

**BIOLOGICAL RESEARCH
AT THE DEPARTMENT OF ENERGY:
LEVERAGING DOE'S UNIQUE CAPABILITIES
TO RESPOND TO THE COVID-19 PANDEMIC**

HEARING
BEFORE THE
SUBCOMMITTEE ON ENERGY
OF THE
COMMITTEE ON SCIENCE, SPACE,
AND TECHNOLOGY
HOUSE OF REPRESENTATIVES
ONE HUNDRED SIXTEENTH CONGRESS

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FRIDAY, SEPTEMBER 11, 2020

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON ENERGY,
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY,
Washington, D.C.

The Subcommittee met, pursuant to notice, at 1:31 p.m., via Webex, Hon. Lizzie Fletcher [Chairwoman of the Subcommittee] presiding.

**COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON ENERGY
U.S. HOUSE OF REPRESENTATIVES
HEARING CHARTER**

Biological research at the Department of Energy: Leveraging DOE's unique capabilities to respond to the COVID-19 pandemic

Friday, September 11, 2020

1:30 PM EST

Cisco Webex

PURPOSE

The purpose of the hearing is to examine the biological research and development activities within the U.S. Department of Energy Office of Science's Biological and Environmental Research (BER) program. The hearing will examine the historic reasons for why the Department has bioscience research capabilities; how this expertise and BER's advanced research tools are being leveraged to respond to the COVID-19 pandemic; and future directions for the Department's biological research activities. The hearing will also inform the development of legislation that will guide the DOE Office of Science's activities in these and other areas.

WITNESSES

- **Dr. Mary Maxon**, Associate Laboratory Director for Biosciences, Department of Energy, Lawrence Berkeley National Laboratory
- **Dr. Debra Mohnen**, Professor, Department of Biochemistry and Molecular Biology, University of Georgia
- **Dr. Glenn C. Randall**, Chair, Committee on Microbiology, The University of Chicago
- **Dr. Kelly C. Wrighton**, Associate Professor, Department of Soil and Crop Science, Colorado State University

BACKGROUND

In response to the COVID-19 pandemic, the U.S. Department of Energy has leveraged its expertise in biological and virology research to address the global health crisis. Activities range from deploying supercomputers to screen thousands of potential drug components to determining viral protein structures and drug targets using high intensity x-rays. Additionally, the department has employed its user facility capabilities in molecular structural determination, genomic sequencing, clinical and non-clinical sample testing, computational modeling and simulation, and epidemiological and logistics support to respond to the pandemic. This research is made possible by leveraging the expertise of facilities such as the Joint Genome Institute, which is

capable of sequencing large quantities of patient samples, and comparing the COVID-19 disease with other genomes (an organism's complete set of DNA, including all of its genes) to identify promising options for immuno-targeting, and constructing models of individual susceptibility.¹

To synergize the biological and advanced computing expertise of its national laboratory network, DOE launched the *National Virtual Biotechnology Laboratory (NVBL)*.² Considered the US Department of Energy's COVID-19 consortium, NVBL strives to mobilize the resources of the department's seventeen national laboratories to engage in COVID-19 research. Projects within the consortium are focused on molecular design for medical therapeutics, COVID-19 testing R&D, epidemiological modeling, and manufacturing.³ One such project involves designing potential inhibitor molecules to inactivate the main SARS-CoV-2 enzyme in viral replication. These potential inhibitors will be experimentally biochemically tested and validated, then improved upon with computational algorithms.⁴

The NVBL consortium is also leveraging the capabilities of bioinformatics platforms, such as the Empowering the Development of Genomics Expertise (EDGE) platform, hosted by Los Alamos National Laboratory, to tailor COVID-19 analytics and allow public health labs to report SARS-CoV-2 genome sequencing data, validate diagnostic assays, and track case counts and genomic data.⁵ NVBL is establishing a data platform to enable the widespread collection and use of reported data attributes that influence public health response outcomes. The platform will include more than 1,200 attributes and process 600,000 data records weekly, while also potentially laying the foundation for a national data infrastructure to support future epidemiological and pandemic modeling.⁶

The hearing will provide an in-depth discussion of why the Department of Energy's biological research capabilities uniquely position the Department to respond to the unprecedented nature of the COVID-19 pandemic, and how leveraging these capabilities may enable DOE to proactively respond to future pandemics, as well as enable continued advancements to our nation's energy security.

BIOLOGICAL AND ENVIRONMENTAL RESEARCH (BER) PROGRAM

The Biological and Environmental Research (BER) program is one of the six interdisciplinary science program offices within the Department of Energy's (DOE) Office of Science. BER's mission is to advance fundamental research and scientific user facilities to "achieve predictive understanding of complex biological, earth, and environmental systems for energy and infrastructure security, independence, and prosperity."⁷ BER's programs are divided between two divisions, the Biological Systems Science Division (BSSD) and the Earth and

¹ <https://science.osti.gov/nvbl>

² [Ibid.](#)

³ <https://science.osti.gov/nvbl/NVBL-Projects>

⁴ <https://science.osti.gov/nvbl/NVBL-Projects/Molecular-Design-Highlights/2020-06-a>

⁵ <https://science.osti.gov/nvbl/NVBL-Projects/COVID-19-Testing-RD-Highlights/2020-06-a>

⁶ <https://science.osti.gov/nvbl/NVBL-Projects/COVID-19-Testing-RD-Highlights/2020-06-b>

⁷ <https://science.osti.gov/nvbl/NVBL-Projects/Epidemiological-Modeling-Highlights/2020-06-b>

⁷ <https://www.energy.gov/sites/prod/files/2020/06/f75/fy-2021-sc-ber-cong-budget.pdf>

Environmental Systems Sciences Division. In support of its research agenda, BER operates and manages three user facilities, the Atmospheric Radiation Measurement (ARM), the Environmental Molecular Sciences Laboratory (EMSL), and the Joint Genome Institute (JGI).⁸

BER is credited for its transformative impact on science. In 1990, BER initiated the Human Genome Project, which helped map the human genome (the complete set of human DNA, including all genes), and initiated the era of modern biotechnology and genomics-based systems biology.⁹ Today, BER's research seeks to understand and uncover "nature's mysteries involving the processes and interdependencies among genomics, plants, ecosystems, watersheds, regional climate, and the earth system." By studying the fundamental properties encoded in an organism's genome, DOE scientists are trying to understand the principles that dictate the translation of the genetic code into functional proteins and metabolic/regulatory networks underlying the systems biology of plants and microbes (microscopic organism, which may exist in its single-celled form or a colony of cells) as they respond to and modify their environments. This understanding will enable the design and reengineering of microbes and plants supporting an extensive clean energy portfolio, including improved bioproduct and biofuels, as well as controlled biological transformation of materials such as nutrients and contaminants in the environment.¹⁰

Biological Systems Science Division

The hearing will focus on the capabilities of the Biological Systems Science Division (BSSD) of BER. BSSD's research focuses on integrating discovery and hypothesis driven sciences with technology development to study plant and microbial systems relevant to national priorities in energy security and resilience. BSSD defines systems biology as the "multidisciplinary study of complex interactions specifying the function of entire biological systems—from single cells to multicellular organisms—rather than the study of individual isolated components."¹¹ Research areas within the division include genome sequencing, proteomics, metabolomics, structural biology, computational models, and high-resolution imaging and characterization.

BSSD supports the Genomic Science program, considered a leading program in systems biology research, which uses genome sequences as the blueprint for understanding the common principles that govern living systems. The program supports single-investigator and team projects in research areas related to bioenergy, environmental microbiome science, and computational biology;¹² and also supports four distinct Bioenergy Research Centers to accelerate research pathways to improve and scale advanced biofuel and bioproduct production processes.

Bioenergy Research Centers

⁸ <https://science.osti.gov/ber/Research>

⁹ the BER's FY 2021 proposal has the year as 1990, other sources site DOE establishing BER in either 1986 or 1987.

