

2020-2021

IMPACT REPORT

Advancing genome engineering to solve humanity's greatest problems

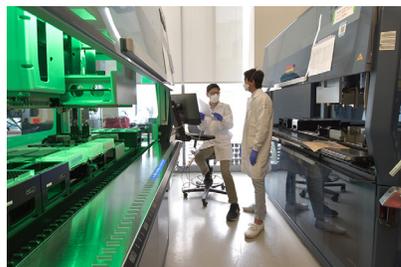
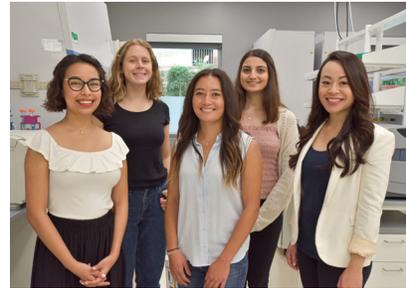


TABLE OF CONTENTS

LETTER FROM THE EXECUTIVE DIRECTOR.....	3
IGI STEPS UP ON COVID-19.....	4
NOBEL & AWARDS.....	5
DISCOVERY.....	6
CRISPR TO THE CLINIC.....	7
HEALTH IMPACTS.....	8
AGRICULTURE.....	9
CLIMATE.....	10
PUBLIC IMPACT.....	11
FACILITIES.....	12



Photo credits

Jennifer Doudna by Christopher Michel (p. 1)
FAST study by Irene Yi, UC Berkeley (p. 1)
Noha Aboelata by Roots Community Health Center (p. 4)
Jennifer Doudna holding Nobel medal by Brittany Hosea-Small (p. 5)

LETTER FROM THE EXECUTIVE DIRECTOR



I knew when I started as the IGI Executive Director in 2020 that I was coming into a special place. The past year made it very clear that the IGI is indeed special, and it's because of the remarkable group of people we have assembled.

In the midst of an unprecedented public health crisis, IGI researchers made groundbreaking scientific discoveries, launched a clinical trial to treat sickle cell disease, developed a new climate strategy, and protected the campus and local community by quickly building a COVID testing lab from scratch. The IGI is not just a research institute, it's a nucleation point for the best scientists to ideate and innovate solutions to the biggest problems facing society, from health inequity to hunger to climate change.

I've learned over my career that the best organizations are those that focus on the Three P's: People, Programs, and Partnerships. The same holds true for the IGI. I want to highlight a few of these that make the IGI one of the most exciting institutes in the world:

- Where else to start than with our Founder, Jennifer Doudna, who won the 2020 Nobel Prize in Chemistry with Emmanuelle Charpentier for their pioneering work developing CRISPR gene editing! The IGI is truly an extension of Jennifer and her vision of using CRISPR to help all humanity through new, affordable cures and sustainable solutions to feed a growing world, and we couldn't be more proud.
- In the last year, IGI hired a Communications Director, an Executive Director, a Public Impact Director, and a Laboratory Director for our Clinical Lab. Our world-class executive team is ready to lead the IGI into a new phase of growth and expansion.
- Publications from IGI's research programs are too numerous to list in entirety but include the tiny, new gene editor CasΦ that can carry larger genomic payloads, subterranean Borgs that could hold keys to reducing agricultural methane emissions, and a new CRISPR-based point-of-care diagnostic that could change the way infectious disease is diagnosed across the globe.
- Philanthropic partners have committed over \$30M of new gifts this year alone, allowing the IGI to take the types of research risks that lead to truly groundbreaking discoveries, successful technology translation, and support of entrepreneurial founders from underrepresented groups.
- Our CRISPR-based sickle cell treatment is heading into a human clinical trial this year, in partnership with UCSF and UCLA, and we are excited to move this forward!

