The Genome Project-write (GP-write)

GP/HGP-write Leadership

Jef Boeke, Ph.D.
Director, Institute for Systems Genetics
Professor, Department of Biochemistry and Molecular Pharmacology
NYU Langone Medical Center

George Church, Ph.D.
Robert Winthrop Professor of Genetics,
Harvard Medical School
Core Faculty Member,
Wyss Institute for Biologically Inspired Engineering at Harvard University
Professor of Health Sciences and Technology, Harvard and the Massachusetts Institute of Technology (MIT)
Associate Faculty Member,
Broad Institute

Andrew Hessel
Distinguished Researcher,
Bio/Nano Research Group
Autodesk

Nancy J Kelley, J.D., M.P.P.
President & CEO
Nancy J Kelley & Associates
Founding Executive Director,
New York Genome Center

Project Contact

Nancy J Kelley, J.D., M.P.P.
info@engineeringbiology.org

Media Contact

Lynn Blenkhorn
lynn.blenkhorn@fkhealth.com
(617) 761-6766

A Grand Challenge: To Understand Life-write

The Genome Project (GP-write) is an open, 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. Additionally, GP-write is developing 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.

Thus, GP-write is an international scientific research project that includes whole genome engineering of human cell lines and other organisms of agricultural and public health significance. The Human Genome Project-write (HGP-write) will be a critical core activity within GP-write focused on synthesizing human genomes in whole or in part. Because of the special challenges surrounding human genomes, this activity includes an expanded examination of the ethical, legal and social implications (ELSI) of the project. It will also be explicitly limited to work in cells, and organoids derived from them only.

From Observation to Action

GP-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.

For example, some applications that may arise from GP/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 transforming 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 which can be applied to 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 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 has been designed to responsibly support and advance GP/HGP-write, with a particular focus on addressing the potential risks and ethical implications of the projects 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 Implementation

GP/HGP-write is being implemented through a new, independent nonprofit organization, the Center of Excellence for Engineering Biology, that is managing planning and coordination efforts.

Initial pilot projects will first be completed to evaluate feasibility and value, similar to other large-scale endeavors such as the HGP-read and the Synthetic Yeast Project (Sc2.0). These projects are being chosen to provide early stage resources valuable for biomedical research and/or biotechnology production. Furthermore, GP/HGP-write is being conducted in phases with milestones, metrics, and assessments.

For more information, please visit: www.gpwrite.org or www.engineeringbiologycenter.org.

GP-write

GP/HGP-write Pilot Projects

Initial GP/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.