¹⁰ <https://www.energy.gov/sites/prod/files/2020/06/f75/fy-2021-sc-ber-cong-budget.pdf>

¹¹ <https://science.osti.gov/ber/Research/bssd>

¹² <https://science.osti.gov/ber/Research/bssd/Genomic-Science>
<https://genomicscience.energy.gov/pubs/GenomicScienceOverview.pdf>
<https://genomicscience.energy.gov/index.shtml>

- [**Center for Advanced Bioenergy and Bioproducts Innovation \(CABBI\)**](#), led by the University of Illinois at Urbana-Champaign. CABBI integrates recent advances in agronomics, genomics, biosystems design, and computational biology to increase the value of energy crops, using a “plants as factories” approach to grow fuels and chemicals in plant stems and an automated foundry to convert biomass into valuable chemicals that are ecologically and economically sustainable.
- [**Center for Bioenergy Innovation \(CBI\)**](#), led by Oak Ridge National Laboratory. CBI conducts research to accelerate the domestication of bioenergy-relevant plants and microbes to enable high-impact, value-added coproduct development at multiple points in the bioenergy supply chain.
- [**Great Lakes Bioenergy Research Center \(GLBRC\)**](#), led by the University of Wisconsin—Madison in partnership with Michigan State University. GLBRC is developing the science and technological advances to ensure sustainability at each step in the process of creating biofuels and bioproducts from lignocellulose.
- [**Joint BioEnergy Institute \(JBEI\)**](#), led by DOE’s Lawrence Berkeley National Laboratory. JBEI deploys advanced tools in molecular biology, chemical engineering, and computational and robotics technologies to transform biomass into biofuels and bioproducts.

Joint Genome Institute

The BSSD subprogram also supports the Joint Genome Institute (JGI), established in 1997 to connect expertise and resources in genome mapping, DNA sequencing, technology development, and information sciences. JGI serves as the central source for genome sequence production capabilities for plants, microbes, and microbial communities. JGI’s capabilities are instrumental to several BER programs, such as the BRCs, and the Institute’s resources are available to the larger research community. JGI is currently engaged in enhancing its expertise to further support microbiome research, and production of complex plant, fungal, and microbial genomes supporting systems biology research within the BRCs and the BER portfolio.

Bioimaging Research

BSSD also supports the Bioimaging Research program, which advances research to develop novel approaches for multifunctional imaging and integrative analysis of the principles guiding gene expression and regulation.¹³ The program supports the development of new imaging, characterization, and sensor techniques, with an emphasis on improvements in quantifying nutrient and metabolite flows in situ in field environments.

¹³ <https://science.osti.gov/ber/bioimaging-research>

Chairwoman FLETCHER. This hearing will come to order. Without objection, the Chair is authorized to declare recess at any time.

Before I deliver my opening remarks, I want to note that the Committee is meeting today virtually. I want to announce a couple of reminders to the Members about the conduct of this hearing. First, Members should keep their video feed on as long as they are present in the hearing. Members are responsible for their own microphones. Please keep your microphones muted unless you are speaking. Finally, if Members have documents they wish to submit for the record, please email them to the Committee Clerk, whose email address was circulated prior to the hearing.

Good afternoon, and welcome to today's hearing on biological research at the Department of Energy (DOE), where we will hear about how these capabilities are being leveraged to respond to the COVID-19 pandemic. I want to thank Ranking Member Lucas, Members of the Energy Subcommittee, and our witnesses for joining us today.

Members of this Subcommittee are enthusiastic about the energy innovations that are coming out of DOE's national laboratories, and rightfully so, given that the labs have provided our country with breakthroughs like supercomputing, inventing new materials, pioneering efficient powerlines, improving automotive steel, and discovering 22 elements. Yes, the periodic table would be much smaller without the national labs.

As the COVID-19 pandemic began to unfold in the United States, it became apparent that DOE's laboratories and programs were also well-positioned to help us respond to the virus. It is perhaps not well-known, but this territory of research is not new to the labs. In fact, as an example, national lab scientists developed a non-toxic foam that neutralizes chemical and biological agents. It was this foam that was used to clean up the congressional office buildings and mail rooms exposed to anthrax in 2001.

Lab scientists are also credited for developing the field of nuclear medicine, producing radioisotopes to diagnose and treat disease, designing imaging technology to detect cancer, and developing software to target tumors while sparing healthy tissue. DOE labs house and operate national user facilities like the Joint Genome Institute (JGI), established by the Department in 1997 as part of the Human Genome Project. Today, institute researchers survey the biosphere and characterize organisms relevant to the DOE science missions of bioenergy, global carbon cycling, and biogeochemistry. They also provide advanced sequencing and computational analysis of genes related to clean energy generation and environmental characterization and cleanup. Leveraging these capabilities has enabled researchers to develop countermeasures against the novel coronavirus like diagnostic tests and allowed them to assess transmission and evolution dynamics as the virus spreads globally.

This hearing will examine the historic reasons for why the Department possesses advanced bioscience capabilities to address the Nation's great challenges and to stimulate innovation, how this expertise and DOE's biological research tools are being leveraged to respond to the COVID-19 pandemic, and what future directions for the Department's biological system research can provide solutions for our Nation's most pressing issues.

I look forward to hearing from our witnesses sharing their expertise on these topics, as well as hearing how the Science Committee can best support DOE's biological research activities to unleash the next generation of innovation.

[The prepared statement of Chairwoman Fletcher follows:]

Good afternoon and welcome to today's hearing on biological research at the Department of Energy, where we will hear about how these capabilities are being leveraged to respond to the COVID-19 pandemic. I want to thank Ranking Member Lucas, Members of the Energy Subcommittee, and our witnesses for joining us today.

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I look forward to hearing from our witnesses sharing their expertise on these topics as well as hearing how the Science Committee can best support DOE's biological research activities to unleash the next generation of innovation.

But, before I recognize Ranking Member Lucas, I would like to take a moment to acknowledge that we are holding this hearing on the 19th anniversary of the September 11 attacks, and to ask for a moment of silence for us to remember and honor those who lost their lives, those whose lives were forever altered, and our first responders, the brave men and women who rushed in to help our fellow Americans.

Chairwoman FLETCHER. Before I recognize Ranking Member Lucas, I would like to take a moment to acknowledge that we are holding this hearing on the 19th anniversary of the September 11 attacks, and to ask for a moment of silence for us to remember and honor those who lost their lives, those whose lives were forever altered, and our first responders, the brave men and women who rushed in on this day to help our fellow Americans.

[Moment of silence observed.]

Chairwoman FLETCHER. Thank you. I'll now recognize Mr. Lucas for an opening Statement.

Mr. LUCAS. Thank you, Chairwoman Fletcher, for hosting this hearing, and thank you for all our witnesses for being with us this afternoon.

During all the challenges and the uncertainties of this pandemic, one thing has stood out: our scientific community has gone above and beyond in the effort to understand, treat, and prevent COVID-19. The Department of Energy and its Office of Science and National Labs have been central to this effort. Today, we have the chance to narrow our focus to DOE's biological research efforts, in particular, the Biological and Environmental Research program, BER.

BER is a high-priority research area within the Office of Science that's consistently received bipartisan support from this Committee. From examining the complex behavior of plants and microbes to developing new approaches to characterizing genomic information, the BER portfolio helps address today's public health challenges while preparing us for the next generation of bioscience R&D (research and development).

Much of this work is carried out through BER's user facilities, including the Joint Genomic Institute, the preeminent facility for sequencing plants and microbes. Originally created to lead DOE's role in the Human Genomic Project, JGI sequencing and analyzes more than 200,000 billion bases of DNA each year, 200,000 billion. That's a huge number.

Another key BER user facility, the Environmental Molecular Sciences Laboratory, or EMSL, offers over 50 premier instruments and modeling resources to assist researchers in understanding complex biological interactions. EMSL also offers access to high-performance computing resources to support advanced experimental research in the biosciences.

