# **GP-write: A Grand Challenge Project to Build and Test Genomes in Living Cells**

May 2018 Scientific Working Meeting Summary

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# **Executive summary**

In May 2017, more than 250 attendees, including scientists, industry leaders, ethicists, communicators, lawyers, artists, and members of the public gathered over two days at the New York Genome Center for the second annual GP-write meeting. Launched a year earlier at a meeting in Boston and an accompanying commentary in <a href="Science">Science</a>, GP-write is focused on using synthesis and genome editing technologies to understand, engineer and test living systems of model organisms, including the human genome, and plants in cell lines. The goal of GP-write is to not only deepen our understanding of life but to develop pragmatic technologies of general use in biology, improving the cost and quality of DNA synthesis, DNA assembly in cells, and testing of many DNA variations on tissue characteristics. At the beginning of 2017 GP-write was named a "project to watch" by <a href="Nature">Nature</a>.

The second meeting explored concrete steps that GP-write can take to solve some of the most important problems facing humanity, including how to uncover the engineering principles of complex genomes, what impact human genetic diversity has on disease, and how to ensure that the advances of genome engineering research are safely and ethically shared with the broader scientific community and the public. Presenters discussed their proposals for pilot projects that would fall under the GP-write umbrella. Organizers also unveiled nine working groups tasked with developing roadmaps for critical aspects of the project, including a scientific executive committee; ethical, social, and legal implications; safety engineering; technology and infrastructure development; high performance computing and data infrastructure; policy development; standards, quality control, and reporting; intellectual property; education; and communications and public outreach.

Following the meeting, there were numerous reports in the press, including Science, NPR, The Atlantic, and Scientific American. In June 2017, GP-write was featured in the cover story for Newsweek, and in April 2018, the work of George Church and GP-write was featured in WIRED magazine. Before the May 2018 meeting, GP-write was also featured in articles by Neo.LIFE and Chemistry World, and the project has also been approached by authors and a documentary film team to chronicle its advances.

The 2018 GP-write Scientific Working Meeting was held on May 1 at Harvard Medical School in Boston, Massachusetts, including over 130 attendees and members of the press. The goal of the meeting was to announce the first official community project, ultra-safe cells which resist natural viruses as well as cancer, aging, radiation, and freezing. In support of that effort, the Wyss Institute and Cellectis, a leading cell therapy company, announced a collaboration to use TALEN gene editing technology to introduce changes into DNA code with high specificity and across an entire genome. It has subsequently been announced that the donation of intellectual property by Cellectis will be made available to the rest of the GP-write consortium. Additionally, organizer Jef Boeke 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 for studying the "dark matter of the genome," a goal shared by GP-write.

At the meeting, the nine working groups presented their charters and roadmaps. Over 100 scientists volunteered their time to these efforts, and completion of these foundational documents was a significant accomplishment and a milestone for the project. Presenters and panelists held question and answer sessions following each roadmap presentation. In addition, members of the international GP-write consortium presented updates on genome writing advances in their home countries, including several large-scale investments in technologies related to GP-write. GP-write now includes affiliates in 15 countries around the world.

Finally, the Industry Advisory Board was introduced, with Labcyte, GenScript, and Twist Bioscience as founding members. These companies have agreed to provide financial and other benefits to GP-write affiliated scientists, such as discounts on instruments and technology and early access to new technologies. The meeting concluded with presentations from industry partners and meeting sponsors, followed by a press conference.

The announcements coming from the 2018 meeting garnered extensive press coverage by publications including Time, Scientific American, Nature, Science, and the MIT Technology Review. GP-write appeared in 378 total articles following the meeting, reaching 384 million readers. GP-write will continue its transparent and positive relationship with the press as a crucial mechanism for engaging with the public about genome synthesis advances.

The GP-write working groups will continue revising their strategic roadmaps in light of the discussions at the meeting, with the goal of publishing the charters and roadmaps on a public

forum in the near future. We invite you to get involved in GP-write and take part in the conversation.

#### Jef Boeke, Ph.D.

Director, Institute for Systems Genetics Professor, Department of Biochemistry and Molecular Pharmacology NYU Langone Health

Nancy J Kelley, J.D., M.P.P.
President and CEO, Nancy J Kelley &
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#### George Church, Ph.D.

