

5.0

GP-write Virtual Conference
October 21-22, 2021



CENTER of EXCELLENCE
for ENGINEERING BIOLOGY



GP-write



Welcome!

Welcome to GP-write 5.0, our first virtual conference. Since our last meeting in 2019, we have launched GP-write Technology, formed Industrial Advisory Board, and developed a whole genome CAD design platform in collaboration with Lattice Automation. We look forward to demonstrating the first version with you at this Conference.

We have an exciting line-up of keynote speakers and global leaders in their fields presenting recent advances in their research. Lightning talk presenters from around the world will share innovative ideas followed by Poster Sessions.

The interactive Gather Town platform will host the Poster Sessions, Biosecurity Roundtable, and offer fun and engaging ways to interact socially in real-time, network, and have lunch on the beach, and even teleport directly into the presentation room!

We hope you enjoy the updates on key scientific and technological advances and have opportunities to participate and interact with colleagues. Thank you for your ongoing support and interest in the mission of Genome Project-write: writing genomes for a better future.

The Leadership Team,

George Church, Andrew Hessel, Farren Isaacs,
Todd Peterson and Amy Cayne Schwartz

Agenda

All times listed in Eastern Standard Time (EST)

Day 1: Thursday, October 21, 2021

10:30 Introduction and Welcome Remarks

Amy Cayne Schwartz, J.D., President of GP-write

Session 1: Genome Design & Foundries

Moderator: Farren Isaacs, Ph.D., Yale University

10:40 Keynote Presentation: Multiplex Writing & Editing Genomes & Epigenomes

George Church, Ph.D., Harvard Medical School

11:30 The Role of Biofoundries in Genome Engineering

Paul Freemont, PhD, Imperial College

12:00 Genome Project-write's Next-Generation Genome Design Platform

Douglas Densmore, PhD, Boston University

Session 2: Lightning Talks

Construction of a Synthetic 57-Codon E. coli and Tools for Microbial Genome-Scale Recoding

Akos Nyerges, Harvard Medical School

Evaluation of serine-integrases activity as genome editing tools in the synthetic minimal cell Mycoplasma mycoides JCVI-Syn3B

Marco de Oliveira, National Institute of Science in Synthetic Biology/EMBRAPA

Nanofluidic sequence-specific sorting of single DNA molecules: The autonomous retrieval of specific DNA sequences from a heterogeneous pool of single-stranded DNA molecules

Hatem Mohamed Gaber Abdelrahman, Zewail City of Science and Technology

Targeted editing and evolution of repetitive genetic elements by filtered editing

Felix Radford, Yale University

Synthetic genomes reveal coupling between transcriptional neighbourhood and transcript isoform expression

Amanda Hughes, EMBL

Development of RNA Biosensors to Detect Cancer Biomarkers Using Cell Free System

Milca Rachel da Costa Ribeiro Lins, Sao Paulo State University (UNESP)

Computational design advances (GPW-CAD)

Hugo Lins de Albuquerque Vieira, Department of Genetics and Morphology, University of Brasília

Mammalian Genome Engineering

Ralf Kuehn, Max-Delbrueck-Center for Molecular Medicine, Berlin, Germany

1:00–2:00 Lunch Break [Gather.Town platform]

**1:00–2:00 Poster Sessions and Sponsor Booths
[Gather.Town platform]**

Session 3: Eukaryotic & Mammalian Genome Engineering

Moderator: June Medford, Ph.D., Colorado State University

2:00 Engineering Next-Generation T Cells for Cancer Immunotherapy

Yvonne Chen, Ph.D., UCLA

2:30 Mammalian Cell Design Using Synthetic Biology

Wilson Wong, Ph.D., Boston University

3:00 Driving epigenetic centromere establishment to facilitate mammalian chromosome engineering

Ben Black, Ph.D., University of Pennsylvania

3:30 Dissecting phenotypes: lessons from functional genomics and synthetic biology

Lars Steinmetz, Ph.D., Stanford University

4:00 Coffee Break and Posters

[Gather.Town platform]

4:30–5:15 Keynote Presentation: The Chemistry of CRISPR for Genome Editing and Detection

Jennifer Doudna, Ph.D., UC Berkeley

5:30 Day 1 Closing Remarks and Adjourn

Day 2: Friday, October 22, 2021

Session 4: Engineering Microbes & Communities

10:00 Welcome Back Remarks

Moderator: Junbiao Dai, Ph.D., Shenzhen Institute of Advanced Technology

10:10 The Journey with Gene Editing Technologies - Xenotransplantation & Cell Therapy Research

Luhan Yang, Ph.D., CEO and Co-Founder of Qihan Biotech

10:40 Designing Biology for Health and Sustainability

Pam Silver, Ph.D., Harvard Medical School

11:10 Controlling gene expression in Bacteria with CRISPR-Cas systems

David Bikard, Ph.D., Pasteur Institute

11:40 Organs on Chips and Future Medicine

Jianhua Qin, Ph.D., Dalian Institute of Chemical Physics, Chinese Academy of Sciences

Session 5: Lightning Talks

Synthetic Biology Software

Matheus de Castro Leitão, Institute of Biological Sciences, University of Brasilia, Brazil

Synthetic Spidroin Production from *Parawixia bistrata* by TXTL system

Valquiria Michalczechen, National Institute of Science in Synthetic Biology/EMBRAPA

Future Organisms: Synthetic Genomics and Responsible Research and Innovation in the UK, the USA and Japan

Robert Smith, University of Edinburgh

Genetic Code Engineering Metrics and Biosafety

Markus Schmidt, BioFaction

Re-write the Yeast Genome for Customised Biosynthesis Control

Xinyu Lu, Imperial College

Synthetic Biology In Pursuit Of The Minimal Cell Cycle

Anastasiya Malyshava, Imperial College

12:30–1:30 Lunch Break [Gather.Town platform]

**12:30–1:30 Poster Sessions and Sponsor Booths
[Gather.Town platform]**

**12:30–1:00 Biosecurity Roundtable: Sponsored by DNA Script
[Gather.Town platform]**

Keynote Presentation

Moderator: Virginia Cornish, Ph.D., Columbia University

**1:30 Keynote Presentation: Base Editing and Prime Editing: Precision Chemistry
on the Genome Without Double-Strand DNA Breaks**
David Liu, Ph.D., Harvard University and The Broad Institute

Session 6: Communities and Ethics in Genome Engineering

2:30 Building Microbial Communities to Understand Community Dynamics and Functions
Ophelia Venturelli, Ph.D., University of Wisconsin, Madison

3:00 Ethical and Regulatory Considerations of Writing Genomes
Barbara Evans, J.D., Ph.D., University of Florida

**3:30–4:00 Coffee Break and Sponsor Booths, Poster Sessions
[Gather.Town platform]**

4:00 Keynote Presentation: Writing the Future with Synthetic DNA
Emily Leproust, Ph.D., Twist Bioscience

5:00 Closing Remarks and Adjourn



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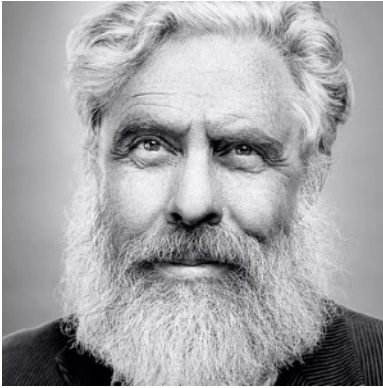
Keynotes



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George Church, Ph.D.