Dr. Kelly Wrighton is here with us today and her work makes great use of the BER resources. Dr. Wrighton is an Associate Professor at Colorado State University and a recipient of the Presidential Early Career Award for Scientists and Engineers. I look forward to hearing more from her on the value of user access to BER's resources.

BER user facilities, along with the other 25 user facilities maintained and operated by the Office of Science, are vital tools of scientific discovery and important drivers of national economic competitiveness. No other system in the world grants this kind of cutting-edge technology access to tens of thousands of researchers each year.

But the other countries have taken notice. Developing the most advanced scientific facilities has become an intense international competition. The nation with the fastest supercomputer or most complete genomic data set for example, will hold a distinct advantage in nearly every field from materials science to predictive atmospheric modeling.

Office of Science programs like BER need robust Federal support for large-scale user facilities, which academia and industry simply cannot afford. This is why the key component of my bill, H.R. 5685, the "*Securing American Leadership in Science and Technology Act*", is a comprehensive authorization of the BER program, which includes a user facility development program and authorization of

important initiatives like the Bioenergy Research Centers. This legislation also doubles funding for the entire Office of Science over the next 10 years. This significant investment is essential to U.S. leadership in Biological and Environmental Research.

Whether it's COVID-19 or the next public health challenge, our understanding of these complex systems is dependent on the basic research conducted by BER and the Office of Science. I urge my colleagues on both sides of the aisle to join me in focusing our limited legislative days on these bipartisan programs.

I once again want to thank our witnesses for being here today, and I look forward to a productive discussion. And thank you, Chairwoman Fletcher, and I yield back the balance of my time.

[The prepared statement of Mr. Lucas follows:]

Thank you, Chairwoman Fletcher for hosting this hearing, and thank you to all our witnesses for being with us this afternoon.

During all the challenges and uncertainties of this pandemic, one thing has stood out: our scientific community has gone above and beyond in the effort to understand, treat, and prevent COVID-19.

The Department of Energy and its Office of Science and National Labs have been central to this effort. Today we have the chance to narrow our focus to DOE's biological research efforts-in particular, the Biological and Environmental Research program, or B.E.R.

B.E.R. is a high-priority research area within the Office of Science that has consistently received bipartisan support from this Committee. From examining the complex behavior of plants and microbes to developing new approaches to characterizing genomic information—the B.E.R. portfolio helps address today's public health challenges while preparing us for the next generation of bioscience R&D.

Much of this work is carried out through B.E.R.'s user facilities, including the Joint Genome Institute, the preeminent facility for sequencing plants and microbes. Originally created to lead DOE's role in the Human Genome Project, JGI sequences and analyzes more than 200,000 billion bases of DNA each year.

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I once again want to thank our witnesses for being here today. I look forward to a productive discussion. Thank you Chairwoman Fletcher and I yield back the balance of my time.

Chairwoman FLETCHER. Thank you very much, Mr. Lucas.

I will now recognize the Chairwoman of the Full Committee, Ms. Johnson, for an opening Statement.

Chairwoman JOHNSON. Thank you very much, Mrs. Fletcher and Mr. Lucas, for holding this hearing today, and thank you to all the witnesses for being with us today.

We meet to discuss the groundbreaking bioscience research supported by the Department of Energy's Biological and Environmental Research program, and how these capabilities are now being used to better understand the novel COVID-19 virus.

DOE stewards many unique facilities related to the biosciences. They range from the Department's world-class genomic sequencing tools that have been decades in the making, to large x-ray light sources that can be used to identify various characteristics of and treatments to the virus. Combining this experimental knowledge with the Department's state-of-the-art supercomputing capabilities provides our Nation with a scientific testbed that is second to none.

This extensive biological research portfolio has been leveraged as part of a broad departmentwide initiative called the National Virtual Biotechnology Laboratory (NVBL) that was created to help address the issues we face from the current global health crisis, as well as those that we can expect in the future. Not only are the activities of the Biological and Environmental Research program so critical for better preparing us to respond to potential future pandemics, but also for our national energy security and for addressing the climate crisis. Among other applications, research carried out under this program will help us develop the low-emissions biofuels of the future, which will be very important if we work to decarbonize the transportation sector and other parts of our economy.

Today, however, our focus is on the program's contribution to the fight against COVID, and I look forward to our witnesses' testimony. I thank you again to our witnesses for being here, and with that I yield back the balance of my time.

[The prepared statement of Chairwoman Johnson follows:]

Thank you Chairwoman Fletcher for holding this hearing today, and thank you to all of our witnesses for being here.

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Chairwoman FLETCHER. Thank you, Chairwoman Johnson.

If there are Members who wish to submit additional opening statements, your statements will be added to the record at this point.

And at this time I would like to introduce our witnesses. Dr. Mary Maxon is the Associate Laboratory Director of Biosciences at Lawrence Berkeley National Laboratory where she oversees Berkeley Lab's biological systems and engineering, environmental genomics and system biology, molecular biophysics and integrated bioimaging divisions, and the DOE Joint Genome Institute. Prior to joining Berkeley Lab, Dr. Maxon worked in the biotechnology and pharmaceutical industries, as well as the public sector in such positions as Assistant Director for Biological Research at the White House Office of Science and Technology Policy where she developed the National Bioeconomy Blueprint.

Dr. Debra Mohnen is Professor of Biochemistry and Molecular Biology at the Complex Carbohydrate Research Center at the University of Georgia. She has studied plant cell wall synthesis, structure, and function for more than 30 years and currently serves as Research Domain Lead for Integrative Analysis and Understanding within the Department of Energy-funded Center for Bioenergy Innovation (CBI).

Dr. Glenn Randall is a Professor of Microbiology and Chair of the Committee on Microbiology at the University of Chicago where, for the past 15 years, he's overseen studies for emerging RNA viruses. This year, Dr. Randall was also appointed the Director of Emerging Infection Research at the Howard Taylor Ricketts Regional Biocontainment Laboratory where he leads the lab's COVID-19 research.

Last but certainly not least, Dr. Kelly Wrighton is a Professor for Soil and Crop Sciences and Microbiome Science at Colorado State University where her research focuses on the chemical reactions catalyzed for microorganisms. Prior to joining Colorado State, Dr. Wrighton was an Assistant Professor of Microbiology at the Ohio State University.

So thank you to all of our witnesses for joining us today. As you should know, you will each have 5 minutes for your spoken testimony. Your written testimony has already been circulated and will be included in the record for the hearing. When you've completed your spoken testimony, we will begin with questions. Each Member will have 5 minutes to question the panel. We will begin with our witness testimony, and we'll start with Dr. Maxon. Dr. Maxon, please begin.

**TESTIMONY OF DR. MARY MAXON,
ASSOCIATE LABORATORY DIRECTOR FOR BIOSCIENCES,
DEPARTMENT OF ENERGY,
LAWRENCE BERKELEY NATIONAL LABORATORY**

Dr. MAXON. Chairwoman Johnson, Ranking Member Lucas, Chairwoman Fletcher, Ranking Member Weber, and Members of

the Committee, thank you for including me in this important hearing. My testimony reflects my views only and not those of the Department of Energy.

DOE's history of biological research is fascinating from pioneering nuclear medicine and understanding the impact of radiation on humans to how biology drives energy solutions and creates new economic opportunities for the U.S. bioeconomy. Because of the foundation and biology built across the national lab complex, the Office of Science Biological and Environmental Research program, BER, is today one of the world's leading supporters of nonhuman bioresearch. That is biology of microbes and plants. BER delivers transformative energy and environmental discoveries and solutions and, along with the broader Office of Science and DOE capabilities, can respond aggressively to national crises such as the current coronavirus pandemic.