Robert Winthrop Professor of Genetics, Harvard Medical School Core Faculty Member, Wyss Institute Professor of Health Sciences and Technology, Harvard and MIT Associate Faculty Member, Broad Institute

#### **Andrew Hessel**

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# **Featured Project Overview**

Jef Boeke and George Church, presenters; Boeke, Church, Farren Isaacs (Yale) and Pam Silver (Wyss Institute), panelists

GP-write is a grand challenge project with the goal of catalyzing demand for technology development in genome writing and testing. Organizers aim to reduce the cost of designing, synthesizing, assembling and testing genomes by 1,000-fold over 10 years. Such technology will enable cutting edge research and advances that will benefit all of humanity.

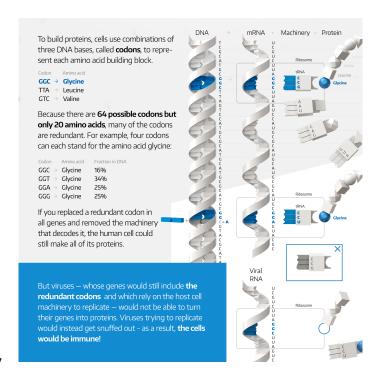
GP-write is a successor to the Human Genome Project ("GP-read"), moving from passively reading genomes to actively writing them. It is also a continuation of more recent projects, such as the Sc 2.0 effort to construct a yeast cell with an extensively engineered genome; the initiative, led by Jef Boeke and others, is now 95-98% complete. Using genome synthesis and other synthetic biology tools, researchers are able to test the functional importance of the so-called "dark matter of the genome," or the non-coding regions of unknown function which are frequently associated with disease. Separately, George Church and colleagues are using genome engineering in pigs to allow them to grow organs for human transplantation, for example by removing inherited viral sequences from the pig genome.

#### Ultra-safe cellS

The meeting began with the unveiling of the first official community project, the ultra-safe cell line. Cells may be rendered virus-proof using a process called recoding. To build proteins, cells use combinations of three DNA bases, called codons, to represent each amino acid building block. For example, the triplet 'GGC' represents the amino acid glycine, TTA represents leucine, GTC represents valine, etc. Because there are 64 possible codons but only 20 amino acids, many of the codons are redundant. For example, four codons can each stand for glycine: GGT, GGC, GGA, and GGG.

GP-write scientists aim to remove redundant codons from all genes (or 'recode' the genes) and removed the tRNA machinery that decodes it. This would allow the cell to make all of its proteins, but viruses – whose genes would still include the redundant codons and which rely on the host cell machinery to replicate – would not be able to translate their genes into proteins. Viruses trying to replicate would instead get snuffed out – as a result, the recoded cells would be immune.

The concept of recoding for viral resistance has already been demonstrated. In 2013, Lajoie and colleagues reported in <u>Science</u> that, by removing all 321 instances of a single



codon from the *E. coli* genome, they could impart resistance to viruses which use that codon. An international team, including the lab of professor George Church, is finishing the removal of six more codons from the E. coli genome, requiring a further 62,000 changes. In comparison, the GP-write proposal of an ultra-safe cell line would require at least 400,000 changes to the human genome. 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.

Ultra-safe cells could have a major impact on human health. 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. And while they are resynthesizing genes, researchers could make the cells safer in other ways, like recoding genes to make the cell less likely to become cancerous, or to resist damage from aging, freezing, and radiation. Other proposed benefits include programming the ultra-safe cells to combat cancer and using them as universal stem cell immunotherapies, or growing synthetic organs or organoids to better study three-dimensional tissues in a laboratory setting.

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.

#### **Community project selection process**

Over the past year, the scientific executive committee met and deliberated on the selection of the first community project, ultimately deciding that recoding was the best proposal. Recoding is ambitious, requiring extensive rewriting of the chosen genome, and both the end product and the new technology developments may have major scientific, health, and societal impacts. While recoding and the tools for accomplishing it would be widely applicable to all species, the scientific executive committee would likely adopt a human induced pluripotent stem cells (iPSC) as the first community project, as iPSCs can be coaxed to grow into many different cell types. Other proposals include mouse embryonic stem cells, acknowledging the major role that mice play in biomedical research, or chinese hamster ovary (CHO) cells, which are used extensively by drug manufacturers for producing pharmaceuticals.