George M. Church, PhD '84, is professor of genetics at Harvard Medical School, a founding member of the Wyss Institute, and director of PersonalGenomes.org, the world's only open-access information on human genomic, environmental, and trait data.

Church is known for pioneering the fields of personal genomics and synthetic biology. He developed the first methods for the first genome sequence & dramatic cost reductions since then (down from \$3 billion to \$600), contributing to nearly all “next generation sequencing” methods and companies. His team invented CRISPR for human stem cell genome editing and other synthetic biology technologies and applications – including new ways to create organs for transplantation, gene therapies for aging reversal, and gene drives to eliminate Lyme Disease and Malaria.

Church is director of IARPA & NIH BRAIN Projects and National Institutes of Health Center for Excellence in Genomic Science. He has co-authored more than 590 papers and 155 patent publications, and one book, “Regenesis”. His honors include Franklin Bower Laureate for Achievement in Science, the Time 100, and election to the National Academies of Sciences and Engineering.

Multiplex Writing & Editing Genomes & Epigenomes

Genome-wide recoding enables secure bio-isolation, new amino acids and multi-virus resistance -- probably in any species. We can also engineer highly repetitive DNA and chirality. To make these tasks easier we are testing combinations of precise edits and large syntheses. We have rates exceeding 22,000 edits per human stem cell (per single transfection). We are designing and testing combinations of genetic and epigenetic diversity in large libraries (informing and informed by machine learning).



Jennifer Doudna, Ph.D.

HHMI Investigator Li Ka Shing Chancellor's Chair in Biomedical and Health Sciences Professor, Depts. of Molecular & Cell Biology and Chemistry UC Berkeley

Dr. Jennifer A. Doudna is the Li Ka Shing Chancellor's Chair and a Professor in the Departments of Chemistry and of Molecular and Cell Biology at the University of California, Berkeley. Her groundbreaking development of CRISPR-Cas9 as a genome-engineering technology, with collaborator Emmanuelle Charpentier, earned the two the 2020 Nobel Prize in Chemistry and forever changed the course of human and agricultural genomics research.

This powerful technology enables scientists to change DNA — the code of life — with a precision only dreamed of just a few years ago. Labs worldwide have re-directed the course of their research programs to incorporate this new tool, creating a CRISPR revolution with huge implications across biology and medicine.

In addition to her scientific achievements, Doudna is a leader in public discussion of the ethical implications of genome editing for human biology and societies, and advocates for thoughtful approaches to the development of policies around the safe use of CRISPR technology.

Doudna is an investigator with the Howard Hughes Medical Institute, senior investigator at Gladstone Institutes, and the President of the Innovative Genomics Institute. She co-founded and serves on the advisory panel of several companies that use CRISPR technology in unique ways.

She is a member of the National Academy of Sciences, the National Academy of Medicine, the National Academy of Inventors, and the American Academy of Arts and Sciences. Doudna is also a Foreign Member of the Royal Society and has received numerous other honors including the Breakthrough Prize in Life Sciences (2015), the Japan Prize (2016), Kavli Prize (2018), the LUI Che Woo Welfare Betterment Prize (2019), and the Wolf Prize in Medicine (2020). Doudna's work led TIME to recognize her as one of the "100 Most Influential People" in 2015 and a runner-up for "Person of the Year" in 2016. She is the co-author of "A Crack in Creation," a personal account of her research and the societal and ethical implications of gene editing.

The Chemistry of CRISPR for Genome Editing and Detection

Fundamental research to understand how bacteria fight viral infections uncovered the function of CRISPR-Cas programmable proteins that detect and cut specific DNA or RNA sequences. I will discuss current research to develop and deploy genome editing molecules for biomedical and other applications. I will also discuss the development of CRISPR-based diagnostics technology to address the current pandemic and improve future preparedness.



David Liu, Ph.D.

Richard Merkin Professor and Director of the Merkin Institute of Transformative Technologies in Healthcare Core Institute Member and Vice-Chair of the Faculty, Broad Institute Thomas Cabot Professor of the Natural Sciences, and Professor of Chemistry & Chemical Biology, Harvard University Investigator, Howard Hughes Medical Institute

David R. Liu's research integrates chemistry and evolution to illuminate biology and enable next-generation therapeutics. His major research interests include the engineering, evolution, and in vivo delivery of genome editing proteins such as base editors to study and treat genetic diseases; the evolution of proteins with novel therapeutic potential using phage-assisted continuous evolution (PACE); and the discovery of bioactive synthetic small molecules and synthetic polymers using DNA-templated organic synthesis and DNA-encoded libraries. Base editing (named one of four 2017 Breakthrough of the Year finalists by Science), prime editing, PACE, and DNA-templated synthesis are four examples of technologies pioneered in his laboratory. Liu graduated first in his class at Harvard in 1994. He performed organic and bioorganic chemistry research on sterol biosynthesis under Professor E. J. Corey's guidance as an undergraduate. During his Ph.D. research with Professor Peter Schultz at U. C. Berkeley, Liu initiated the first general effort to expand the genetic code in living cells. He earned his Ph.D. in 1999 and became assistant professor of chemistry and chemical biology at Harvard University in the same year. He was promoted to associate professor in 2003 and to full professor in 2005. Liu became a Howard Hughes Medical Institute investigator in 2005 and joined the JASONS, academic science advisors to the U.S. government, in 2009. Liu has been elected a member of the U.S. National Academy of Sciences, the U.S. National Academy of Medicine and fellow of the American Association for the Advancement of Science. He has earned several university-wide distinctions for teaching at Harvard, including the Joseph R. Levenson Memorial Teaching Prize, the Roslyn Abramson Award, and a Harvard College Professorship. Liu has published more than 200 papers and is the inventor on more than 75 issued U.S. patents. His research accomplishments have earned distinctions including the Ronald Breslow Award for Biomimetic Chemistry, the American Chemical Society David Perlman Award, ACS Chemical Biology Award, the American Chemical Society Pure Chemistry Award, the Arthur Cope Young Scholar Award, the NIH Marshall Nirenberg Lecturer, and awards from the Sloan Foundation, Beckman Foundation, NSF CAREER Program, and Searle Scholars Program. In 2016 and 2019 he was named one of the Top 20 Translational Researchers in the world by Nature Biotechnology, and in 2017 was named one of Nature's 10 researchers in world and to the Foreign Policy Leading Global Thinkers. He is the scientific founder or co-founder of several biotechnology and therapeutics companies, including Beam Therapeutics, Prime Medicine, Editas Medicine, Pairwise Plants, Exo Therapeutics, and Chroma Medicine.

Base Editing and Prime Editing: Precision Chemistry on the Genome Without Double-Strand DNA Breaks

In this lecture I describe the development and therapeutic application in animals of two precision gene editing technologies that perform chemistry on the genome of living cells without requiring double-strand DNA breaks. We developed base editors, proteins that enable point mutations to be installed or corrected at target positions in genomic DNA. We also engineered a mitochondrial base editor that enables the first purposeful changes in the sequence of mitochondrial DNA of living cells. By integrating base editors with ex vivo and in vivo delivery strategies, we have addressed animal models of human genetic diseases including sickle-cell disease and progeria, resulting in rescue of these diseases in mice. I will also describe prime editing, a gene editing technology that directly writes new genetic information into a specified DNA site without requiring double-strand DNA breaks. Prime editing can mediate any base substitutions, small insertions, and/or small deletions in living cells in vitro and in vivo, and has also been applied for therapeutic correction of pathogenic alleles. Illuminating the cellular determinants of prime editing outcomes has led to next-generation prime editing systems with enhanced editing efficiency and product purity.



