomes lead to further understanding and applications of genomic information?

A collaborative group called the Center of Excellence for Engineering Biology, led by New York University synthetic biologist Dr. Jef D. Boeke, formally announced the Human Genome Project-Write (HGP-write) in the June 2016 issue of *Science (1)*. This project aims to synthesize large-scale genomes through an international, multidisciplinary collaboration.

Writing genomes is not a novel concept; viral and bacterial genomes were synthesized in 2003 and 2010, respectively, with the yeast whole genome currently under construction. Current technology for de novo gene synthesis primarily uses large-scale single-stranded DNA oligonucleotide synthesis and assembly, while innovations of alternate approaches to oligo synthesis and gene assembly have been developed at variable costs. However, molecular technologies mastered thus far are not sufficient to construct large-scale eukaryote genomes.

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Recognizing the interdependence of technology and potential applications of large-scale synthesis, the group proposes parallel efforts to advance methodologies and reduce costs while implementing pilot projects aimed at synthesizing genome fractions with immediate value for biomedical research or development. Proposed projects include: exploring the function of noncoding genetic regions through construction of full gene loci; constructing full chromosomes to model disease; and development of a panhuman reference genome. Pilot projects aim to synthesize a targeted 1% of the human genome to stimulate progress toward applications such as ex vivo human organ growth, engineered viral immunity, and engineered cancer resistance. This includes the creation of an ultrasafe cell line to be the "basic and potentially universal platform for human biotechnology" *(1)*.

Concerns about the commercial and scientific value of large-scale DNA synthesis have been raised. A key question debated is whether there exist any immediate industrial or clinical utilities for which large-scale DNA synthesis is required. Other discussions focus on whether a centralized project is necessary as the technological progression of gene synthesis and engineering is indeed already happening worldwide. The collaborators forthrightly recognize that the HGP-write raises ethical concerns as perceived by the scientific community and lay public, including the extreme that genome synthesis equates to creating a synthetic human being. The HGP-write project team indicates a commitment of time and funding to ethical, social, and legal implications which enable broad public discourse and early, ongoing consideration.

Significant historical advancements in medical science have been promoted by international multiinstitutional projects such as HGP-read. Evaluation and consideration of the proposed HGP-write should be undertaken to assess whether the goals are scientifically appropriate, ethically sound, and technologically feasible. Will HGP-write bring a new era of biomedical technology? The answer will be revealed in the near future.

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