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Ultra-safe Cells Resistant to Natural Viruses Announced as First GP-write Grand-scale Project

Roadmaps for Future Activities Shared by Nine Working Groups at GP-write 2018 Scientific Meeting

NEW YORK, May 1, 2018 – The Center for Excellence in Engineering Biology and the leadership of Genome Project-write (GP-write) today announced its first grand-scale community-wide project, to develop "ultra-safe cells" that resist natural viruses and potentially radiation, freezing, aging and cancer.

"The ultra-safe cell lines, made using technologies broadly applicable to plant, microbial and mammalian species, are aimed at complete resistance to all viruses and prions, and partial resistance to senescence and cancer, plus biocontainment—significantly updating the goals in the GP-write 2016 paper, in Science magazine," said Professor Jef Boeke, Ph.D., director, Institute for Systems Genetics, Department of Biochemistry and Molecular Pharmacology, NYU Langone Health, and one of four members of the GP-write Leadership Group.

"Ultra-safe cells could have a major impact on human health," said another organizer, Professor George Church, core faculty of the Wyss Institute for Biologically Inspired Engineering, Harvard Medical School and one of four members of the GP-write Leadership Group. For example, some medicines are manufactured in specialized cellular factories. Viruses can contaminate the cells, in one case causing an estimated $1 billion in losses and cutting off patients from their medicine. Because of the risk, companies must undertake costly monitoring for viruses. "Ultra-safe cells could thus make pharmaceuticals safer, cheaper and more reliable," says Church.

In support of these efforts, the Wyss Institute and Cellectis announced a collaboration at the GP-write Scientific Working Meeting, which will give the Church lab access to Cellectis proprietary TALEN gene editing technology that can introduce changes into the DNA code with high specificity and across an entire genome, including multiple changes at a time.

According to Boeke, "The overall GP-write project is focused on writing, editing and building large genomes. We will generate a wealth of information connecting the sequence of nucleotide bases in DNA with their physiological properties and functional behaviors, enabling the development of safer, less costly and more effective therapeutics and a broad range of applications in other areas such as energy, agriculture, healthcare, chemicals and bioremediation." The ultra-safe cell project will be modeled in part on the success of the Sc2.0 project, led by Boeke at Langone. Multiple institutions will be conducting various aspects of this virus-safe cell work as part of GP-write, including NYU Langone Medical Center and the Wyss Institute of Biologically Inspired Engineering.

"We believe in proceeding transparently and responsibly," said, Nancy J Kelley, also an organizer, and lead executive of the Center of Excellence for Engineering Biology which coordinates GP-write. "GP-write efforts include supporting the formation and work of multi-institutional and interdisciplinary

research teams working in a highly integrated fashion, responsive to and engaged with a broad public outreach. We have sought feedback from bioethicists, policy experts, journalists and the public."

Creating virus-resistant cells is accomplished by a process called DNA recoding. Previously, Church and colleagues demonstrated the feasibility of recoding in the bacteria *E. coli*, whereby 321 changes to the bacterial genome were able to confer viral resistance. The proposed recoding of a different species, such as a plant or mammalian genome, would be significantly more ambitious. "Recoding every protein in the human genome, for example, would require 400,000 changes," says Church. Specific redundant codons would have to be removed from all 20,000 human genes. The GP-write organizers hope to complete their work within 10 years.

Project organizers point to potential benefits besides virus resistance. **Recoding will require large-scale changes to the genome, creating opportunities for researchers to make the cells safer in other ways.** Proposals include recoding genes to make the cell less likely to become cancerous, or enabling the cell to resist damage from aging, freezing and radiation.

Another proposed benefit of the ultra-safe cell line, and GP-write more broadly, would be the commercial development of new genomics analysis, design, synthesis, assembly and testing technologies, with the goal of making these technologies affordable and widely available to the scientific community.

Recoding human cells will require significant improvements to technology for synthesizing and testing artificial genomes. In gene synthesis, DNA nucleotides are biochemically stitched together one at a time. The result is similar to natural DNA, but the process is currently very slow. By driving innovation and increasing demand, GP-write hopes to make this process faster and cheaper. After synthesis, the DNA can be assembled into genes or entire chromosomes, and then tested in living cells. GP-write scientists will also work to improve the tools for genome assembly and testing, but in some cases, the technology doesn't exist yet. This year the participants aim to complete the radical rewriting of the 12-million base-pair genome of baker's yeast. In comparison, the human genome has 3 billion base pairs in one set of chromosomes.

In other developments at the meeting, Jef Boeke, Matthew Maurano and colleagues at NYU Langone Health announced an **award of $8M over five years from NIH's National Human Genome Research Institute** to fund a Center of Excellence in Genome Science. The Center, which will be housed in the laboratories of Boeke, Maurano and the GenomeFoundry@ISG, will focus on developing synthetic big-DNA tools to investigate the genetic basis of diverse genetic diseases and to dissect the "dark matter of the genome."

Nine working groups shared and discussed their roadmaps and charters moving forward, which they have developed since attending last year's meeting. Working groups include: The Scientific Executive Committee; Ethical, Legal and Social Advisory Board/Policy; Technology and Infrastructure Development; High Performance Computing and Data Infrastructure; Safety Engineering; Standards, Quality Control and Reporting; Intellectual Property; Communications and Public Outreach; and Education.

An Industry Advisory Board was also announced, with Labcyte, GenScript and Twist Bioscience as the first members.

For more about the 2018 GP-write Scientific Meeting see engineeringbiologycenter.org.

About GP-write

The GP-write Leadership Group includes Jef Boeke, Founding Director, Institute for Systems Genetics, New York University School of Medicine; George Church, Core Faculty Wyss Institute for Biologically Inspired Engineering, Harvard Medical School; Andrew Hessel, CEO, Humane Genomics,

Inc. and Nancy J Kelley, President and CEO, Nancy J Kelley & Associates. GP-write is being implemented through the Center of Excellence for Engineering Biology, which supports the formation and work of multi-institutional and interdisciplinary research teams working in a highly integrated fashion, responsive to and engaged with a broad public outreach. To date, nearly 200 scientists, affiliated with more than 100 institutions/companies in 15 countries, are participating in GP-write. GP-write and the Center of Excellence for Engineering Biology may be followed at engineeringbiologycenter.org.

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