Emily Leproust, Ph.D.

CEO and co-founder of Twist Bioscience

As an early pioneer in the high-throughput synthesis and sequencing of DNA, Dr. Leproust is disrupting markets to enable the exponential growth of DNA-based applications including chemicals/materials, diagnostics, therapeutics, food and digital data storage. In 2020, BIO presented her with the Rosalind Franklin Award for Leadership. Foreign Policy named her one of their 100 Leading Global Thinkers and Fast Company named her one of the

Most Creative People in Business. Prior to Twist Bioscience, she held escalating positions at Agilent Technologies where she architected the successful SureSelect product line that lowered the cost of sequencing and elucidated mechanisms responsible for dozens of Mendelian diseases. She also developed the Oligo Library Synthesis technology, where she initiated and led product and business development activities for the team. Dr. Leproust designed and developed multiple commercial synthesis platforms to streamline microarray manufacturing and fabrication. She serves on the Board of Directors of CM Life Sciences and is a co-founder of Petri, an accelerator for start-ups at the forefront of engineering and biology.

Dr. Leproust has published over 30 peer-reviewed papers – many on applications of synthetic DNA, and is the author of numerous patents. She earned her Ph.D. in Organic Chemistry from University of Houston and her M.Sc. in Industrial Chemistry from the Lyon School of Industrial Chemistry.

Writing the Future with Synthetic DNA

Emily will discuss the innovation around DNA synthesis, or "writing," touching on the newest applications including storing digital data in DNA, the applications of DNA writing on drug discovery, how long oligonucleotides can enable double CRISPR screens and what is to come from Twist to serve the GP Write community.



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Speakers



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Paul Freemont, Ph.D.

Imperial College, Biofoundry

Professor Paul Freemont is the co-founder of the Imperial College Centre for Synthetic Biology and Innovation and co-founder and co-director of the National UK Innovation and Knowledge Centre for Synthetic Biology (SynbiCITE; since 2013) and co-director of the London BioFoundry (since 2016) at Imperial College London. He is also currently the Head of the Section of Structural and Synthetic Biology in the Department of Infectious Diseases at Imperial College. He was previously the Head of the Division of Molecular Biosciences and Centre for Structural Biology having joined Imperial from Cancer Research UK London Research Institute (now known as the Crick Research Institute) where he was a Principle Investigator and Head of Group. His research interests are focused on developing synthetic biology foundational tools, automation and biofoundries and cell-free systems for specific applications including biosensing and metabolic engineering. He is author of over 270 scientific publications and is an elected member of European Molecular Biology Organisation and Fellow of the Royal Society of Biology, Royal Society of Chemistry and Royal Society of Medicine and is an Honorary Fellow of the Royal College of Art. He was a co-author of the British Government's UK Synthetic Biology Roadmap and was a recent member of the Ad Hoc Technical Expert Group (AHTEG) on synthetic biology for the United Nations Convention for Biological Diversity (UN-CBD).

The role of Biofoundries in Genome Engineering

Synthetic biology is an interdisciplinary field that is primarily built upon foundational advances in molecular biology combined with engineering design. The field considers living systems as programmable at the genetic level and has been defined by the development of new platform technologies, automation and data-driven design. Synthetic genomics is a key area of intense research with the design and assembly of genome's and chromosomes for both fundamental biological understanding as well as specific biotechnology applications. These activities have spurred a rapid growth in the development of Biofoundries comprising integrated automation infrastructure for synthetic biology workflows aimed at accelerating the synthetic biology design cycle. This rapid growth has led to the foundation of the Global Biofoundry Alliance comprising 30 non-for-profit academic biofoundries worldwide. In this talk I will discuss the objectives of the GBA and illustrate how biofoundries can accelerate genome writing. I will also briefly show how biofoundries can be pivoted to provide emergency infrastructure in a global pandemic.



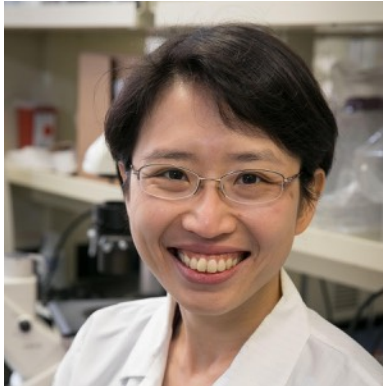
Doug Densmore, Ph.D.

Boston University

Douglas Densmore is a Kern Faculty Fellow, a Hariri Institute for Computing and Computational Science and Engineering Faculty Fellow, and Associate Professor in the Department of Electrical and Computer Engineering at Boston University. His research focuses on the development of tools for the specification, design, assembly, and test of synthetic biological systems. He aims to raise the level of abstraction in synthetic biology by employing standardized biological part-based designs which leverage domain-specific languages, constraint-based genetic circuit composition, visual editing environments, microfluidics, and automated DNA assembly. This leads to a new research area he calls “Hardware, Software, Wetware Co-design”. He is the director of the Cross-disciplinary Integration of Design Automation Research (CIDAR) group at Boston University, where his team of staff scientists, postdoctoral researchers, graduate students, and undergraduate interns develop computational and experimental tools for synthetic biology. He is the lead PI for the NSF Expeditions “Living Computing Project” and a Senior Member of the IEEE and ACM. He is also the founder of the “Design, Automation, Manufacturing, and Prototyping” (DAMP) lab. He has co-founded three commercial synthetic biology-based companies (Lattice Automation, Asimov, and Biosens8). He is a co-founder and board member of the non-profit Nona Research Foundation and the non-profit Bio-Design Automation Consortium.

Genome Project-write: Next-gen CAD

This talk will outline the collaboration between GP Write and Lattice Automation to design, build, and deploy a state-of-the-art computer-aided design platform for genome design. In addition to a demo of the software progress to date, this talk will discuss the challenges around biosecurity, connections to external service providers, hosting remote applications, and performance at the genome-scale. The talk will conclude with the features to be added in subsequent engagements and how the community can best contribute to this effort.



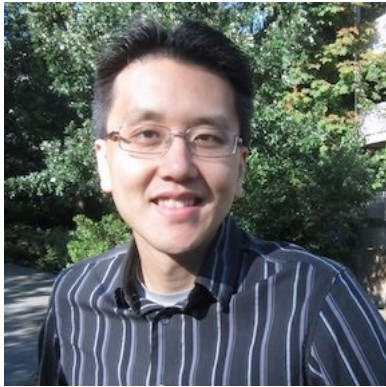
Yvonne Chen, Ph.D.