My main goal for my first year as Executive Director of the IGI was to start new programs that address some of society's biggest challenges. No bigger challenge faces us than climate change. A team led by our Directors of Sustainable Agriculture and Microbiology, Brian Staskawicz and Jill Banfield, respectively, has devised a path to achieve a net-zero farm and accelerate biological carbon capture and sequestration on agricultural lands. Based on our first fundraising win, we have started a set of projects that include reducing farmer inputs like fertilizers and irrigation, enhancing photosynthesis, and increasing carbon storage in soil, and are busy working to support additional projects on genomic approaches to climate change mitigation.

COVID-19 was not in anyone's plans, but the IGI team rose to the challenge, setting up the country's first CLIA-certified COVID-19 diagnostic testing lab on a non-medical campus. The lab and its staff have run over 320,000 COVID tests for the Berkeley campus and East Bay community. The IGI is also now on the leading edge of sequencing variants in the Bay Area to help inform campus and local public health officials of impending dangers. What an amazing year to be part of the IGI!

Brad Ringeisen
Executive Director, Innovative Genomics Institute



IGI BY THE NUMBERS

85

IGI-affiliated principal investigators

88

Current IGI research projects

15

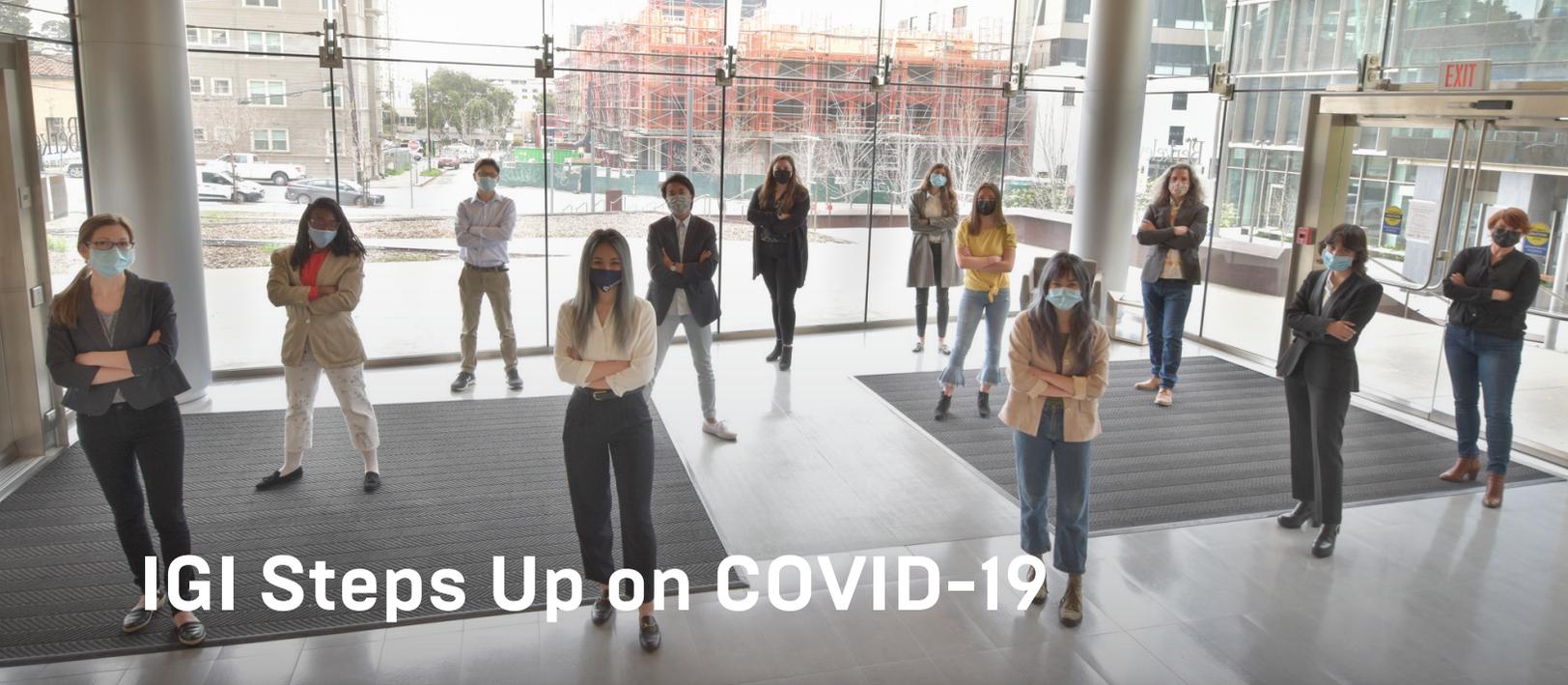
New gifts

11

New crop traits developed

1

Nobel Prize



IGI Steps Up on COVID-19

The IGI not only does cutting-edge genomic science, but does so with a social purpose. In March, 2020, as the COVID-19 pandemic was gaining a foothold in the US, the IGI faced a choice: shut down research or step up and use our skills and our facility to serve the public good in a time of great need. The decision was immediate and unanimous.

Over the past 18 months, our newly CLIA-certified and CAP-accredited Clinical Laboratory has run over 320,000 tests. We freely shared our laboratory blueprint, developed new testing protocols, hired Petros Giannikopoulos to lead the Clinical Laboratory, and funded over 20 different rapid-turnaround research projects on SARS-CoV-2.



*Petros Giannikopoulos, M.D.
Clinical Lab Director*

Next-Gen Diagnostics

The pandemic revealed troubling gaps in the global community's ability to quickly and accurately diagnose infections during an outbreak. Work on new CRISPR-based diagnostic technologies became suddenly critical. In response:

- The Ott and Doudna labs published a new CRISPR-based test for COVID-19 that uses a smartphone camera to provide accurate and rapid results.
- Multiple IGI labs collaborated to develop a new method of simple, highly sensitive, on-site testing for COVID-19 and other diseases that avoids lengthy lab analysis time.

Tracking the Virus

As the SARS-CoV-2 virus spread around the world, IGI researchers and UC Berkeley and UCSF tracked its every move using genomic sequencing. Every sample with a positive test result from the IGI Clinical Laboratory was sequenced, published, and shared with other institutes around the world as part of a global effort to help track the evolution and spread of new variants.



*Stacia Wyman, Ph.D.
Senior Genomics Scientist*

Supporting Our Community

In addition to providing testing to the UC Berkeley campus, the IGI served first responders and partnered with community health providers such as Roots Community Health Center in Oakland to offer testing in underserved neighborhoods experiencing extremely high positivity rates.



"Our walk-up site in Oakland has a 14.4% positivity rate."

Noha Aboelata, Roots Community Health Center

NOBEL & AWARDS

When Jennifer Doudna met Jill Banfield for coffee at the Free Speech Movement Cafe in 2006 to discuss an unusual pattern of repeats found in some microbial genomes called CRISPR, there was no notion at the time of how significant that meeting would become.

Against the backdrop of an unprecedented and challenging year, the early morning of October 7, 2020, stands out as the unquestioned highlight of the year for the IGI, when our Founder and President Jennifer Doudna along with her collaborator Emmanuelle Charpentier were awarded the Nobel Prize in Chemistry for their work developing CRISPR-Cas9 as a genome editing tool.

"This great honor recognizes the history of CRISPR and the collaborative story of harnessing it into a profoundly powerful engineering technology that gives new hope and possibility to our society."

Jennifer Doudna,
Founder

A Rewarding Year

Other IGI Investigators also received notable awards and appointments over the past year:

- IGI Investigator Pamela Ronald became the first woman to be named a World Agriculture Prize laureate.
- Jenny Hamilton, an IGI postdoc in the Doudna lab, was named a 2020 STAT Wunderkind.
- Cara Brook, an IGI postdoc in the Glaunsinger lab, was named a 2020 L’Oreal For Women in Science fellow.
- IGI Investigators Barbara Baker and N. Louise Glass were elected to the National Academy of Sciences.