Berkeley Lab's founder Ernest Lawrence in 1931 invented the cyclotron, a particle accelerator that is the original ancestor of today's DOE light sources, the large hadron collider, and particle accelerators around the world. Understanding the cyclotron's potential beyond physics, Lawrence asked his younger brother John, an M.D., to harness it for bioresearch, a move that changed modern medicine forever and laid the foundation for DOE's biosciences capabilities.

In 1937, John used radioisotopes from the cyclotron to successfully treat a bone marrow disorder and later used beams of energized neutrons to treat leukemia, the first cancer treatment with beams from a particle accelerator. And with that, the field of nuclear medicine was born.

Bioresearch wasn't limited to human health. At Lawrence's urging, Melvin Calvin and his colleagues used a radioisotope of carbon to trace how sunlight drives photosynthesis, winning a Nobel Prize in 1961.

Because of BER's deep expertise in bioresearch and the Department's role in large interdisciplinary initiatives, the Nation turned to DOE and then later to the NIH (National Institutes of Health) to sequence the human genome. DOE's part of the Human Genome Project was focused on a collaboration among three national labs to create the Joint Genome Institute, the JGI. JGI contributed 13 percent of the total Human Genome Project and, now managed by Berkeley Lab, is the largest facility in the world dedicated to genome sciences for energy and environmental solutions. With roughly 65 billion genes from microbes alone—and that's significant given the basis of every—almost every biomanufacturing process starts with genes and circuits of genes harnessed to make useful bioproducts, including fuels and therapeutics.

Today, Berkeley Lab's Joint Bioenergy Institute, JBEI, a BER Bioenergy Research Center, has leveraged DOE's bio-expertise, facilities, and whole systems approach to lower the cost of bio-based isopentenol, which has an energy density close to gasoline. Ten years ago, one gallon of isopentenol produced in the lab cost about \$300,000, and today, it's closer to \$3 a gallon.

DOE is now able to respond to the coronavirus in similar ways to the Human Genome Project response and JBEI's systemic approach, that is with diverse teams working together under the Na-

tional Virtual Biotechnology Lab established by Office of Science Director Chris Fall and directed by Deputy Director Harriet Kung. The NVBL has brought together all of the national labs to advance innovations in coronavirus testing, new targets for therapeutics, epidemiological and logistical support, and to address supply chain bottlenecks. The national labs are now leveraging DOE user and collaboration facilities to understand the ancient origins of coronaviruses to identify possible COVID-19 treatments quickly, develop biomanufacturing processes for new therapeutics, and investigate new materials and reagents for viral detection.

DOE's bio-capabilities promise to give rise to future new tools to reproducibly study biological systems in controllable, fully instrumented lab ecosystem environments, something not possible today anywhere in the world. These new fabricated ecosystems are envisioned to help understand microbiomes and how they control soil carbon cycling and could also be used to detect, identify, and mitigate new pathogens in soil systems.

In summary, DOE's bioresearch enterprise has a significant history and an urgent, vital future for delivering scientific solutions to drive the U.S. bioeconomy. Thank you very much.

[The prepared statement of Dr. Maxon follows:]

BIOLOGICAL RESEARCH AT THE DEPARTMENT OF ENERGY: LEVERAGING DOE'S UNIQUE
CAPABILITIES TO RESPOND TO THE COVID-19 PANDEMIC

September 11, 2020

A Hearing of the
Subcommittee on Energy
Committee on Science, Space, and Technology
United States House of Representatives

Testimony of
Dr. Mary Maxon
Associate Laboratory Director for Biosciences
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Introduction

Chairwoman Johnson, Ranking Member Lucas, Chairwoman Fletcher, Ranking Member Weber, and distinguished members of the committee, thank you for holding this important hearing and for inviting me to testify about the Department of Energy's (DOE) Office of Science's biology research and development enterprise. And, thank you for your strong and unwavering support for science and discovery, and for your commitment to developing the next diverse generation of scientists, engineers, and other critical STEM practitioners.

I am Mary Maxon, and I am the Associate Laboratory Director for Biosciences at Lawrence Berkeley National Laboratory (Berkeley Lab). Berkeley Lab was founded in 1931 and has been managed ever since by the University of California for the DOE. Our researchers develop sustainable energy and environmental solutions, create useful new materials, advance the frontiers of computing, and probe the mysteries of life, matter, and the universe. Over 14,000 scientists from around the world rely on the Lab's national scientific user facilities for their own discovery science.

My testimony represents my views only and does not represent the views or positions of the Office of Science or of the Department of Energy.

Throughout my career – first as a microbiology student and as a researcher within academia and industry, later as a policymaker in government, and today in research management – I've witnessed the progress made in biosciences. It has been extraordinary. Things possible today would have flabbergasted me as a young Ph.D. candidate at the University of California. Among

the important facts that I did not know as a young student, but that I know now, is that many of the advances in biology would not have happened without the DOE's Office of Science and without our national laboratories. Although understood by too few, DOE's Office of Biological and Environmental Research is critical to the nation's innovation engine and to its international economic competitiveness. I will strive today to describe just how important DOE's role is in driving biological innovation, addressing challenges in energy and environmental sustainability, and building the nation's biobased economy.

Today, my testimony will attempt to tell this story by addressing:

1. *How early, mission-driven federal investments created the DOE biology enterprise we benefit from today;*
2. *How DOE and the nation is leveraging the investments made in facilities and human expertise to advance today's mission priorities; and*
3. *How the Office of Science Biological and Environmental Research program is delivering solutions to society, including responding to national crises such as the Coronavirus pandemic, and helping to drive the nation's bioeconomy.*

In overview, the foundation of DOE's biosciences capabilities has been and continues today to be built on: investing in early career talent and entrusting them with solving tough problems; bringing researchers, engineers, and operations together in dynamic teams; and inventing novel, unique and useful new technologies that advance discovery and invention -- including scientific user facilities. These tools are sophisticated, often large in scale or scope, and cost-prohibitive for academia or industry to build and maintain. No other federal agency or international entity can match the Department's record on this score.

Perhaps the most important assets at the national laboratories, however, are the men and women who conduct the research, as well as those who provide the much needed administrative, financial, technical, and health and safety support. Although the narrative of the brilliant solo scientist persists in today's culture, in fact most scientific research is conducted by multi-disciplinary teams of people rather than single investigators. Scientific discovery is fueled by creativity and perseverance, and extraordinary progress is most often made when diverse perspectives allow problems to be seen from a variety of different angles. Cultivating talent and promoting inclusion and diversity are central to the creation of a successful work environment. Among the national labs, Berkeley Lab was the first to publish its workforce diversity demographics. We know that successful innovation depends on the ability to create a community that brings together people with diverse backgrounds and different approaches to problem-solving.

The Coronavirus Pandemic and the National Virtual Biotechnology Laboratory

The Department's ability to respond effectively to the coronavirus pandemic illustrates the power of and value to the nation of biology research capabilities, expertise, and resources at the national laboratories. With emergency funding from the Congress, the Department of Energy, the Office of Science, including its Biological Environmental Research program (BER) have, pretty much on the fly, organized a highly effective and sophisticated response to the pandemic.

Leveraging the remarkable breadth of expertise, capabilities, and resources from every national laboratory, the Department, under the leadership of Office of Science Director Chris Fall, established the National Virtual Biotechnology Laboratory (NVBL) to coordinate and expedite SARS-CoV-2 and COVID-19 related research across the Office of Science. NVBL is supporting the development of innovations in testing capabilities, identifying new targets for medical therapeutics, providing epidemiological and logistical support, and addressing supply chain bottlenecks by harnessing extensive additive manufacturing capabilities. Examples of this incredible response will be included throughout this testimony and will illustrate the Department's deep bench of biosciences expertise and unique scientific user facilities.