Associate Professor of Microbiology, Immunology, and Molecular Genetics, University of California, Los Angeles

Dr. Yvonne Chen is an Associate Professor of Microbiology, Immunology, and Molecular Genetics at the University of California, Los Angeles. She is also a faculty, by courtesy, in the Department of Chemical and Biomolecular Engineering. Yvonne is also the co-director of the Tumor Immunology program in the Jonsson Comprehensive Cancer Center at UCLA, and a member researcher of the Parker Institute for Cancer Immunotherapy. The Chen Laboratory applies synthetic biology and biomolecular engineering techniques to the development of novel mammalian-cell systems for clinical use, and led the first investigator-initiated clinical trial on CAR-T cell therapy at UCLA. The Chen Lab's work on engineering next-generation T-cell therapies for cancer has been recognized by the NIH Director's Early Independence Award, the NSF CAREER Award, the Hellman Fellowship, the ACGT Young Investigator Award in Cell and Gene Therapy for Cancer, the Mark Foundation Emerging Leader Award, and the Cancer Research Institute Lloyd J. Old STAR Award. Prior to joining UCLA in 2013, Yvonne was a Junior Fellow in the Harvard Society of Fellows. She received postdoctoral training at the Seattle Children's Research Institute, and in the Department of Systems Biology at Harvard Medical School. Yvonne received her B.S. in Chemical Engineering from Stanford University and her Ph.D. in Chemical Engineering from the California Institute of Technology.

Engineering Next-Generation T Cells for Cancer Immunotherapy

The adoptive transfer of T cells expressing chimeric antigen receptors (CARs) has demonstrated clinical efficacy in the treatment of advanced cancers, with anti-CD19 CAR-T cells achieving up to 90% complete remission among patients with relapsed B-cell malignancies. However, challenges such as antigen escape and immunosuppression limit the long-term efficacy of adoptive T-cell therapy. Here, I will discuss the development of and clinical data on next-generation T cells that can target multiple cancer antigens and resist antigen escape. I will also present recent work on tuning CAR signaling activities via rational protein design to achieve greater *in vivo* anti-tumor efficacy. This presentation will highlight the potential of synthetic biology in generating novel mammalian cell systems with multifunctional outputs for therapeutic applications.



Wilson Wong, Ph.D.

Boston University

Wilson Wong is an Associate Professor in the Biomedical Engineering Department at Boston University, and a core member of the BU Biological Design Center. His lab is focused on developing synthetic biology tools in mammalian systems for cell-based immunotherapy. He received his B.S. degree in Chemical Engineering from UC Berkeley and a Ph.D. degree in Chemical Engineering from UCLA under the guidance from Dr. James Liao. He

did his postdoctoral work with Dr. Wendell Lim and Arthur Weiss at UCSF. He is the recipient of the NIH Director's New Innovator and NSF CAREER Award.

Mammalian Cell Design Using Synthetic Biology

Genetically engineered cells hold great promise for improving therapeutics, diagnostics, animal models, and industrial biotechnological processes. Here I will describe our efforts in engineering powerful and versatile genetic circuits for improving the safety and efficacy of cell and gene therapy. I will also share some of our recent work on designing genetic circuits for enhancing chemical and CRISPR screens.



Ben Black, Ph.D.
University of Pennsylvania

Following undergraduate studies at Carleton College, Ben Black did a Ph.D. dissertation at the University of Virginia on pathways for nuclear protein export in the lab of Bryce Paschal. After a four-year postdoctoral fellowship with Don Cleveland at UCSD in the Ludwig Institute for Cancer Research, Ben started his own group at UPenn to continue the work he had started in the area of chromosome biology. At UPenn, Ben is the Eldridge Reeves Johnson Foundation

Professor of Biochemistry & Biophysics, co-director of the Penn Center for Genome Integrity, co-director of Penn's graduate training program in Structural Biology & Molecular Biophysics, and member of the Penn Epigenetics Institute and Abramson Cancer Center. He has also taught in or co-directed more than a dozen different courses in the Biomedical Graduate Studies (BGS) programs, School of Arts & Sciences, and Medical School. He has served on NIH review panels and as a reviewer for many national and international funding agencies. He is an Associate Editor of *Science Advances* and the *Biochemical Journal*, on the editorial board of *Molecular & Cellular Biology* and *Cells*, and serves as a reviewer for >25 scientific journals, including *Nature*, *Science*, and *PNAS*. He has given invited lectures at numerous universities and meetings in the USA and in more than a dozen foreign countries. He has been recognized for his work with a fellowship from the American Cancer Society, a Career Award in the Biomedical Sciences from the Burroughs Wellcome Fund, a Rita Allen Foundation Scholar Award, the Michael S. Brown New Investigator Award, the Charles E. Kaufman Foundation Initiative Award, the inaugural Perelman School of Medicine Dean's Innovation and Penn's Discovering the Future Awards, and the Stanley N. Cohen Biomedical Research Award.

Driving Epigenetic Centromere Establishment to Facilitate Mammalian Chromosome Engineering

Chromosomes are inherited through cell divisions via connections made between their centromeres and the microtubule-based spindle that segregates the genome to daughter cells. Centromere location is defined by the presence of an array of nucleosomes in which CENP-A replaces histone H3. In this talk, I will highlight work in my lab that builds on studies of the pathway for epigenetically propagating centromere identity. We have taken information gleaned from our molecular studies to guide the design of new types of mammalian artificial chromosomes (MACs) that advance our understanding of centromeres and inform synthetic biology approaches where these tools can be useful. I will highlight recent efforts to use our new MACs to break down prior barriers, including extending to useful cell types a direct, "bottom-up" MAC formation approach that was not possible (or was extremely inefficient) with earlier strategies. Lastly, I describe efforts in progress to directly form MACs in mammalian embryos, with the goal of streamlining the generation of transgenic animals harboring MACs and the useful genetic payloads that they can carry.



Lars M. Steinmetz, Ph.D.

Professor of Genetics, Stanford University, USA

Co-director Stanford Genome Technology Center, USA

Senior Scientist EMBL Heidelberg, Germany

Dr. Lars M. Steinmetz is a Professor of Genetics at Stanford University, Co-Director of the Stanford Genome Technology Center, and Senior Scientist at the European Molecular Biology Laboratory (EMBL). His laboratories have a strong track record in developing and applying cutting-edge experimental, statistical, and computational methods in genomics. Many of the technologies he has pioneered have since become gold standards that are widely applied by others and have led Dr. Steinmetz to co-found three companies: Sophia Genetics, currently the world's largest clinical genomics network, Levitas bio, a new diagnostics company based on magnetic levitation technology, and Recombia Biosciences a new start-up based on gene editing technologies developed in the lab. In addition, Dr. Steinmetz promotes transatlantic research as Director of the Life Science Alliance, a joint research initiative which fosters innovative science and exchange between Stanford and EMBL.

Dissecting Phenotypes: Lessons from Functional Genomics and Synthetic Biology

Leveraging the power to design, build and manipulate DNA, we are interrogating genome function with unprecedented precision at the scale of entire genomes. Using gene editing technologies we are dissecting the effects of thousands of single nucleotide variants in a genome-wide manner to understand natural and disease associated genetic variability. As we enter a new era of gene therapy in precision health, we are ever conscious of the off-target mutations or unintended repair outcomes resulting from CRISPR technologies, and present methods to measure and enhance editing efficiency and precision. Finally, with a designer yeast capable of reorganizing its genome on-demand, we characterize how isoform selection changes when evolved linear genome organization is suddenly disrupted. Synthetic genomics enables us to test genome function directly and systematically, ultimately unlocking deep insight into genomes that will transform how we understand ourselves and our environment.



Luhan Yang, Ph.D.