GROUNDBREAKING DISCOVERY CONTINUES AT THE IGI



Developing CRISPR genome editing was just the beginning. IGI researchers are expanding the genomic toolkit through continued discovery and innovation.

Meet the Borg

Researchers in the Banfield lab discovered a huge extra-chromosomal DNA element unlike anything described before. Named “Borgs” for their ability to assimilate host genes, Borgs appear to supercharge methane oxidation by archaea and could provide new approaches to reducing greenhouse gas emissions from soils.

E. coli that Eat CO₂

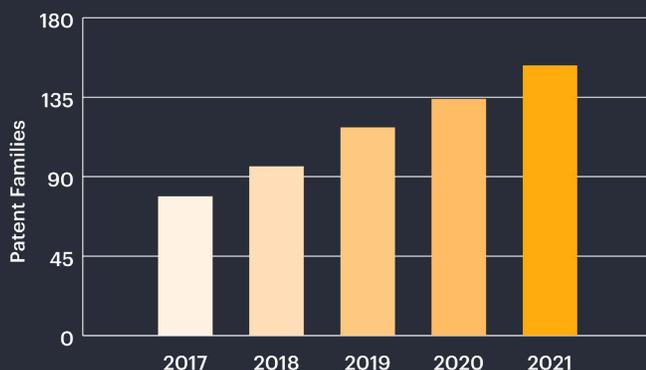
IGI Investigator Dave Savage and collaborators re-engineered *E. coli* bacteria to capture and use carbon dioxide from the air, suggesting a potential impact on climate change and the recycling of atmospheric CO₂ for green-tech applications.

A New, Tiny Editor

IGI researchers found a tiny protein named CasΦ in the largest known bacteriophages (see image above) — the most compact working Cas variant yet discovered. Smaller Cas proteins can help overcome delivery challenges by being easier to ferry into cells to perform genome editing.

A Powerhouse of Innovation

The IGI continues to grow its patent portfolio of innovations with applications in life science research, human health and sustainable agriculture.



Real-World Impact

In 2017, Benjamin Oakes was named as one of the first IGI Entrepreneurial Fellows, with the goal of creating tools to drive a new era of precision genome editing.



Today, he’s the Co-founder, President, and CEO of Scribe Therapeutics, which raised \$100M in 2021 to further develop Scribe’s unique gene editing and delivery technologies through its proprietary CRISPR by Design™ platform. Scribe is now focused on advancing its engineered CRISPR technologies and a pipeline of therapeutics for neurodegeneration, ophthalmology, cardiometabolic disorders, and additional diseases with high unmet need.



Bringing CRISPR to the Clinic

The IGI's health strategy is to use the institute's unique interdisciplinary and multi-institutional power to accelerate CRISPR cures. This includes developing targeted CRISPR-based cures and platform technologies in the IGI Center for Translational Genomics (CTG) to enable the rapid development of affordable therapeutics.

Developing an Accessible Cure for Sickle Cell Disease

Today, the IGI is at the forefront of the drive to cure sickle cell disease while researching other next-generation CRISPR cures.

There are now a small number of people cured of sickle cell by the first clinical trial of a CRISPR-based therapy, but the work is far from done: these treatments are prohibitively expensive and can only be done in a few facilities in the world.

"Our work is not driven by profit but by the very real possibility of making the lives of millions around the world better, people who have too long been ignored by medical science."

Fyodor Urnov,
IGI Director of Technology & Translation

CRISPR Clinical Trial

In 2021, the IGI and collaborators at UCSF Benioff Children's Hospital and the UCLA Broad Stem Cell Research Center became the first non-profit group to launch a clinical trial for a CRISPR-based sickle cell therapy. Others around the world are developing sickle cell therapies, but the goal of the UC consortium is unique: to develop new affordable and equitable cures. The trial of a direct repair to the mutation that causes sickle cell disease begins in late 2021, and research on new in vivo delivery methods is underway at the IGI.