The panelists discussed some early logistics about how the project might unfold. Taking inspiration from the successful model used by the Sc 2.0 leadership, Boeke suggested that different research groups might be assigned their own chromosome to complete, dividing the community project into manageable fragments and allowing each group the freedom to accomplish its goal in innovative ways. This approach would require an agreement at the outset of certain design schemes and engineering specifications to be standardized across the participating groups. Under this model, there would likely be one central group responsible for decision making, although all participants would have the ability to contribute to the deliberations about design choices. In Sc 2.0, there was also independent verification of the sequencing for each component that member groups delivered. Additionally, participating labs were required to raise their own funding.

"One of our criteria for picking projects was it both be intellectually interesting and practically important." - Professor George Church While maintaining a fundamental interest in technology development around genome synthesis, the scientific executive leadership thought it was important to galvanize involvement in GP-write by deciding on one overarching community project. The working group considered several alternatives to the recoded cells, including cells with mirrorimage DNA, human cells equipped with photosynthesis or other metabolic pathways, or "ancestral" human cells

containing the (presumed) original versions of all genes. Ultimately, recoding was unanimously endorsed, because it will involve the entire GP-write community and have an immediate practical impact.

Discussions also centered on the ethical dimensions of the proposed ultra-safe cell line project. For example, if the recoded cells are human in origin, which person's cells (and therefore, their genome) would form the basis of the project? Professor Church raised the possibility of including participants from the Personal Genome Project, which requires rigorous informed consent before participants can contribute their genetic information. Additionally, while industry involvement in the project is welcomed, the leadership has stressed that the advances of GP-write should be shared as widely and freely as possible. Panelists discussed patenting options, such as patent pools or unrestricted licensing, that might incentivize the participation of corporate partners while allowing researchers free access to scientific tools and data.

The next phase of the project will involve making concrete decisions about how to proceed, including who will be involved, what the design specifications will be, and how participants will raise funding.

# **Working Group Presentations**

Sharing the results of deliberations from the past year, a clear theme of the working group presentations was the interest in brokering new links between the committees, given the highly interdisciplinary nature of the project. For example, numerous working groups have been grappling with questions regarding intellectual property or public communications, as part of charting a roadmap for their specific mission. Future progress will build on the connections forged at the May 1 meeting between members of each working group.

# Ethical, Legal, and Social Implications (ELSI)

Carolyn Chapman (NYU Langone), presenter; Gigi Gronvall (Johns Hopkins), Jeantine Lunshof (MIT), Robert Smith (University of Edinburgh), panelists

In the 2016 Science commentary, various ELSI concepts were proposed, including inclusive decision-making, equitable distribution of benefits, intellectual property considerations, appropriate regulation of biohazards, and harmonization of goals shared by both scientists and the public. Subsequently, the ELSI working group, with participants including lawyers, ethicists, philosophers, scientists, and policy and biosecurity experts, have revised and expanded their mission into a charter and strategic roadmap. Stated goals include maintaining an ongoing integrated bioethics approach that is responsive to new developments; conducting reviews of the ethical landscape surrounding synthetic biology and related projects; engaging with the public around ELSI topics; and making recommendations, both to other GP-write working groups, as well as to institutional, local, state and national policymakers.

GP-write will advance the foundational tools and technologies for genome design, synthesis and testing that will have many potential future uses, many of which cannot even be imagined today. The ethical issues associated with this project should be addressed as they arise instead of debating whether

"The time for ethics is upon us."

- Carolyn Chapman

scientific progress should be stopped because of what could potentially happen in 100 years. Transparency, responsible communication, and clear goals are needed in order to respond to ethical issues in a timely manner. Public engagement in GP-write will require a new, 21st-century bioethics framework that fosters participation by the public.

Much as GP-write takes scientific inspiration from the Sc 2.0 project, so too can the ELSI group use as inspiration the statement of ethics and governance that was required of Sc 2.0 participants. Published in the journal <u>Genetics</u>, the agreement covers matters including societal benefits of Sc 2.0 inventions, relinquishing of intellectual property claims, biosafety standards, and mechanisms of governance. Panelist Robert Smith called for an evaluation of the impact of Sc 2.0 governance structures on the science that was actually undertaken.

Carolyn Chapman also explained classic bioethics frameworks and described how they would relate to GP-write, while noting that other working groups are likely grappling with the same issues. Topics raised include minimization of risk, consideration of who will bear the burden of

any externalities of GP-write, autonomy of research subjects, and alignment with societal goals and values.