Co-Founder and CEO of Qihan Biotech, Co-Founder and former CSO of eGenesis

Dr. Luhan Yang is CEO and Co-Founder of Qihan Biotech, a leader in applying multiplexable genome editing technology to cell therapies and organ transplantation. Prior to her current position, Yang served as Co-Founder and Chief Scientific Officer of eGenesis, a company advancing a multiplexed gene editing platform for the creation of human-compatible organs. Before co-founding both companies with Dr. George Church and becoming an entrepreneur, Yang was a post-doctoral fellow at Harvard, where she co-invented the highly programmable genome-engineering tool, CRISPR/Cas9, for use in mammalian cells, and pioneered the first isogenic human stem cell lines to model human diseases at the tissue level.

Her work has been recognized with numerous awards and honors including the Fortune “40 Under 40” list (2020), “Young Global Leader” by the World Economic Forum (2017), “The Bloomberg 50” (2017), “10 Scientists to Watch” by Science News (2017), and the Forbes “30 Under 30” list (2014). Yang holds B.S. degrees in Biology and Psychology from Peking University and a Ph.D. in Human Biology and Translational Medicine from Harvard Medical School.

The Journey with Gene Editing Technologies - Xenotransplantation and Cell Therapy Research

Over the years, numerous remarkable achievements have been made in the Gene Editing field, and the technology continues to evolve rapidly. From Engineering extensively genome-modified pigs as bioreactors to “grow” xenogeneic cells, tissues, and organs for safe and effective clinical application To producing next-generation “immune-privileged” human cells and tissues for cell therapy, CRISPR/Cas9 has been our most irresistible “weapon” to support the cutting-edge advances in the field.



Pam Silver, Ph.D.

Harvard Medical School and The Wyss Institute at Harvard

Pamela Silver is the Adams Professor of Biochemistry and Systems Biology at Harvard Medical School and the Wyss Institute for Biologically Inspired Engineering. She received her BS in Chemistry and PhD in Biochemistry from the University of California. Her work has been recognized by an Established Investigator of the American Heart Association, a Research Scholar of the March of Dimes, an NSF Presidential Young Investigator Award, Claudia Adams Barr

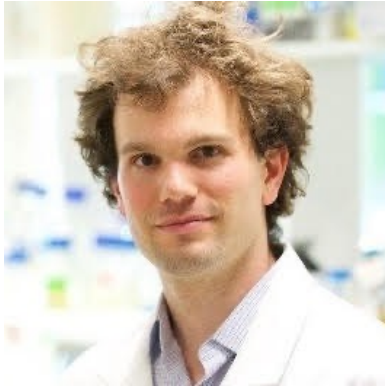
Investigator, an NIH MERIT award, the Philosophical Society Lecture, a Fellow of the Radcliffe Institute, and election to the American Academy of Arts and Sciences.

She is among the top global influencers in Synthetic Biology and her work was named one of the top 10 breakthroughs by the World Economic Forum. She serves on the board of the Internationally Genetics Engineering Machines (iGEM) Competition and is member of the National Science Advisory Board for Biosecurity.

She has led numerous projects for ARPA-E, iARPA and DARPA. She is the co-founder of several Biotech companies including most recently KulaBio and serves on numerous public and private advisory boards.

Designing Biology for Health and Sustainability

We have deployed large gene libraries to develop a platform to predict the potential pathogenicity of emerging viruses. In doing so, we have created cell lines useful for large DNA introduction and evasion of the associated innate immune response. Second, we have designed gene libraries encoding both natural and designed proteins that confer unique features to preservation of human cells. Together, these technologies and results will be of use to many aspects of large chromosome synthesis.



David Bikard, Ph.D.

Institut Pasteur, Head of the Synthetic Biology Lab

David is a young investigator at the Institut Pasteur in the department of Microbiology where he started his group in 2014.

David graduated from AgroParisTech and obtained his PhD from Paris Diderot University for his work performed at the Institut Pasteur on the integron bacterial recombination system. He then joined the laboratory of Luciano Marraffini at the Rockefeller

University as a postdoctoral fellow where he started to work on CRISPR systems. David is interested in applying engineering principles to better understand and fight pathogenic bacteria.

Controlling Gene Expression in Bacteria with CRISPR-Cas Systems

CRISPR-Cas systems have been engineered as powerful tools to control gene expression in bacteria. The most common strategy relies on the use of Cas effectors modified to bind target DNA without introducing DNA breaks. These effectors can either block the RNA polymerase or recruit it through activation domains. CRISPR-Cas tools can be further engineered to obtain fine-tuned control of gene expression or target multiple genes simultaneously. Several caveats in using these tools have also been revealed, including off-target effects and toxicity, making it important to understand the design rules of engineered CRISPR-Cas effectors in bacteria. In particular, we recently investigated the mechanism underlying the toxicity of Cas9 in some bacteria. We could show how off-target binding with as little as 5nt of identity between the guide and target can block the expression of essential genes. Despite these caveats, CRISPR-Cas systems have found numerous applications in bacterial genetics. We recently performed high-throughput CRISPRi screens to investigate the evolution of gene essentiality in the *E. coli* species. This work uncovered how gene essentiality can change between different strains of the same species, a phenomenon driven mostly by the horizontal transfer of genes able to modulate the essentiality of core genes. Altogether this work illustrates how obtaining a deep understanding of CRISPR-Cas tools enables powerful applications and opens novel research directions.



Jianhua Qin, Ph.D.

Dalian Institute of Chemical Physics, Chinese Academy of Sciences

Jianhua Qin is a Chair professor in Dalian Institute of Chemical Physics (DICP), Chinese Academy of Sciences (CAS), and Director of Biomicrofluidics Research Center in DICP. She is the Fellow of Royal Society of Chemistry (FRSC) and Associate Editor of Lab on a Chip. She is the chair of Biosensor, Biochip and Nanotechnology (BBN) division, Chinese Society of Biotechnology. Dr. Qin has published more than 150 peer-review papers and filed 35 patents to date. Her

research interests lie in the interface of organs-on-chips, stem cell organoids, biomaterials and biomedical applications.

Organs on Chips and Future Medicine

Organs-on-chip technology are ideally suited for the study of organ biology, drug testing and precision medicine. They can recapitulate many key aspects of the human tissue microenvironment and can be used to simulate high-level tissue and organ-level physiology. This talk will present the properties and functions of different organs on chips for the purpose of engineering biology and disease modeling. The design processes with attention of the particular device, cells, organoids and materials used are also presented. This technology has great potential to advance the engineering of living system, understanding of organ physiology and pathology, which provides a promising platform for human biology, organ engineering and synthetic biology.



Ophelia S Venturelli, Ph.D.

Assistant Professor of Biochemistry & Chemical & Biological Engineering & Bacteriology, University of Wisconsin-Madison

Dr. Ophelia Venturelli is an Assistant Professor in Biochemistry, Bacteriology and Chemical & Biological Engineering at UW-Madison. She began her appointment in July 2016 after completing a Life Sciences Research Foundation Fellowship at UC Berkeley in the laboratory of Dr. Adam P. Arkin. The Venturelli Lab aims to understand and engineer microbiomes using a combination of high-throughput experimental techniques, computational modeling and synthetic biology. Dr. Venturelli's postdoctoral research focused on microbial community dynamics and strategies to manipulate intracellular resource allocation. She received her PhD in Biochemistry and Biophysics in 2013 from Caltech with Richard M. Murray, where she studied single-cell dynamics and the role of feedback loops in a metabolic gene regulatory network. Dr. Venturelli received the Shaw Scientist Award (2017), ARO Young Investigator Award (2017), NIH Outstanding Investigator Award (2017) and WARF Innovation Award (2019).