Building a Platform for CRISPR Cures

There are over 5000 genetic diseases, the majority of which remain poorly addressed by current therapies. It can take a decade or more to develop a new therapy. How can we speed the development of CRISPR cures?

This is the challenge being tackled by the IGI Center for Translational Genomics (CTG), a cutting-edge computational and wet lab facility developing a platform technology approach to accelerate the process of developing safe and effective CRISPR-based cures.

Neglected Diseases

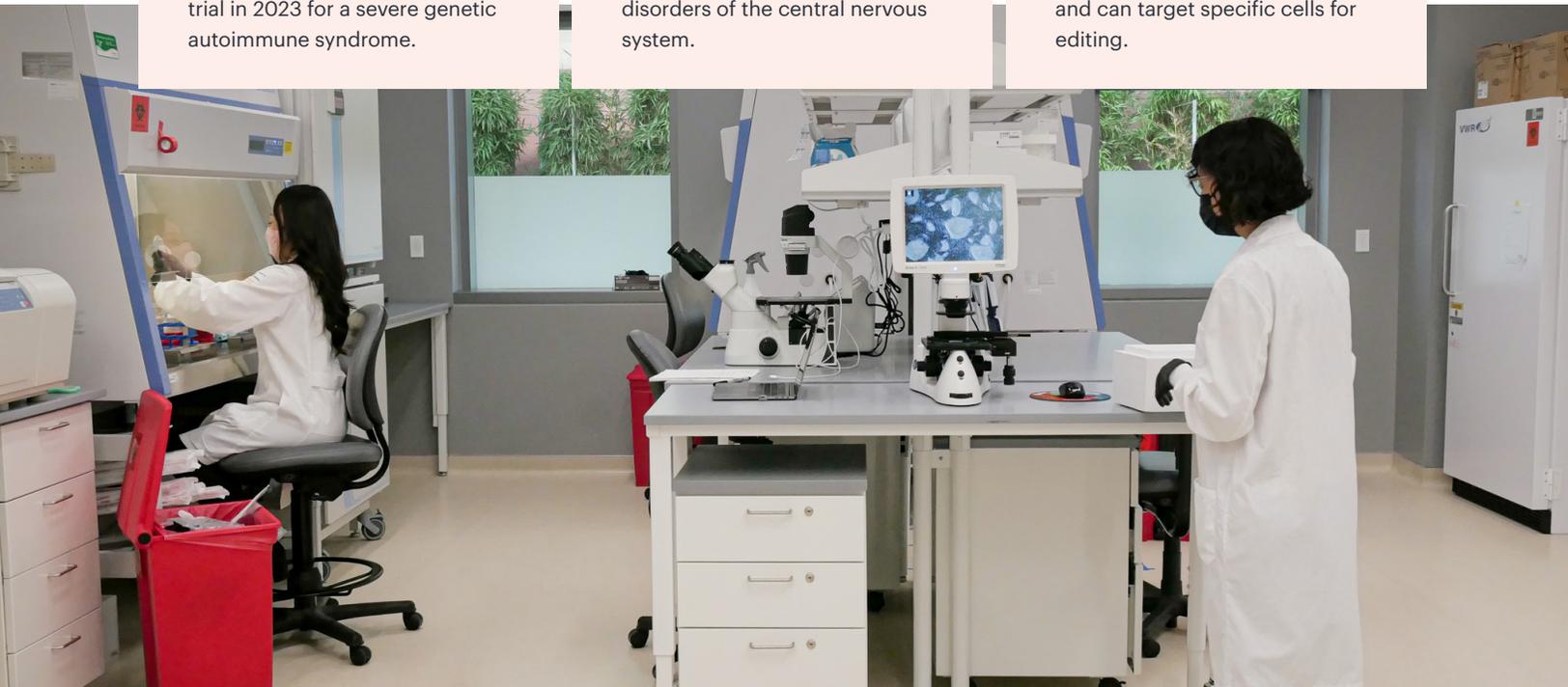
Rare diseases are overlooked by the standard drug development process. The IGI is committed to creating new pathways to cures, whether it affects 1 or 1 million people. IGI researchers are developing a CRISPR-based cure slated to enter a clinical trial in 2023 for a severe genetic autoimmune syndrome.