Biology at DOE: A History

DOE's involvement in biological research has a grand and fascinating history, and there are many incredible examples from across the national laboratory complex. These examples reflect the importance that biology has played for the Department, from understanding and addressing the impacts of radiation exposure for humans and its effects on natural environments, to how biology drives energy solutions and creates new economic opportunities for the nation's bioeconomy. Much of the biology research at Lawrence Berkeley, Oak Ridge, Argonne, Pacific Northwest, Brookhaven, and at other national labs began by tackling the challenges of a post-WWII world and by leveraging the unique resources and expertise that existed because of significant federal investments made during the war and afterward. However, because I represent Berkeley Lab and know its stories best, my testimony will focus on its particular role in the history and future of biological research within the Department of Energy.

The Advent of Nuclear Medicine

A foundational moment in the building of DOE's biological capabilities took place on August 26, 1931, 89 years ago, when the University of California took a big gamble on its then youngest full professor: Ernest Lawrence, the namesake of Berkeley Lab. They built for him a lab where he

could scale up the experimental tool he invented and for which he would later win the Nobel Prize – the cyclotron, a circular particle accelerator in which beams of electrons smash into materials at 99.9999% the speed of light to reveal their atomic, molecular and chemical secrets. Lawrence's cyclotrons are the great grandfathers of the Large Hadron Collider and light sources such as the Advanced Photon Source at Argonne and the Advanced Light Source at Berkeley Lab.

As Lawrence's cyclotrons grew and became more powerful, their transformational value for science solidified. The team around them got bigger, too, and included experts from many fields: machinists; chemical, electrical, and civil engineers; electricians; chemists, physicists, and materials scientists; as well as accountants, secretaries, and other administrative staff. Big team science was under way, and a new scientific research paradigm was launched.

Throughout the 1930s, 40s, and 50s, cyclotrons were facilitating the discovery of new elements at an amazing rate – among them technetium, neptunium, and plutonium. (Sixteen elements on the periodic table were discovered at Berkeley Lab – more than any other institution in the world.) Producing new radioactive isotopes became a matter of rote. Lawrence understood the potential of the cyclotron and these products beyond basic physics. He turned to family, his younger brother John, an M.D., to explore and capitalize on the power of the cyclotron for biological research – a move that changed modern medicine forever and laid a critical piece of the foundation for DOE's focus on biosciences.

John Lawrence joined his brother at Berkeley in 1935 after teaching at Yale where he studied the effects of radiation on the pituitary gland. John had become interested in the potential use of cyclotron-produced radioisotopes and nuclear radiation in the treatment of cancer when he and a colleague discovered that a beam of neutrons had a much more destructive effect on tumors than an equivalent dose of x-rays. In 1937, John Lawrence used the radioisotope phosphorus-32 to successfully treat polycythemia vera, a bone marrow disorder. In 1939, he used beams of energized neutrons to treat a patient with leukemia, the first treatment of cancer with beams from a particle accelerator. These advances attracted funding to build new cyclotrons and state of the art research labs from renowned institutions and philanthropists such as the National Cancer Institute and steel magnate William Donner, whose son Joseph had died of cancer in 1929.

Although the Manhattan Project dominated Lawrence's lab and cyclotrons for a time, John, his Berkeley colleagues, and researchers at other national labs continued to build the field of nuclear medicine and advance other medical processes and treatments during the war and over the following decades. Among their many accomplishments were:

- the use of particle beams to successfully treat acromegaly (the abnormal growth of the hands, feet, and face) and Cushing's disease;
- establishing world leading research capabilities across several national labs focused on the effects of radiation on humans;
- the invention of the Anger Camera – a revolutionary medical imaging tool invented by Hal Anger in 1957 - that is still the predominant nuclear medicine imaging machine;
- identifying the roles that HDL and LDL cholesterol may play in heart disease¹; and
- the discovery and production at Brookhaven National Laboratory of the isotope technetium-99m (Tc-99m). Used to create images from inside the human body, Tc-99m is used in tens of millions of medical diagnostic procedures annually, making it the most commonly used medical radioisotope in the world.²

Although DOE ended its direct role in funding a broad program of nuclear medicine research, it continues to fund important radioisotope research, development, and production as part of a key federal program that produces isotopes that are otherwise unavailable or in short supply for U.S. science, medicine, and industry. Additionally, health research-focused organizations like the National Institutes of Health and the Howard Hughes Medical Institute fund important research and facilities at the national laboratories to advance their mission objectives, including the development and operation of specialized biomedical beamlines at light sources.

Unlocking the Mysteries of Photosynthesis

Even during the heady days of advances in medicine at the national laboratories, biological research wasn't just limited to human health. Presaging today's DOE biosciences portfolio, which is primarily focused on non-human biology, Ernest Lawrence is reputed to have told biochemist Melvin Calvin in September 1956 that it was "time to do something useful with radioactive carbon." Scientists understood the potential use of one of Carbon's isotopes, Carbon-14, as a "tracer," a substance that can be tagged to organic molecules and used to follow those molecules through different stages of a chemical process. Understanding the mysteries of photosynthesis was the objective.

Using carbon-14 as the tracer, Calvin organized a team of researchers to map the path that carbon takes through a plant during photosynthesis. Over the next few years, in the process of creating their map, Calvin and his team showed that sunlight acts on the chlorophyll in a plant to fuel growth, rather than on carbon dioxide as was previously believed. For leading the research that deciphered the photosynthetic process, Calvin received the 1961 Nobel Prize in chemistry. The Calvin-Benson-Bassham Cycle we learn about in school bears his name.

¹ <https://academic.oup.com/in/article/128/2/439S/4724045>

² <https://www.bnl.gov/newsroom/news.php?a=24796>

DOE's Office of Science Biological and Environmental Research: The Modern Era

At the beginning of the national laboratory system, and as evidenced at the creation of the Atomic Energy Commission (AEC) in 1946, DOE's mission imperatives and the national laboratories' capabilities in biological research and development were well understood within government. The enabling legislation for the AEC specifically called out the "utilization of fissionable and radioactive materials for medical, biological, and health purposes." Congressional direction continued to support this view, or slight variations on it, in reauthorization bills over the years. The inclusion of biosciences within the repertoire of the Department was codified again, with a particular focus on energy and the environment, in the legislation that created the Department of Energy in 1977 and in subsequent legislation ever since. The Engineering Biology Research and Development Act sponsored by this Committee and passed by the House on December 9, 2019, is another recent example of Congressional intent that the Department play a critical role in biosciences for the nation.

With roots stretching back to the beginning of the national laboratory complex, the Office of Sciences' Biological and Environmental Research program (BER) is today one of the world's leading supporters of non-human biological research and development – that is, the biology of microbes, plants, and other non-human organisms. As described below in more detail, the BER of today supports world leading scientific user facilities and funds cutting edge biosciences research activities at the labs and at universities across the nation.

Sequencing the Human Genome

Because of BER's deep experience in managing biological research and its leadership role in driving large, interdisciplinary initiatives such as designing and building particle accelerators, it was no surprise that the nation turned to DOE, and later to the National Institutes of Health (NIH), when setting eyes on the daunting task of sequencing the human genome. Deep understanding within the Congress of the national labs' capabilities in addressing this grand challenge helped as well.

BER had begun seriously considering the Department's interest in deciphering the human genome as early as 1984 as it became clearer that new analytical tools and scientific methods were needed to advance mission-focused research in biological mutations caused by radiation. A DOE-sponsored meeting in December 1984, later dubbed the Alta Conference for its Utah location, convened leading geneticists of the day to discuss new approaches to genomics research and to begin to map a path forward. BER followed on with additional conversations, workshops, and road-mapping and eventually by funding more genomics research across its

laboratories. DOE and the national labs were more than ready when the national human genome initiative took off.