Additionally, Chapman and panelist Jeantine Lunshof have engaged in "lab-based ethics," working closely with the Church and Boeke labs, respectively, as interactive ethics collaborators. Their work has led to a number of articles in <u>academic</u> as well as <u>mainstream</u> publications. Panelists also pushed for substantive engagement with the public, especially now that concrete goals of the project have been defined, and for dedicated funding for ELSI efforts.

## **Technology and Infrastructure Development**

Nili Ostrov (Harvard Medical School), presenter; Jeff Schloss (independent consultant), Axel Trefzer (Thermo Fisher), Giovanni Stracquadanio (University of Essex), and Ben Gordon (MIT-Broad Foundry), panelists

GP-write aims to reduce the cost of engineering and testing large genomes in cell lines more than 1,000-fold within 10 years. As opposed to developing a singular technology for completing GP-write projects, the technology development working group is doing the opposite: they are pursuing an inclusive, open approach by soliciting feedback from practitioners in the field about what technologies are not yet available and what are the limitations of existing technologies. To gather this feedback, they have published an <u>online survey</u> to facilitate in the needs assessment.

Conceptually, the technology roadmap is divided into four categories - design, synthesis, editing, and assembly and delivery. The technologies that fall under each category are evaluated for readiness of application to GP-write projects, e.g. those that can be deployed today, those that require improvement or investment, and those that do not yet exist.

**Computational design:** While small scale genetic engineering is common practice, more ambitious efforts are currently impractical, such as design of whole chromosomes or complex cellular functions. Collaborative design tools are being pioneered by Sc 2.0, but future improvements will be required. Ultimately, tools to accurately predict sequence-to-phenotype relationships, or to find errors in the design similar to debugging computer code, would be massively enabling for the project and for the field.

**DNA synthesis:** Small-scale DNA synthesis is quite advanced and widely commercially available, but we are currently incapable of quickly building entire chromosomes. Anticipated advances include enzymatic DNA synthesis methods, longer and faster synthesis rates, and increased parallelization and automation, with the overall goal of a 1,000-fold reduction in cost.

**Genome editing:** Existing tools, such as programmable nucleases (Cas9, TALEN, ZFN), are capable of introducing specific changes into the genome, but not at the scale that would be required for genomic recoding. Introducing large numbers of precise edits into a single chromosome in a single cell may be accomplished either by advances using current tools, or by developing novel genome writing tools that operate within cells.

Ideally, improved editing will obviate the need to make large stretches of synthetic DNA from scratch.

Assembly and delivery: Technology for inserting large fragments of DNA into living cells, for example entire chromosomes, is currently the least developed of the four categories. Techniques for insertion into budding yeast do exist, but future advances may allow for rapid delivery and assembly of DNA into the desired host cells on the scale of millions of base pairs. Other challenges include ensuring that synthetic DNA behaves the same as natural DNA, such as properly dividing when cells reproduce, adopting an appropriate three-dimensional structure in the nucleus, and joining with proteins that typically attach to the genome.

Panelists spoke of the robust participation and excitement in their working group, expressing optimism about achieving the goal of a major reduction in synthesis costs by noting that much of the technology currently in use is decades old, and could be due for an overhaul. To achieve its goals, the technology development group will need to collaborate closely with those who are designing and implementing the community projects.

#### **High Performance Computing and Bioinformatics**

Chris Dwan (Bridgeplate), presenter; Jake Beal (BBN Raytheon), Bryan Bishop (LedgerX), panelists

In similarly audacious projects, such as the Human Genome Project (HGP), HapMap, ENCODE, and TCGA, information technology has been a crucial enabler. However, it has also been a regular source of tension, frustration, and unexpected expense. For example, 3% of the HGP budget was initially set aside for information technology; by the final accounting, it had consumed around 30% of the funding. By learning from the example of GP-write's predecessors, the working group hopes to avoid or mitigate many of these struggles.

"Hopefully our challenges of scale will not come from the IT side."

- Chris Dwan

Technologies that other working groups aspire to develop, such as predicting protein expression from DNA sequences, are currently at the edge of human capability. Rapid advances in computing are poised to aid and enable the efforts of GP-write. For example, machine learning or artificial intelligence may yield insights for researchers that

humans wouldn't be capable of identifying in very large data sets. Blockchain is another emerging technology with major implications for a collaborative, international scientific project such as GP-write. Attendees were warned to tune out some of the hype about emerging computer science, and to keep in mind that algorithms cannot remove the mistakes from a low quality data set; as the saying goes, "garbage in, garbage out."