Neurodegenerative Disease

As part of the Alliance for Therapies in Neuroscience, a new 10-year partnership between UCSF, UC Berkeley, Roche, and Genentech, a team at the IGI will be working to develop new CRISPR-based therapies for debilitating brain diseases and disorders of the central nervous system.

Next-Generation Delivery

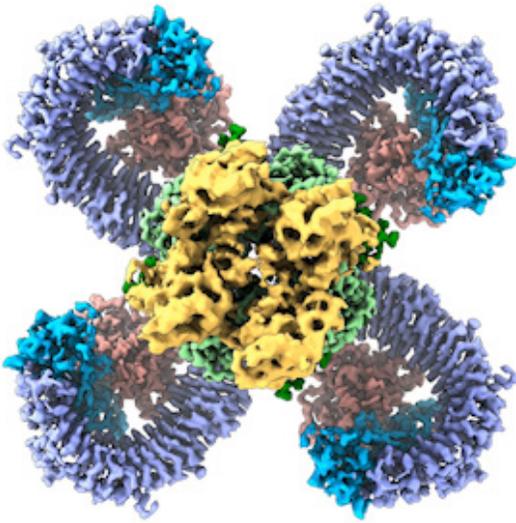
IGI researchers are making significant leaps on the most challenging hurdle for new CRISPR-based therapies: delivery. In 2021, members of the Doudna and Marson labs demonstrated that virus-like particles can deliver genome-editing tools effectively and can target specific cells for editing.



Entrepreneurship with a Purpose

A breakthrough that never reaches the public is a missed opportunity. The IGI helps innovations reach the world by supporting IGI mission-aligned entrepreneurs.

- The 2021 Tory Burch Fellowship at the IGI supports scientific genomic business founders who are committed to solving gender inequity. The first recipient, Nabiha Saklayen, is the cofounder of Cellino, a personalized regenerative medicine company with a focus on accessibility and affordability.
- The IGI is launching a new entrepreneurship program thanks to the support of an anonymous donor, and will be hosting the first cohort of entrepreneurial fellows in Q3-Q4 2022, focusing on underrepresented founders of early-stage genomics-focused companies.



Stopping Plant Pandemics

Humans aren't the only ones dealing with a deadly pandemic. Three of the world's major crops — wheat, bananas, and chocolate — are facing their own. New research from the IGI provided the first detailed look at the plant immune receptor ROQ1. This work shed light on how plants recognize pathogens — and how scientists can help them fight off other attackers.

Protecting Wheat Harvests

With new grants totaling \$3.2 million, IGI PIs Brian Staskawicz and Ksenia Krasileva are working to develop disease-resistant wheat, using gene-editing technology to stack multiple pathogen resistance genes in crop plants. With this approach, the plant can fight back even when the pathogen mutates.



Removing Cyanide from Cassava

CRISPR has the potential to improve the nutritional value of food crops. Cassava, a staple food for roughly 1 billion people around the world, naturally accumulates cyanide, which can cause serious long-term health effects. IGI's genome editing techniques can stop cassava's production of cyanide, something traditional breeding techniques have not been able to achieve.



In 2021, IGI's work on climate change entered a new era. Kick-started by a \$3 million gift, the IGI has launched three new projects aimed at developing scalable nature-based solutions to mitigate climate change with the goal of a net-zero farm.