Although there were skeptics of DOE's role in the project and a lot of jockeying within the Administration and the Congress for control and funding, the Department and NIH signed a Memorandum of Understanding in 1988 about how to move forward collaboratively. With strong and united support within the Congress and the Administration, the federal Human Genome Project, with a goal of determining the exact order of the DNA letters and the genes encoded in the human genetic blueprint, was established in 1990.³

DOE's part of the Human Genome Project was eventually focused on a collaboration among the three University of California managed national laboratories, Lawrence Berkeley, Lawrence Livermore, and Los Alamos and their genome research laboratories. This collaboration was formerly organized as the Joint Genome Institute (JGI) in 1997. The significant economies of scale achieved by bringing these efforts together under one roof enabled the JGI to be the first to publish the sequence analysis of the target chromosomes [5](#), [16](#), and [19](#), in the journal *Nature*. JGI's contribution represented 13% of the total Human Genome Project.

With the completion of the Human Genome Project in 2003, leaders at DOE and within the Congress and the Administration understood that the specialized tools, expertise, and capabilities of JGI could be powerfully leveraged to address grand challenges and grand opportunities in energy solutions and environmental sustainability. So, in 2004, the Department established JGI as a national user facility, similar to the light and neutron sources at national labs that this Committee has examined in previous hearings, to focus on non-human health genomics grand challenges and opportunities.

The Joint Genome Institute

JGI, now a Berkeley Lab-managed user facility, has grown to serve a community of 2,000 users annually from almost every state and from around the world. Like the other national user facilities, researchers submit proposals for using the JGI and are awarded access through a peer-reviewed competitive process. In addition to direct users, there are nearly 18,500 data users worldwide who in 2019 downloaded 2.16 million files and a total of 400 terabytes of data. The vast majority of JGI proposals are supported under the auspices of its Community Science Program (CSP) to characterize organisms (plants and microbes) relevant to the DOE science mission areas of bioenergy, global carbon cycling, and biogeochemistry.

³ <https://plato.stanford.edu/entries/human-genome/>

The JGI further extends its capabilities through the “Facilities Integrating Collaborations for User Science” (FICUS) initiative. FICUS enables a “one-stop shopping” approach whereby an applicant, in one proposal submission, can request multiple complementary technical resources at JGI and in partnership with the Environmental Molecular Sciences Laboratory (EMSL). EMSL is another national user facility supported by the BER located at Pacific Northwest National Laboratory (PNNL). Through FICUS a user could access metabolomics technologies along with protein characterization and imaging technologies at EMSL and DNA sequencing and synthesis resources at the JGI. The JGI-EMSL FICUS collaboration, now in its eight year, has supported over 70 joint proposals. Owing to this success, the FICUS initiative has been extended to include the National Energy Research Scientific Computing center to focus on data analysis projects.

Over 15 years, the JGI transformed from an organization that was responsible for one project (sequencing its three human chromosomes) to a national user facility completing over 43,500 projects and generating over 2,100 peer-reviewed scientific publications. Here are some selected examples from the diversity of projects that JGI enables.

Revolutionized our understanding of ecosystems. Using its powerful DNA sequencing capacity and novel computational analysis strategies, JGI has shed light on the interactions in numerous complex ecosystems, enabling comparisons of nutrient cycling in agricultural and prairie soils and drought tolerance of plants grown under these different conditions. In addition, providing the means to gauge greenhouse gas emissions produced by microbes in Arctic permafrost and Bay Area wetlands, and determining the microbes capable of coping with oil spills and natural seeps in the Gulf of Mexico.

Cataloging the diversity of life. There are more microbes in a handful of soil than there are stars in the Milky Way, but we know far less about the former. In 2007, JGI began working to change that by establishing GEBA, a worldwide Genome Encyclopedia of Bacteria and Archaea. Currently, the information gathered by the GEBA initiative along with others has funneled into the Integrative Microbial Genomes (IMG) data system that currently has over 61 billion genes and counting. This repository represents a springboard for adding new branches to the microbial tree of life and understanding the function of the newly characterized species in our environment.

Coronavirus genomes. With the goal of developing computational and machine learning/artificial intelligence approaches to study the evolutionary patterns of SARS-CoV-2, JGI researchers are using their genomics expertise to analyze over 80,000 coronavirus genomes to investigate genome similarities and differences. Knowledge gained through this research may have useful purposes in addressing the coronavirus pandemic, including diagnostics, vaccines,

and possible treatments. JGI received NVBL support for exceptional operations to continue research during the pandemic this past year

Sequencing plant species. The poplar was the first tree ever sequenced. This was done at the JGI in 2006. We now have the genetic sequences of hundreds of different plant species that form the foundational knowledge needed to develop bioenergy crops with desired traits. This genomic knowledge is being used by the DOE Bioenergy Research Centers (BRCs) to develop optimal plant species and conversion processes for the efficient production of biofuels and bioproducts that can bolster and catalyze growth in the US bioeconomy. The BRCs are among the JGI's largest dedicated partnerships.

The Bioenergy Research Centers

Established by BER in 2007, the BRCs conduct basic science but with “use inspired” goals and objectives. Simply put, the BRCs’ holy grail is to develop viable integrated approaches for the production of advanced biofuels and bioproducts from biomass that are cost equivalent to and/or better performing than existing alternatives. Jay Keasling, the CEO of the Joint BioEnergy Institute (JBEI), the Berkeley Lab led BRC, says that the ultimate goal is to use every single carbon atom present in the biomass feedstock, be it found in switchgrass, poplar, sorghum, or pine, to make affordable and scalable biofuels and bioproducts. Achieving this would create significant new economic opportunities for American farmers and for the nation’s rural communities and catalyze rapid growth in the US bioeconomy.

There are four BRCs, they are:

[Center for Advanced Bioenergy and Bioproducts Innovation \(CABBI\)](#), led by the University of Illinois at Urbana-Champaign.

[Center for Bioenergy Innovation \(CBI\)](#), led by Oak Ridge National Laboratory

[Great Lakes Bioenergy Research Center \(GLBRC\)](#), led by the University of Wisconsin—Madison in partnership with Michigan State University.

[Joint BioEnergy Institute \(JBEI\)](#), led by DOE’s Lawrence Berkeley National Laboratory

Each center has a unique focus, yet they work collaboratively on shared scientific and technology challenges, and in syncing up with industry to stay focused on scientific avenues that will most likely scale and ultimately become commercially transferable.

The BRCs’ record of accomplishment speaks for itself. Since 2007 they have collectively published 3,424 academic papers, disclosed 728 inventions, and filed 521 patent applications.

Nineteen companies have spun out of the BRCs, including twelve from JBEI. Since its founding, JBEI has contributed many scientific achievements, including:

- *Engineering bioenergy crops to increase sugar-containing polymers and decrease lignin in plant cell walls*
- *Developing a feedstock agnostic pretreatment technology based on ionic liquids that is affordable and scalable*
- *Developing optimized microbial routes for the conversion of biomass-derived sugars and lignin-derived intermediates into advanced, “drop-in” blendstocks for gasoline, diesel, and jet fuels*

Here are some selected examples from the diversity of projects that JBEI has enabled:

Lower-cost, higher-performing biofuel. In terms of meeting the cost and performance goals, one example is the cost of isopentenol, a leading advanced drop-in biofuel candidate. Ten years ago, the cost of one gallon produced in the lab was approximately \$300,000. Today, it’s closer to \$3.00 per gallon. Isopentenol has an energy density close to that of gasoline and burns more efficiently than ethanol in certain combustion engines. It can also be chemically converted into an advanced aviation biofuel that enables more efficient jet engine combustion that can extend the range of airplanes. Performance has also improved for other leading biofuel candidates.

Better adjuvants for possible Coronavirus vaccines. Adjuvants are used in some vaccines to help create a stronger immune response. Adjuvants help vaccines work better. Many vaccine adjuvants are extracted from plants and are in short supply. Berkeley Lab scientists are working with a pharmaceutical company to engineer yeast to produce a very effective vaccine adjuvant so that there will be a sufficient supply of the adjuvant for the billions of doses that will be needed to address the coronavirus pandemic. The yeast that will produce the vaccine is a variant of the yeast that JBEI originally engineered to produce a variety of biofuels.