Building Microbial Communities to Understand Community Dynamics and Functions



Barbara J. Evans, Ph.D, J.D., LL.M.

Professor of Law and Stephen C. O'Connell Chair, University of Florida Levin College of Law

Barbara J. Evans is Professor of Law and Stephen C. O'Connell Chair at University of Florida's Levin College of Law and Professor of Engineering at UF's Herbert Wertheim College of Engineering. Her work focuses on data privacy and the regulation of machine-learning medical software, genomic technologies, and diagnostic testing. She is an elected member of the American Law Institute, a

Senior Member of the Institute of Electrical and Electronics Engineers and was named a Greenwall Foundation Faculty Scholar in Bioethics for 2010–2013. Before coming to academia, she was a partner in the international regulatory practice of a large New York law firm and is admitted to the practice of law in New York and Texas. She holds a BS in electrical engineering from the University of Texas at Austin, an MS & PhD from Stanford University, a JD from Yale Law School, an LLM in Health Law from the University of Houston Law Center, and she completed a post-doctoral fellowship in Clinical Ethics at the MD Anderson Cancer Center.

Ethical and Regulatory Considerations of Writing Genomes

Biosecurity Roundtable

Biosecurity Roundtable Hosted by DNA Script

12:30 - 1:00 pm EST on Oct 22, 2021

At this year's GP-write 5.0 virtual event, DNA Script will host a roundtable session to discuss biosecurity as it relates to genome writing technologies with a focus on GP-write's newly launched CAD platform and DNA Script's SYNTAX system for benchtop DNA synthesis. Among the objectives of the roundtable will be to discuss potential approaches to ensuring biosecurity without restricting research and development or putting data at risk.

DNA SCRIPT

A world map with a light teal background. Overlaid on the map are several circular logos, each composed of a grid of small, multi-colored squares (red, orange, yellow, green, blue, purple). These logos are placed over various continents, including North America, South America, Europe, Asia, and Australia. The text "GP-write 5.0" is centered over the map in a large, bold, black font.

GP-write 5.0

Lightning Talks/ Poster Boards



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GP-write

Targeted editing and evolution of repetitive genetic elements by filtered editing

Felix Radford, Yale University

Abstract: Genome editing technologies introduce targeted chromosomal modifications in diverse organisms yet are constrained by the inability to selectively modify repetitive genetic elements. We present filtered editing, a genome editing method that modifies a specified DNA site possessing high sequence similarity to other genetic elements by embedding group 1 self-splicing introns into repetitive sequences to construct unique genetic addresses that can be selectively modified. We used filtered editing to generate multisite modifications in a tethered ribosome in *E. coli* using CRISPR/cas9 and multiplex automated genome engineering (MAGE), while leaving the seven native ribosomal operons unperturbed. Self-splicing of the intron post-transcription yielded scarless RNA molecules, generating complex libraries of targeted combinatorial ribosome variants. Using this method, we were able to drive continuous *in vivo* evolution of ribosome function, without interference with the native translation apparatus. This work sets the stage to engineer mutant ribosomes able to polymerize abiological monomers with diverse chemical structures and expands the scope of genome engineering by enabling precise editing and evolution of repetitive DNA sequences.

Synthetic genomes reveal coupling between transcriptional neighbourhood and transcript isoform expression

Amanda Hughes, EMBL

Abstract: While DNA 'parts' are successfully used to engineer synthetic gene circuits, distal epigenetic factors, including neighbouring transcript architecture, also contribute to transcriptional regulation. To disentangle sequence from contextual effects, we profiled the transcriptomes of 64 synthetic yeast strains that had undergone stochastic rearrangements of the synthetic *synIXR* chromosome, using long-read, direct RNA sequencing. Across 612 genomic perturbations, transcript isoform properties were associated with transcriptional context and were predictable from the transcriptional neighbourhood. Leveraging these insights, we constructed a synthetic circuit in which neighbouring transcription controls 3'-UTR length. Our results demonstrate that the transcriptional context generated by linear genome organization influences transcript isoform expression levels and boundaries. Understanding the influence of transcriptional contexts could guide more precise genome engineering. Additionally, it could be co-opted to embed sequence information into alternative transcript isoforms that are responsive to regulation at neighboring loci, potentially establishing a new design concept.

Evaluation of serine-integrases activity as genome editing tools in the synthetic minimal cell *Mycoplasma mycoides* JCVI-Syn3B

Marco de Oliveira, National Institute of Science in Synthetic Biology/EMBRAPA

Abstract: The identification of a set of essential and quasi-essential genes for the assembly of the minimal cell approximation *Mycoplasma mycoides* JCVI-syn 3B put us closer to understanding the basic molecular requirements to life. In that context, we propose the use of serine-integrases as tools able to silence a group of genes simultaneously in a directed and inducible way to complement the 'one gene per cell' analyses allowed by the transposon bombardment originally used. Sets of integrative plasmids carrying a mCherry gene flanked by the recombination sites of serine-integrases INT9 and INT13, as well as the respective integrase gene under control of a tetracycline inducible promoter were used. Upon induction, INT9 was able to activate mCherry expression by inverting its sequence orientation. INT13 induction didn't turn mCherry expression on, although reporter inhibition in one of the positive controls suggests an influence of the sites rather than INT13 ineffectiveness.

Construction of a Synthetic 57-Codon *E. coli* and Tools for Microbial Genome-Scale Recoding

Akos Nyerges, Harvard Medical School

Abstract: At the meeting, we will present the construction of a fully recoded, 57-codon *Escherichia coli* genome, in which seven codons are replaced with synonymous alternatives in all protein-coding genes.

For this aim, the entirely synthetic recoded genome was assembled as 87 50-kb episomal segments, individually tested for functionality, and then integrated into the genome. The development of a specialized integration system and our workflow's optimization allowed us to integrate recoded segments in vivo with 100% efficiency within a few days. We are now combining recoded genomic segments with a novel technology that builds on our latest developments in recombineering and CRISPR-associated nucleases. In parallel with genome construction, we developed novel computational and experimental methods to identify fitness-decreasing recoding issues and troubleshoot these in a massively parallel manner. As we approach the final assembly of a virus-resistant *E. coli* genome, we are also implementing dependency on non-standard amino acids for stringent biocontainment.

In sum, our work will soon I.) demonstrate the first 57-codon organism, II.) establish a tightly biocontained and virus-resistant chassis for new-to-nature protein production, and III.) open a new avenue for the bottom-up synthesis and refactoring of microbial genomes, both computationally and experimentally.

Development of RNA Biosensors to Detect Cancer Biomarkers Using Cell Free System

Milca Rachel da Costa Ribeiro Lins, Sao Paulo State University (UNESP)

Abstract: Cancer/testis (CT) antigens are biomarkers independent of cancer location and provide clues about its severity. GAGE (CT) antigens are expressed in the early stage of several types of cancer associated with X chromosome disorders. This makes GAGE a promising target for the development of an effective cancer early diagnosis biosensor through the rapid detection of GAGE mRNA using a cell free system. We designed RNA switches using the NUPACK package to control the expression of a luciferase reporter gene. The switches were designed to keep gene expression OFF until it pairs with the trigger RNA. The trigger RNA was defined as a 40nt-long sequence of the GAGE mRNA. To test the RNA switches, we will set an in vitro gene expression reaction to which a synthetic RNA trigger will be added in different concentrations. With that, we will access the efficiency and sensitivity of the switches to the trigger.