~33%

Global greenhouse gas emissions from the food system

12%

Global methane emissions that come from rice farming

The IGI Approach

1. **Reduce:** Create solutions to minimize emissions while maintaining food security
2. **Restore:** Build soil carbon storage back to pre-modern levels
3. **Revive:** Enhance crop yield with affordable climate-friendly strategies

Current Projects

CRISPR-Based Carbon Capture

Using genome editing and soil microbial farming to enhance carbon uptake by plants and soil microbes

- Genomic and chemical analysis of the soil microbiome of rice paddies to enhance carbon storage and reduce GHG emissions (Banfield Lab, UC Berkeley)
- Using CRISPR genetic screens and editing to optimize crop photosynthesis for increased food yield and enhanced carbon capture (Savage Lab, UC Berkeley)

Pathway to a Net-Zero Farm

Reducing farmer inputs and greenhouse gas (GHG) emissions, using rice farms as a model system

- Investigating the effect of rice root system architecture on microbes to reduce methane emissions (Ronald Lab, UC Davis)
- Gene stacking in rice to reduce pesticide and fertilizer usage (Staskawicz Lab, UC Berkeley)

"While we have viable solutions for reducing greenhouse gas emissions for many sectors, agriculture stands out as a glaring exception. Plants and microbes can be part of the solution, and genomic technologies can scale to meet the size of the challenge."

Brad Ringeisen
IGI Executive Director

Climate Workshop

To ensure that IGI research priorities are aligned with societal needs, we invited over 80 thought leaders with multi-disciplinary expertise to attend our first ever climate workshop. Following the workshop, IGI leadership met with the US Secretary of Agriculture, Tom Vilsack, and formed a partnership with One CGIAR, a premier international agricultural organization with the capacity to translate IGI research discoveries into climate-friendly agricultural solutions for farmers in developing countries.

PUBLIC IMPACT



We believe that true impact requires incorporating societal, ethical, and environmental considerations into our scientific research.

Policy

The IGI, American Society of Hematology Research Collaborative, and FDA are collaborating to “Accelerate Innovations for Sickle Cell Disease (SCD) with Real-World Evidence.” Stakeholders from industry, academia, government, and the patient community seek consensus on generating actionable, regulatory-grade evidence for genomic therapies for SCD. Improving real-world data collection can prevent adverse outcomes, aid enrollment selection, and expedite new, lower-cost therapies.



Engagement

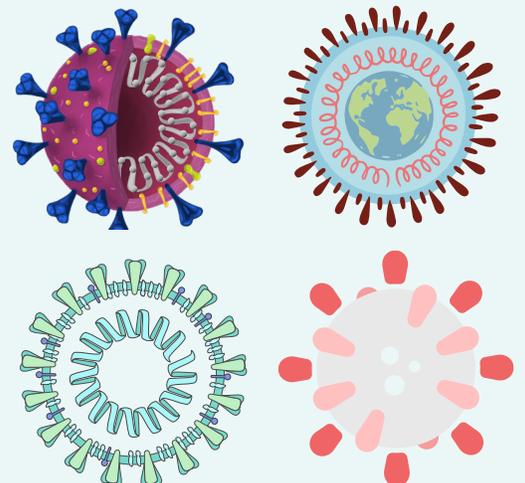
The IGI joined the Coalition for Responsible Use of Gene Editing in Agriculture, which is developing industry best practices for the responsible use of gene editing technology that complement regulatory oversight in the agriculture space. Developers will be verified using the new framework, which is intended to increase transparency and credible oversight. The IGI will be involved in soliciting input from stakeholders, approving the framework, and developing policies for oversight.



