



The Genome Project-write (HGP-write)

HGP-write Leadership

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A Grand Challenge: To Understand Life-write

The Genome Project-write (HGP-write) will be an open, academic, international scientific research project led by a multi-disciplinary group of scientific leaders who will oversee a reduction in the costs of engineering and testing large genomes in cell lines by over 1,000-fold within ten years. This will include whole genome engineering of human cell lines and other organisms of agricultural and public health significance. Additionally, HGP-write will develop new technologies and an ethical framework for genome-scale engineering, as well as transformative medical applications. The overarching goal of such an effort is to understand the blueprint for life provided by the Human Genome Project (HGP-read).

Biology's first large-scale project, HGP-read aimed to "read" a human genome. Successfully completed in 2003, HGP-read is now widely recognized as one of the great feats of exploration, one that sparked a global revolution in science and medicine, particularly in genomic-based diagnostics and therapeutics.

But our understanding of the human genome – and the full benefits to humanity to be obtained from this knowledge – remains far from complete. Many scientists now believe that to truly understand our genetic blueprint, it is necessary to "write" DNA and build human (and other) genomes from scratch. Such an endeavor will require research and development on a grand scale.

From Observation to Action

HGP-write is expected to generate considerable knowledge by connecting the sequence of bases in DNA with their physiological and functional behaviors. Importantly, scientists will be able to move beyond observation to action, and facilitate the use of biological engineering to address many of the global problems facing humanity.

Some applications that may arise from HGP-write that could have a significant impact on human health include, but are not limited to, growing transplantable human organs, engineering immunity to viruses in cell lines, engineering cancer resistance into therapeutic cell lines, and enabling high-productivity, cost-efficient vaccine and pharmaceutical development using human cells and organoids that makes precision medicine more affordable and universal.

Responsible Innovation

Genome synthesis is a natural extension of the genetic engineering tools that have been safely used within the biotechnology industry for the past 40 years and have provided significant benefits to society. However, recent technological advancements, such as standardized genomic parts and CRISPR/Cas9 genome editing technology are the field and creating uncertainty in how these technologies will be applied.

For example, society is presently grappling with the ethical implications of CRISPR/Cas9 genome synthesis is a natural extension of the genetic engineering tools that have been safely used within the biotechnology industry for the past 40 years and have provided significant benefits to society. However, recent technological advancements, such as standardized genomic parts and CRISPR/Cas9 genome editing technology are on human germ-line gene editing.

As human genome-scale synthesis appears increasingly feasible, a coordinated scientific effort to understand, discuss, and apply large genome editing technologies is timely, and public discourse regarding such an endeavor is both expected and encouraged. However, responsible innovation requires having more than ethical, legal and social implications (ELSI) discussions; it also involves identifying common goals important to scientists and the public through timely and detailed consultation among diverse stakeholders. Having these conversations well in advance of any deliverable will help society better prepare for the emerging capability.

As such, the project infrastructure will be designed to responsibly support and advance HGP-write, with a particular focus on addressing the potential risks and ethical implications of the project as they arise. For example, a percentage of all research funds could be dedicated to these issues. Additionally, there should be equitable distribution of any benefits in view of diverse and pressing needs in different regions across the globe.

Project Launch

The goal is to launch HGP-write in 2016 with \$100 million in committed support. Funding is expected to come from public, private, philanthropic, industry and academic sources from around the globe.

HGP-write will be implemented through a new, independent nonprofit organization, the Center of Excellence for Engineering Biology. The Center, which will operate virtually at first, will manage initial planning and coordination efforts. Additional Centers could be included in the future.

Initial pilot projects, which will focus on synthesizing ~1% of the human genome, will first be completed to evaluate feasibility and value, similar to other large-scale endeavors such as the HGP and the Synthetic Yeast Project (Sc2.0). HGP-write will be conducted in phases with milestones, metrics, and assessments. Furthermore, these projects will be chosen to provide early stage resources valuable for biomedical research and/or biotechnology production.

We celebrate 2016 – the 26th anniversary year of HGP-read – as a major leap forward for human knowledge and health. In the same spirit, we look forward to the launch of HGP-write as another giant step for humanity.

For more information, please visit: <http://www.hgpwrite.org> or <http://engineeringbiologycenter.org>.

HGP-write Pilot Projects

Initial HGP-write pilot projects under consideration include:

- Using induced pluripotent stem cells (iPSCs) to create an 'Ultrasafe' human cell line;
- Synthesizing "full" gene loci with accompanying noncoding DNA to understand the role of noncoding genetic variation in common human diseases and traits
- Constructing specific chromosomes or complex cancer genotypes to more comprehensively model human disease
- Transforming gene therapy with freedom to deliver many genes and control circuits to improve safety and efficacy
- Developing a pure wild-type genome, bearing the homozygous ancestral allele at each position; and
- Producing specialized chromosomes encoding one or several pathways, such as all genes required to make a prototrophic human cell (ability to synthesize all compounds necessary for growth, including vitamins and amino acids), or to transform the pig genome to make it more amenable for human organ transplantation.