“Bio-advantaged” chemicals. Lygos, one of JBEI’s twelve spin-off companies, produces “bio-advantaged” chemicals, where chemicals from petroleum cannot compete with those produced through biochemistry. JBEI scientific discoveries and technology development underpin much of Lygos’ capabilities. The company is currently commercializing its first product, malonic acid, and its platform for synthetic biology is being exploited to develop a number of new products. Malonic acid, traditionally made from petroleum feedstocks, is an important precursor to many valuable products. The Lygos malonic acid is not only made from a renewable feedstock, but also employs a biomanufacturing process that results in the production of less hazardous waste and fewer exposures for workers to toxic chemicals.

Still, the BRCs have work to do. A major objective is using their versatile platform technologies and leveraging their expertise in biofuels to accelerate research into high-value biobased chemicals and bioproducts, such as those driving toward commercialization at Lygos. Developing these high-value products can drive economies of scale that could help to simultaneously bring down the costs of biofuels and speed their delivery to consumers. In addition to being an important part of a more sustainable economic model for biofuels, bioproducts have the additional benefit of storing carbon in durable goods and products such as paints, flooring, furniture, recyclable plastics, etc.

Today and Tomorrow: Bringing Big Science to Biology

Today, research assets at all of the national laboratories are leveraged for biosciences discovery and invention. These assets are not just limited to those funded by BER, like JGI, the BRCs, EMSL, and others. Biological research at the labs leverage investments made by the Basic Energy Sciences, Fusion Sciences, High Energy Physics, and Advanced Scientific Computing Research programs among others within the DOE Office of Science. Collectively, the expertise, national scientific user facilities, and other capabilities of the Office of Science serve as research and technology development platforms for researchers from academia and industry from throughout the US and the world. They also represent, figuratively and literally, a machine learning ecosystem where results, failures, and successes are shared, learned from, and disseminated.

Imaging Biology to Drive Advances

A leading example that isn't supported by BER funding but rather by the Office of Science's Basic Energy Sciences program are the bioscience capabilities at DOE's light sources. These descendents of Lawrence's cyclotrons are invaluable to the nation's biological research community of academics, industry, and national lab researchers. As the Committee has heard in previous hearings, almost every pharmaceutical treatment on the market today has been developed utilizing light sources to determine the structure of potential drug targets. Collectively, the light sources have determined the structures of tens of thousands of proteins. Leading pharmaceutical companies utilize the Advanced Light Source at Berkeley Lab to develop their candidate drugs, for example. The examples of direct implications for drug development are too numerous to list, but include successful treatments for melanoma and vaccine development for ebola.

In addition, new femtosecond X-ray free electron laser sources, another type of light source, such as the Linear Collider Light Source at SLAC National Laboratory, are now used to collect

data from millions of protein crystals per day, resulting in multi-terabyte datasets. For context, a femto-second is one quadrillionth of a second. Yes, it is hard to fathom. These experiments have also been essential in explaining key features of photosynthesis, and will ultimately help lead to improved alternative energy sources.

There are many examples of how these unique resources are being leverage to address the coronavirus pandemic:

Coronavirus structures. These key national assets have been put to use during the current pandemic helping scientists discover the structures of many of the 27 individual proteins in the Coronavirus that cause COVID-19. This can improve diagnostics and treatments by identifying weaknesses in structures and opportunities to disrupt the inner workings of the virus that control how it infects, replicates, and spreads -- helping to speed the development of vaccines and therapeutics. The DOE synchrotron light sources received NVBL support for exceptional operations to continue research during the pandemic this past year, partially supporting these efforts.

In situ protein responses. Beyond the light sources, BER's investment in fundamental biological science and Pacific Northwest National Laboratory's (PNNL) long-standing expertise in molecular research and computational biology has made it possible to explore protein structure characteristics of the Coronavirus and how they can be disrupted. Researchers at PNNL are using robust computational capabilities and a technique called nuclear magnetic resonance spectroscopy to see a single protein in incredible detail, even looking at specific segments of the protein and monitoring responses of those proteins during experiments.

Automation and Computation

Because of BER's investments and the national laboratories' ingenuity, genome sequencing and other biology research processes that once took days, weeks, months, or years now happen in seconds, minutes, hours, or days. Robots perform intricate chemical manipulations by the thousands an hour, replacing the hands-on work of eager postdocs working over days. These tools quickly weed out the combinatorial wheat from the chaff, freeing researchers up for more productive tasks and speeding science along its way.

New imaging and characterization tools now produce terabytes of biological data instead of the gigabytes of previous methods. The revolution in cryo-electron microscopy (using frozen samples in microscopes that use electrons instead of light) for biological systems has led to the routine generation of terabytes of data per microscope per day. For context, one terabyte is equal to a trillion bytes – roughly 1,400 compact discs worth of information. A new detector at

the Berkeley Lab Molecular Foundry's National Center for Electron Microscopy (NCEM) enables scientists to record atomic-scale images in microseconds, or millionths of a second – 60 times faster than possible with previous electron detectors. According to Andrew Minor, NCEM facility director, this new detector, known as the “4D Camera” (for Dynamic Diffraction Direct Detector) is the fastest electron detector ever made.

This abundance of data - its exponential growth and complexity - is a big challenge that also presents a great opportunity for scientific and technological advancement. The computing capabilities at the DOE Office of Science's large computing centers supported by the Office of Science's Advanced Scientific Computing Research program – the National Energy Research Scientific Computing Center (NERSC) at Berkeley Lab and the Leadership Computing facilities at Argonne and Oak Ridge national laboratories, interconnected with ASCR's high-speed network facility, the Energy Sciences Network (ESnet) – are tremendous resources for biology. These supercomputers and DOE's deep bench of computational resources, applied mathematics, software development, and networking capabilities are world class and move biosciences forward by leaps and bounds.

The NVBL and the COVID-19 HPC Consortium, a collaboration among industry, academic, and government HPC centers, are aggressively leveraging Office of Science and other DOE computing resources, such as the supercomputers at the NNSA labs, to address the coronavirus pandemic. Examples include:

Understanding 55 million years of coronaviruses. To ascertain whether COVID-19 may have characteristics similar to the seasonal flu, researchers at Berkeley Lab have been studying how SARS-CoV-2 fits into the history of coronavirus evolution, about 55 million years of diversification. If ancient coronaviruses have swapped genetic material frequently, there is good reason to believe that they will continue to do so. To do this, scientists are utilizing NERSC to computationally generate billions of possible histories that can each explain the data, and then analyze these scenarios to determine which are most likely to have actually taken place. The results so far are in line with the emerging scientific consensus that while recombination has taken place among coronaviruses, it has not happened recently or often, and is unlikely to be a major factor in how SARS-CoV-2 adapts to human hosts.

Identifying possible COVID-19 treatments quickly. At Oak Ridge and Argonne national laboratories, DOE's light sources and leadership computing capabilities have been leveraged to quickly respond to the coronavirus pandemic. One line of inquiry investigated the potential for drugs that typically treat ulcers and acid reflux for their potential antiviral properties. Through computer simulations of SARS-CoV-2 viral proteins and human proteins, the team rapidly ruled out these drugs as possible anti-viral treatments in COVID-19 patients without the need for

testing them further. These efforts continue as part of a multi-lab NVBL effort to identify promising lead compounds for COVID-19 therapeutics.

Although large-scale computing is critical, more and more we understand that there is a rapidly growing need for mid-range, interactive computing, referred to by some as edge-computing, that is not currently best served by the large compute capabilities at DOE's high-performance computing centers. One reason is the rapid growth in omics data (which reflect genes working interconnectedly to express a function or trait), and another is the growing need for data processing and analysis capabilities on site – at the JGI and at NCEM for instance. The 4D Camera mentioned previously generates images at 100,000 frames per second and consequently requires high-speed networks with 400Gbps to 1 Tbps capacity like ESnet to access a supercomputer center like NERSC to process these images in near real-time. On-site, edge computing at NCEM could more efficiently prepare the data for delivery over ESnet. The same is true at JGI and at EMSL.