Education & Outreach

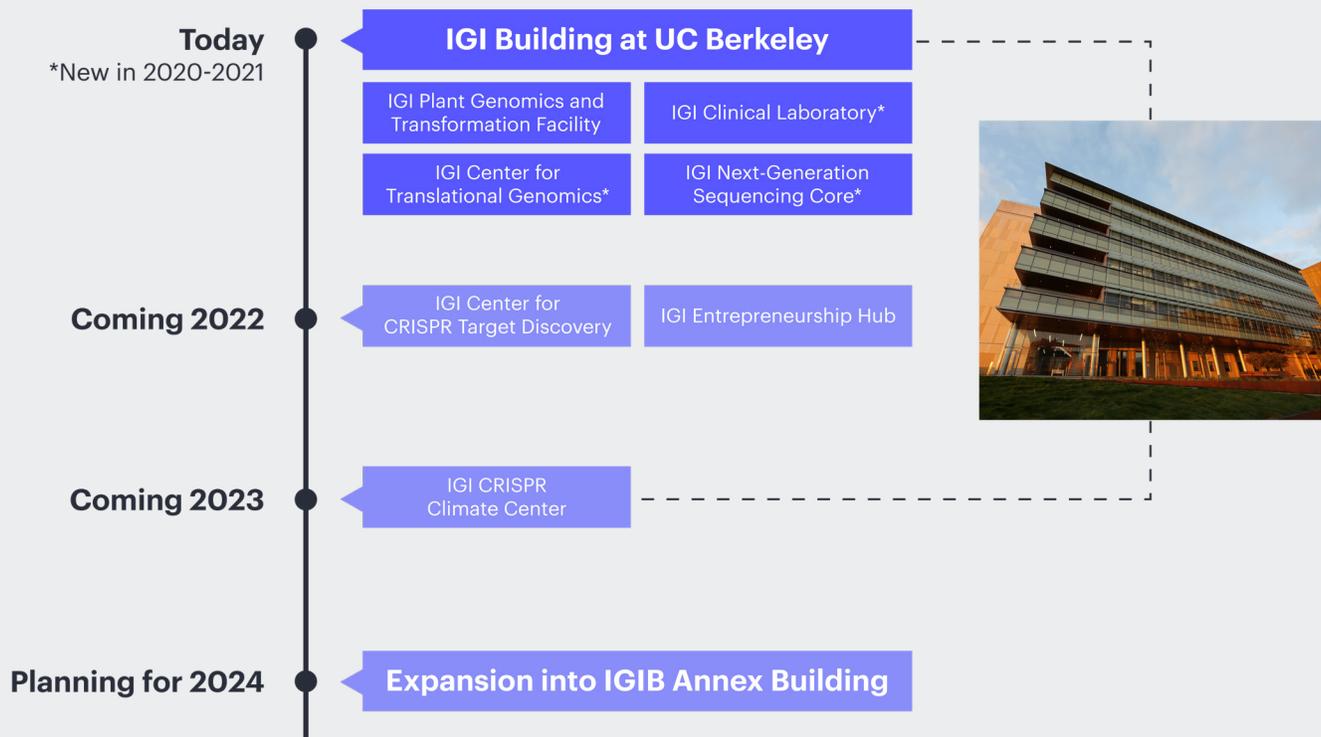
Our online education program released several new digital resources this year, including; a 360° field trip to the IGI, a sickle cell science and ethics video, a Spanish version of our popular illustrated glossary, and “CRISPR Made Simple,” a kid-friendly overview of CRISPR and genome editing and the first chapters of “CRISPRpedia,” which explains all things CRISPR in detailed text, downloadable illustrations, and video.

The IGI Education team also created a suite of coronavirus graphics and made these images freely available, to fill a need for accurate coronavirus visuals. Our COVID-19 illustration page has been viewed more times than any other page on the IGI website in the past year, and our drawings have been used on websites, social media, and in scientific publications around the globe.



New Facilities and Planning for Growth

The IGI is planning for growth. We want to bring genomic innovations from the bench to the clinic and to the field, as well as expand our entrepreneurship programs. We are studying the exciting possibility of adding an IGI annex adjacent to the current IGI building to support our future as an institute.



Growth Through New Gifts

IGI’s continued growth and broad portfolio of research projects is made possible through the generous support of philanthropic organizations and individuals. New gifts were critical to our response to the COVID-19 crisis and to meet the needs of UC Berkeley and community partners. This graph shows the areas that the over \$30 million in new gifts helped support over the past 18 months.