One information technology challenge identified in the group roadmap is the need for authorized access to data while maintaining openness, trust, and accountability. This ties in with the need to ensure that GP-write data is used appropriately: that privacy rules are being adhered to with

regards to sensitive human data, and that clear rules governing the chain of custody of information are established. Panelists also discussed best practices for ways that IT professionals can complement academic groups in analyzing and disseminating data for GP-write and other large collaborations. These included creating forward-thinking that is reusable, flexible, and matches the functional needs of the practicing scientists. At the same time, the working group chair Chris Dwan expressed his belief that a centralized system for storing or manipulating data would be unwise and unworkable for a large, complex project such as GP-write. A federated system of distinct computer programs that can nonetheless communicate with each other provides an excellent model for how GP-write may proceed. Such an approach warrants an investment in thoughtful metadata standards to facilitate the searching and sharing of the associated data.

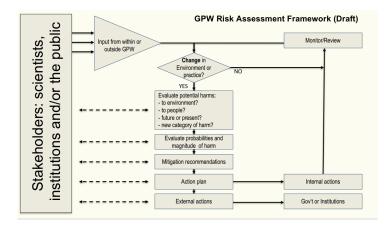
# Safety Engineering

Farren Isaacs (Yale), presenter; Daisuke Kiga (Waseda University), Neal Stewart (University of Tennessee), Peter Carr (Lincoln Laboratory), Brad Schmier (Memorial Sloan Kettering), and Michael Chou (Harvard Medical School), panelists

Safety considerations are common to all biomedical research, not just that associated with GP-write, but the safety engineering working group aims to identify and address the unique aspects of the project, falling into the categories of risk assessment, technical safeguards, and safety. Significantly, success at installing safeguards in genetically modified organisms to protect researchers, the public, and the environment will enable their broad and safe use and expand the impact of GP-write. To assess these risks, the group plans to take inspiration from existing

infrastructure around safety, for example the university regulations on biosafety, which were themselves inspired by the 1975 Asilomar meeting about the ethics and safety of recombinant DNA. At the meeting, a draft safety engineering decision tree for GP-write was proposed, incorporating systems of governance and input from numerous stakeholders, including the public.

Current defense methods inside the lab include the use of lab-confined cells (e.g.



modified cells that cannot replicate outside of a Petri dish) and physical safeguards such as biosafety cabinets, while biocontainment strategies, like sterile seeds in GMO plants, prevent unwanted expansion in open systems such as agriculture. Newly developed techniques from synthetic biology were also discussed, including engineered genomic 'kill switches' to prevent from cells from escaping the lab. Additionally, it was pointed out that recoding, as laid out in the community project proposal, is naturally inclined towards biocontainment, because the recoded organism could be engineered to depend on a synthetic nutrient supplied by the researcher. Even still, the technology that GP-write pioneers may enable others to create modified

organisms without such safeguards, and an important discussion for the group going forward will center around how to proceed responsibly with future capabilities in mind.

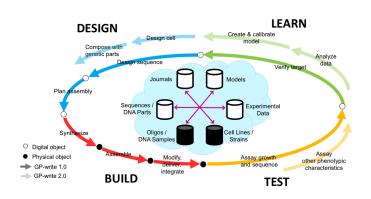
While the group is committed to maximum responsibility and transparency, panelists stressed the importance of facilitating a public conversation that doesn't give a disproportionate degree of fear about GP-write, instead assigning realistic probabilities about potential risks. As an example, community science organizations have been an important venue for the public to interact with scientists and gain a better understanding of scientific process and safeguards.

## Standards, Quality Control, and Reporting

Jake Beal (BBN Raytheon), presenter; Leslie Mitchell (NYU Langone), Bryan Bartley (BBN Raytheon) and Jonathan Karr (Icahn Institute), panelists

In the coming years, GP-write could potentially involve many different individuals in varying roles across multiple simultaneous projects, and the field of genome engineering could experience major improvements in technology and shifting bottlenecks, e.g. from synthesis cost to genome design challenges. Therefore, the decisions made today about technical standards could have major ramifications for GP-write, and the working group presented its framework regarding how it plans to approach this important topic.