Computational design advances (GPW-CAD)

Hugo Lins de Albuquerque Vieira, Department of Genetics and Morphology, University of Brasília

Abstract: Genome reduction is an established approach both to study gene essentiality and for generating truncated genomes amenable to biosynthetic uses, such as biofactories. In *Saccharomyces cerevisiae*, much has been done for synthetic genome assembly, yet large-scale genome reduction is still impaired by the incomplete knowledge of which sequences comprise the set of essential and quasi-essential genes. This problem is multifactorial and an open subject. For instance, the SCRaMbLE (Synthetic Chromosome Rearrangement and Modification by loxP-Mediated Evolution) analysis performed on the yeast's synthetic chromosome three (synIII), removed at once genes considered nonessential resulting in cell death. This analysis has also shown the increased incidence of chromosomal alterations when performed on yeast carrying synIII and synIXR, indicating it is not the appropriate method to evaluate gene essentiality. We propose a defined criteria for synthetic lethality assumption based on gene ontology functional analysis and interaction networks aiming for better design of synthetic genomes.

Mammalian Genome Engineering

Ralf Kuehn, Max-Delbrueck-Center for Molecular Medicine, Berlin, Germany

Abstract: C57Bl/6 inbred mice are most frequently used as mammalian model in genetic and biomedical research. However, resulting from inbreeding their genome harbours numerous homozygous mutant alleles supposed to reduce viability and fecundity as compared to outbred mice. In order to generate an optimized C57Bl/6 inbred mouse line we aim for the repair of point and insertional mutations in 46 genes using CRISPR/Cas9 mediated gene editing in zygotes. First we focused on the deletion of endogenous retroviral elements (ERV) that disrupt gene expression by integration of their 5 - 7 kb genome into intronic regions. Using gRNAs cutting on either side of an element we have currently deleted 29 ERVs including the emv2 tumor virus from the C57Bl/6 genome. In addition we aim to correct point mutations at larger scale without the need for homology-directed repair using A base editors that include Cas9 variants with extended PAM recognition. Presently we test the proficiency of base editors to correct point mutations at 17 loci in C57Bl/6 zygotes. Ultimately all of the repaired alleles will be combined into a new C57Bl/6+ line that will be phenotypically characterized in comparison to the parental strain.

Synthetic Biology Software

Matheus de Castro Leitão, Institute of Biological Sciences, University of Brasilia, Brazil

Abstract: Targeting inserts to genomic regions allowing their expression without altering endogenous gene expression is a desirable design approach for the integration of exogenous genes into host cells. Such regions, classified as Genomic Safe Harbours (GSHs), have been identified by viral insertion site, analysis of loss of gene function, or by similarity to GSHs from other organisms. Available GSHs are predominantly located in intragenic loci and close to oncogenes, raising concerns about unstable expression and unpredictable phenotypes. Given the ongoing analytical expansion from monogenic towards polygenic modules precipitated by synthetic biology, the necessity of tools for systematic and optimized identification of GSHs became clear. To expand the potential GSHs available in human cells, the present work developed SHIP, a computer program to identify potential GSHs in intergenic regions. Here, using a combination of machine learning and knowledge-based genome annotation features, SHIP predicts GSHs and is a general-purpose tool to guide experiments.

Synthetic Spidroin Production from *Parawixia bistrata* by TXTL system

Valquiria Michalczechen, National Institute of Science in Synthetic Biology/EMBRAPA

Abstract: Spider silk proteins have unique structural characteristics that make them ideal for the development of new biomaterials. However, some of the genes are highly repetitive motifs encoding high molecular weight, which is one of the limiting factors for in vivo production. A new sequence of hybrid protein MaSp 1+ 2 (8×) from Brazilian *P.bistrata* was produced by TXTL. This methodology was able to produce the spidroin in a few hours, what wasn't possible in the production by bacteria *E. coli* BL21(DE03), that failed. The TXTL is an in vitro system that transcribes and translates genetic material, allowing the synthesis of complex compounds that could be limiting for a living cell. The next steps are protein purification, fiber spun, and mechanoelastic and morphological investigation by SEM and MFA. These protein and synthetic fibers have application in biomaterials in industrial areas, covering energy and sustainability, robotics, medicine, and biomedical technology.

Future Organisms: Synthetic Genomics and Responsible Research and Innovation in the UK, the USA and Japan

Robert Smith, University of Edinburgh

Abstract: Future Organisms is the first dedicated social science project on synthetic genomics. Assembling researchers from the UK, the USA and Japan, its aim is two-fold: to carry out a social scientific investigation into synthetic genomics and to develop new approaches to Responsible Research and Innovation (RRI) through this investigation. Our research is organised into three workstreams: Countries, Creatures and Capacities. The Countries workstream examines national and international policy and funding strategies for synthetic genomics and the expectations embedded within them. The Creatures workstream explores the ways in which synthetic genomics alters human relationships with other organisms by positioning humans as designers of other species. The Capacities workstream addresses the role of social scientists within the field. The project is funded by the UK Economic and Social Research Council and the US NSF, and started in July 2021. We look forward to discussing future organisms with the GP-write community.

Genetic Code Engineering Metrics and Biosafety

Markus Schmidt, BioFaction

Abstract: Genetic code engineering aims to produce organisms that translate genetic information in a different way from that prescribed by the standard genetic code. This endeavor could eventually lead to genetic isolation, where an organism that operates under a different genetic code will not be able to transfer functional genes with other living species, thereby standing behind a genetic firewall. It is not clear however, how distinct the code should be, or how to measure the distance. We have developed a metric (Δ code) where we assigned polarity indices (clog D7) to amino acids to calculate the distances between pairs of genetic codes. We then calculated the distance between a set of 204 genetic codes, including the 24 known distinct natural codes, 11 extreme-distance codes created computationally, nine theoretical special purpose codes from literature and 160 codes in which canonical amino acids were replaced by noncanonical chemical analogues. The metric can be used for building strategies towards creating semantically alienated organisms, and testing the strength of genetic firewalls. This metric provides the basis for a map of the genetic codes that could guide future efforts towards novel biochemical worlds, biosafety and deep barcoding applications.

Re-write the Yeast Genome for Customised Biosynthesis Control

Xinyu Lu, Imperial College

Abstract: Synthetic genomics is a field in synthetic biology aiming to assemble whole genomic DNAs while manipulating the genome content into a customised way. *Saccharomyces cerevisiae* yeast, a model organism with its whole genome sequence determined and well understood, is a good candidate for genome de novo redesign and synthesis. Here, we demonstrate the feasibility of defragmenting a yeast genome and the benefits of co-regulating a synthetic cluster that can be exploited for genome optimisation. We generated two functional synthetic chromosome clusters by genetically re-locating the genes associated with histidine and tryptophan biosynthesis. A master regulation switch was engineered to achieve the targeted and independent co-regulation of the gene expression. We also introduced an inducible recombination system to create dynamic changes within the clusters for studying the rules that underly the natural eukaryotic genome organisation. These investigations would improve our ability to design and build custom synthetic genomes in the future.