For example, the standards working group proposed a map of the various anticipated conceptual steps taken by project participants, noting points in the process at which groups will likely interface and therefore share data or materials that may be standardized. Additionally, project participants will interact with various databases or repositories, where standards may be desirable. For each of these steps, the working group recommended several options: adopt an existing standard, extend an existing one to the particulars of GP-



write, or create a new one when necessary. For problems with greater uncertainty or a longer time frame, the group recommends waiting until making standardization decisions when they become necessary. Maximizing the usefulness of the standards will require working with all of the stakeholders in the project, including scientists exchanging materials and bioinformaticians performing modeling of engineered cells.

#### **Intellectual Property**

Kristin Neuman (MPEGLA), presenter; Bryan Bishop (LedgerX), Amy Schwartz (Center of Excellence for Engineering Biology), panelists

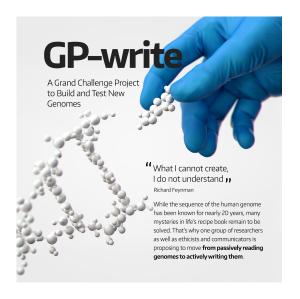
"Sharing" and "access" are the key words adopted by the intellectual property working group with regards to the inventions coming from GP-write. There should be a level playing field for all GP-write participants – from citizen scientists to academic institutions to corporations – to collaborate on scientific discovery and technology development. Creating this level playing field, however, will require balancing appropriate incentivization for industry to engage and invest in desirable, downstream commercial development of products and services based on the output from GP-write.

Working group chair Kristin Neuman presented a statement of principles and policies that GP-write participants might adopt, including a pledge of IP-nonassertion for some types of research, a framework for how GP-write will handle IP factors like patents and trade secrets, expectations and requirements for material exchange, and considerations of the ethical and social aspects of GP-write IP. The announcement of the first community project will be helpful in that it could provide a blueprint around which to model the intellectual property framework, which could then be adapted for future projects. Ultimately, there is a strong desire for friction-free transfer of data and materials between scientists, as well as with the public.

#### Public Communications and Outreach

Jeff Bessen (Harvard), presenter

GP-write has benefited from recent positive press, including cover stories in WIRED Magazine and Newsweek. While the scientific news media is an important mechanism for interacting with the public, the communications working group has been building up its capabilities for producing its own content and messaging. To that end, two original scientific infographics were unveiled at the meeting, with one covering the aims and methods of GP-write, and the other explaining the first community project, the virus-proof cell. GP-write outreach should be guided by several core operating principles, including



transparency, scientific accuracy, clarity and simplicity, and acknowledging the values of the target audience. Public communications efforts will be critical for facilitating the ELSI debate about GP-write with the public.

The communications group is tasked with conveying key messages about GP-write to the public, including the goals and anticipated benefits of the project, the wide range of stakeholders involved, the commitment to transparency and openness, and the credibility of the Center of Excellence for Engineering Biology as the parent organization of GP-write. In practice, these messages may be spread through activities such as coordinating with the press, working with external partners such as universities or museums, and posting on social media. In the future, outreach may take the form of something more ambitious, such as a video game based around genome engineering.

#### **Education**

Ellen Jorgensen (Biotech Without Borders), presenter

Educating non-scientists about DNA and genome engineering is a crucial part of helping the public understand the advances that GP-write hopes to accomplish. Educational materials may also improve the profile of DNA-based science and spread awareness of the large impact that synthetic biology and genetic engineering has on the clothes people wear, the food they eat, the medicines they take, and the plastics they use every day. This broader awareness may then feed into excitement about the bold aims of GP-write scientists.

The output of the education working group may take the form of curricula geared towards different grade levels of students, incorporating science education as well as the ethical and social implications of the research. Educational materials will be high quality, engaging, and accessible to as many students as possible, not just those with in advanced class with access to expensive scientific instruments. There already exist numerous similar educational initiatives from which to draw materials and inspiration.

#### **GP-write International Presentations**

Around the globe, national governments, local governments, industry partners, and academic institutions have recognized the future promise of synthetic biology research, and have prioritized funding for scientists and infrastructure in areas such as genome engineering.

#### **Australia**

Natalie Curach, Macquarie University

Macquarie University has a strong synthetic biology presence, including contributions to the Sc 2.0 project, and the university considers synthetic biology a "future-shaping



research priority," with strong support from the government of New South Wales. Macquarie is in the process of gathering support for the first national genome foundry. Universities across Australia and New Zealand have been participating in synthetic biology for some time, and the consortium CSIRO has established a \$13M investment in synthetic biology. At the national level, the Australian government is currently drafting a national science agenda on synthetic biology and the accompanying infrastructure. Additionally, researchers have assembled to form the Synthetic Biology Australian association, hosting regular meetings, and in late 2018, the next Sc 2.0 meeting will be held in Sydney.

#### **Brazil**

Elibio Rech. EMBRAPA

As a member of the National Institute of Science and Technology on Synthetic Biology, Elibio Rech described his involvement in several Brazilian synthetic biology initiatives. These include engineering of the soy genome enabled by predictive modeling and systems-level understanding, using DNA-modifying proteins to control gene regulation in plant and mammalian cells, and producing "mini-chromosomes" to deliver large DNA fragments into plants.

#### Canada

Bogumil J. Karas, Western University, and Peter Zandstra, University of British Columbia

Numerous research teams across Canada are engaging in synthetic biology research of relevance to GP-write, including new methods for storing and transferring large fragments of DNA and for automating genome editing. The University of Concordia is host to the Centre for Applied Synthetic Biology, including Canada's only genome and synthetic biology foundry. In recognition of the growing interest in Canada, the first GP-write Canada meeting has been scheduled in August 2018.

#### China

Bing-Zhi Liu, Tianjin University

Chinese academics have played major roles in previous international genome engineering collaborations, including work on 6 of the 16 chromosomes for the Sc 2.0 initiative. In recognition of this leadership in synthetic biology, the national government has established a national policy on synthetic biology, including approximately \$360M USD in grants for research. The program on synthetic biology roadmap calls for grant applications pertaining to fundamental research in genome synthesis, technology development, and industry and medical applications. Numerous Chinese universities have made major investments in synthetic biology throughout the country.

#### India

Binay Panda, Ganit Labs

Binay Panda of Ganit Labs, which began in 2010 as a non-profit genome science center in Bangalore, presented an application of synthetic biology research: the study of natural chemical production by native Indian trees. Delhi will host a genome engineering meeting in December 2018.

#### Japan

Yasunori Aizawa, Tokyo Institute of Technology

The Japanese Science and Technology Agency has established a national project called "Large-scale genome synthesis and cell programming," advised by leading scientists with expertise throughout the various synthetic biology disciplines. The amount of funding for the next 7.5 years is approximately \$50 million which will be provided to 15 senior and 25 young researchers. At the university level, professors at Tokyo Institute of Technology participated in the synthesis of chromosome 4 in the Sc 2.0 project, and several labs have joined with industry partners to form the Genome Architect Group.

### **Singapore**

Jee Loon Foo, National University of Singapore

Singapore aims to be a leading hub for synthetic biology, encouraging partnerships between academic and industry partners under the umbrella of the NUS Bio-Foundry. Researchers have partnered up with clinicians to address diabetes, for example, which could have a major impact on the country in the coming decades. With regards to genome engineering, researchers are currently pursuing modifications to microbes in the human gut, and additionally, NUS scientists helped construct chromosome 15 for the Sc 2.0 project.

## **United Kingdom**

Susan J. Rosser, University of Edinburgh

THe UK published its synthetic biology roadmap in 2012, which called for interdisciplinary research in synthetic biology and an increase in UK DNA synthesis capacity. The government has committed over \$90M USD to synthetic biology centers in the UK, as well as \$24M for four DNA foundries. The Edinburgh Genome Foundry, for example, can produce large DNA fragments using its highly automated platform. In addition, the Wellcome Trust Sanger Institute has prioritized numerous scientific goals shared by GP-write genome engineers. Upcoming meetings include the International Foundries Meeting at Imperial College in June 2018, and a planned UK Synthetic Genomics workshop.

# **Industry Partnerships**

# **Industry Advisory Board**

The May working group meeting saw the announcement of the GP-write Industry Advisory Board. The founding members are Labcyte, GenScript, and Twist Bioscience. These companies have agreed to provide financial and other benefits to GP-write affiliated scientists, such as discounts on instruments and technology and early access to new technologies. In addition, representatives from Thermo Fisher Scientific, SBOL, and DNA Script expressed their interest in working with GP-write scientists.

#### **Collaboration with Cellectis**

Cellectis CEO André Choulika announced a partnership between the clinical-stage biopharmaceutical company, which focuses on developing immunotherapies, and Professor George Church of GP-write and the Wyss Institute of Harvard University. Under the collaboration, Church and other GP-write scientists will be given access to the company's TALEN genome editing tools to accelerate the pace of genome-scale modifications.

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