Synthetic Biology In Pursuit Of The Minimal Cell Cycle

Anastasiya Malyshava, Imperial College

Abstract: Synthetic biology offers an alternative approach to answering fundamental research questions about biology by 'learning from building'. Here we use the methodology from the Sc2.0 project to build and understand the minimal set of genes needed to achieve autonomous cell cycle oscillations in *Saccharomyces cerevisiae*. We focused first on genes involved in the dynamics of cyclin waves. 4 pairs of B-type cyclin genes, and several regulators were deleted by CRISPR from their native loci in the yeast genome and simultaneously re-assembled into a synthetic gene cluster. To then explore the effects of removing combinations of genes we used the Sc2.0 SCRaMbLE method, which uses Cre recombinase to delete and rearranges genes in the synthetic cluster. We showed that the genetic complexity of the yeast cell cycle can be reduced. Our ultimate aim is to use this synthetic approach to converge in vivo on the minimal eukaryotic cell cycle gene set.

Nanofluidic sequence-specific sorting of single DNA molecules: The autonomous retrieval of specific DNA sequences from a heterogeneous pool of single-stranded DNA molecules

Hatem Mohamed Gaber Abdelrahman, Zewail City of Science and Technology

Abstract: De novo DNA synthesis is a foundational technology for discovering and engineering biology. Current DNA synthesis technologies rely on the the chemical synthesis of oligonucleotides on microarrays and the enzymatic assembly of these microarray-derived oligonucleotides into full-length dsDNA sequences. Microarray-derived oligonucleotides are error-rich (containing sequence mutations about one mutation every 200 bases as a result of the error-prone chemical synthesis), highly-complex (heterogeneous in sequence), and very low in concentration (femtomoles per oligonucleotide sequence) as a result requires mandatory post-synthesis processing steps before proceeding to the subsequent enzymatic assembly step.

The post-synthesis processing of microarray-derived oligonucleotides include sequence verification as a quality control step for selecting against imperfect sequences in the oligonucleotide pool, partitioning of the heterogeneous oligonucleotide pool into separate sequence-orthogonal sub-pools for carrying out different DNA assembly reactions without the risk of cross-hybridization in the oligonucleotide pool, and PCR amplification to increase the oligonucleotide concentration to the optimal level necessary for the subsequent DNA assembly reactions.

Sequence-specific sorting of single DNA molecules as a mechanism for the autonomous retrieval of specific DNA sequences from a heterogeneous pool of single-stranded DNA molecules (e.g. oligonucleotides) is proposed here for automating the post-synthesis processing steps of microarray-derived oligonucleotide pools to allow for both the autonomous retrieval of perfect sequences from imperfect sequences in the oligonucleotide pool as well as the autonomous partitioning of the highly-complex oligonucleotide pool into different sub-pools for carrying out different assembly reactions.



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Ansa Biotechnologies is developing a new way to make DNA that will be faster, cleaner, and more accurate than existing methods. Currently, DNA is manufactured via a chemical method that has remained mostly unchanged for 40 years. Ansa's enzyme-based approach promises to dramatically accelerate innovation in biological research and biotechnology, including therapeutics, diagnostics and biomanufacturing.

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Conventional technologies are nowhere near keeping pace with the explosive growth in data generation. As a result, humanity is quickly losing the ability to store and analyze all valuable data it creates. CATALOG was founded in 2016 by MIT scientists and has become the first company develop a commercially viable DNA-based solution to this problem. CATALOG is drawing on the natural characteristics of DNA to build a data and compute platform more energy efficient, affordably scalable, and highly secure compared to conventional electronic platforms. For more information about CATALOG, visit www.catalogdna.com.

www.catalogdna.com

DNA SCRIPT

DNA Script

Founded in 2014, DNA Script is a leading DNA synthesis company with a vision of engineering biology to accelerate breakthroughs in life science. The company is pioneering an alternative to traditional DNA synthesis called enzymatic DNA synthesis, or EDS, allowing this technology to be accessible to labs with the first benchtop enzymatic synthesis instrument, the SYNTAX System. By putting DNA synthesis back in the lab, DNA Script aims to transform life science research through innovative technology that gives researchers unprecedented control and autonomy.

www.dnascript.com

Biosecurity Roundtable Hosted by DNA Script

At this year's GP-write 5.0 virtual event, DNA Script will host a roundtable session to discuss biosecurity as it relates to genome writing technologies with a focus on GP-write's newly launched CAD platform and DNA Script's SYNTAX system for benchtop DNA synthesis. Among the objectives of the roundtable will be to discuss potential approaches to ensuring biosecurity without restricting research and development or putting data at risk.



IndieBio

About IndieBio: SOSV's IndieBio is the world's leading startup development program for synthetic biology and biotech startups. Our mission is to solve the world's biggest challenges through biology as a technology by empowering scientists to become entrepreneurs who drive innovation to improve human and planetary health. The IndieBio program uniquely provides startups with a fully equipped lab, world class mentors and significant seed funding to take brilliant biotech ideas from concept to commercialization.

<https://indiebio.co>



Inscripta

Inscripta is a life science technology company enabling scientists to solve some of today's most pressing challenges with the first benchtop system for genome editing. The company's automated Onyx platform, consisting of an instrument, consumables, assays, and software, makes CRISPR-based genome engineering accessible to any research lab. Inscripta supports its customers around the world from facilities in Boulder, Colorado; San Diego and Pleasanton, California; and Copenhagen, Denmark. To learn more, visit Inscripta.com and follow @InscriptaInc.

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Lattice

Lattice Automation, Inc. was founded in 2013 with the mission to provide complete solutions to fundamentally change the way that biological designs are conceived, designed, physically created, and managed. Our technology builds upon state-of-the-art techniques in computer science, electrical engineering, and bioengineering. A primary interaction model for Lattice is the creation of state-of-the-art software for customers engineering novel biological solutions to therapeutic, materials, energy, and agricultural needs. In this capacity, Lattice has designed customized DNA assembly planning software, laboratory information management (LIMS) systems, genome editing design tools, novel e-commerce APIs, and interfaces between laboratory automation equipment. Lattice also provides open-source software in the areas of DNA sequence visualization, nucleic acid folding prediction, and plasmid design. Lattice also provides project management, programming, and technical consulting expertise to augment existing software teams and provide support in software engineering, algorithm design, and data science.

Lattice is a recipient of National Science Foundation Phase 1 and Phase 2 SBIRs, a participant in NSF's iCORPS Program, and has successfully engaged with over 8 unique projects in 5 years.

<https://latticeautomation.com>



Twist Bioscience

Twist Bioscience is a leading and rapidly growing synthetic biology and genomics company that has developed a disruptive DNA synthesis platform to industrialize the engineering of biology. The core of the platform is a proprietary technology that pioneers a new method of manufacturing synthetic DNA by “writing” DNA on a silicon chip. Twist is leveraging its unique technology to manufacture a broad range of synthetic DNA-based products, including synthetic genes, tools for next-generation sequencing (NGS) preparation, and antibody libraries for drug discovery and development. Twist is also pursuing longer-term opportunities in digital data storage in DNA and biologics drug discovery. Twist makes products for use across many industries including healthcare, industrial chemicals, agriculture and academic research.

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