The Explosion in Data Volumes and Complexity

Another Challenge created by so much data is its distribution and dissemination. There has certainly been progress in providing biological data to researchers online and in ways that are transparent, user friendly, and useful. However, large gaps persist. Information that would be critical to scientists, although published and publicly available, may often exist in an unorganized, uncatalogued way – hard to access and manipulate. It may have well been hidden due to the difficulty of searching through thousands of seemingly unrelated scientific papers and disconnected databases. BER is tackling this challenge head on by leading the development of user-friendly databases as tools to store, catalogue, analyze, and make easily accessible critical biological information. A key feature of this effort is to make data FAIR - findable, accessible, interoperable, and reusable. Essentially FAIR allows many more discoveries to be made in addition to those for which the data were originally gathered.

One example is BER's Systems Biology Knowledgebase ([KBase](#)). KBase is an open software and data platform that enables researchers to predict and ultimately design biological functions. KBase's unified data model allows users to perform integrated analyses across plants, microbes, and their communities with a wide range of tools that interoperate across the tree of life, and to publish their data, methods, results, and thoughts in consistent, citable, executable, and reusable ways that allow scientists to build on the work of others. KBase's openness enables external developers to integrate their analysis tools, facilitating distribution and comparative tool analysis.

A second example is the newly established National Microbiome Data Collaborative (NMDC). As you may have heard, especially in relation to your gut and other human biology, microbiomes play important and often determinant roles in the environments in which they exist. This is also true for plants, their growth and resiliency, the health of other minute organisms, and for larger environmental ecosystems. But, most microbes and how they work together in microbial communities, within microbiomes, remain clouded in mystery.

The mystery is understandable. As mentioned previously in the discussion about JGI, a handful of soil may contain as many microbes as there are stars in our galaxy – perhaps a staggering two hundred billion. Just that statistic alone demonstrates the size of the data problem. But, add to that the need to decipher how the constituent microbes communicate, how they strategize, and how or why they act independently or in concert, and ultimately what is the impact of their actions on a plant, a field of biocrops, or an entire watershed, and one can begin to get a better sense of the challenge. We’ve made progress, however, and over the past few decades microbiome data have grown exponentially. But the sheer amount of data available and the challenge of analyzing and interpreting it productively still present a significant bottleneck.

The NMDC, a partnership led by Berkeley Lab along with Pacific Northwest, Los Alamos, and Oak Ridge national laboratories, is developing an open-access data framework to capture and share microbiome data and analyses. The goal is to facilitate more efficient use of microbiome data, regardless of the purpose for which they may be originally generated, for a wide variety of important applications in energy, environment, health, and agriculture. To tackle this data integration challenge, NMDC leverages DOE’s existing data-science resources and the high-performance computing systems mentioned above. The NMDC’s guiding principles are: making data FAIR; connecting data and compute resources; and engendering strong community engagement that supports open science and shared ownership.

A collaboration with NMDC and the BioScales project at Oak Ridge National Laboratory aims to understand how genes influence ecosystem-level processes in plant-microbiome systems. For example, understanding the genes that allocate carbon to plant root systems can ultimately enable engineering of plants to increase biological carbon capture and create more resilient feedstocks for biofuels and bioproducts production. A major objective is to engineer the more efficient uptake of nitrogen to reduce the need to use nitrogen fertilizers that cause environmental problems including toxic algal blooms.

Microbiome R&D: The Next Frontier?

BER's establishment of the NMDC is a reaction to a science community need, but it is also a response to the federal government's call for a more focused and collaborative all-of-government approach to microbiome research and technology development. Recognizing that siloes among the federal research agencies limit the sharing of data and hamper collaboration and joint efforts to tackle similar science and technology challenges in microbiome R&D, the White House established the Microbiome Interagency Working Group in February of 2016. And, in April of 2018, 21 federal agencies, including USDA, DOE, DOD, NASA, and NSF, but also including USAID, the Veterans Administration, and the FBI among others, released the *Interagency Strategic Plan for Microbiome Research FY 2018-2022*. The plan recommended three "areas of focus to transform microbiome discoveries to solutions":

1. *Supporting interdisciplinary and collaborative research to enable a predictive understanding of the function of microbiomes in diverse ecosystems to enhance public health, food, and environmental security and grow new bioeconomy product areas.*
2. *Developing platform technologies to generate critical insights and to improve access to and sharing of microbiome data across ecosystems.*
3. *Expanding the microbiome workforce through educational opportunities, citizen science, and public engagement.*

The Interagency Strategic Plan proposes coordination in microbiome research activities across 21 U.S. government agencies, "describing the interagency objectives, structure and operating principles, and research focus areas." The goal is to identify capabilities that may be leveraged across government and "represents an opportunity to increase Federal efficiency."

DOE BER, with strong support from the Congress, is doing its part to fulfill the goals of the Interagency Strategic Plan, but more is needed to ensure that the United States retains its current leadership in this critical area of research and technology development.

Fabricated Ecosystems to Speed Biology-Based Solutions

As evidenced through the successful programs and scientific output at JGI, the BRCs, EMSL, KBase, and now NMDC, BER and the national labs are making great strides in managing the large amounts of and ever-increasing complexity of data. However, significant challenges in biology remain, including leveraging experiments, sensing, data, computation, and other capabilities in real time, in situ, to reproducibly observe biology in action and to more quickly test hypotheses and learn from failures and success.

This need has led to the creation and utilization of fabricated, in situ, hyper-sensored environments -- environments created in the lab that can replicate conditions in the field.

Trent Northen, a Presidential Early Career Award in Science and Engineering awardee and a rising star in the world of microbial science at Berkeley Lab, has designed and proselytizes the EcoFAB initiative. EcoFAB aims to build model laboratory ecosystems at laboratories around the world to study environmental microbiomes and learn more about soil carbon cycling and how to develop low input sustainable crop production. To meet this goal, EcoFAB has developed a small, hand-sized lab-scale device, a fabricated ecosystem, to study soil-plant-microbe interactions in a reproducible and controllable system.

Fabricated ecosystems, such as the small EcoFABs, or much larger systems like EcoPODS currently the size of phone booths and in prototype production, hold promise for replicating important ecosystem dynamics. Observing microbiomes, plants, and other organisms under different conditions, scientists will be able to define principles for microbial community assembly and structure, understand the functions of genes, microbes, and metabolomes, and predict microbiome health. EcoFABs and EcoPODs have the potential to bring together communities of scientists working on shared systems, enabling more effective knowledge transfer and the ability to build upon previous findings. By expanding our understanding of the assembly, structure, and functions of microbiomes, significant scientific and technical advances will be made in studies of biomedical technologies, environmental health, agriculture, energy, and nutrient cycling.

Currently the United States leads the development of this new, larger-scale approach to biological research. With its focus on novel technology creation and open, accessible, and shared capabilities and learnings, these fabricated ecosystem research tools are exemplars of BER's and the national laboratories' secret sauce – the approach to science that began with Ernest and his brother John, and with Melvin Calvin and his team of collaborators. DOE is investing significant resources in this novel approach. The Office of Science's Science Laboratories Infrastructure program is funding the construction of a new research building at Berkeley Lab to house these fabricated ecosystems in an integrated way. The Biological & Environmental Program Integration Center (BioEPIC) is currently in the advanced planning stage.

With BER's support and through the support of this and other Congressional committees, the U.S. can retain its leadership and reap the benefits of developing these new resources, and of being first in the delivery of new science, new technologies, new processes, and new products.

Fueling the United States Bioeconomy

Today, the biological mission drivers for DOE, the Office of Science, and BER of creating a more diversified energy future and ensuring environmental sustainability are as important as ever.

They also offer even more potential for driving economic growth and advancing the nation's international innovation competitiveness. Because of the BER's decades of critical investments in biology R&D at the national laboratories and at universities, DOE is playing an outsized role in the development of the nation's bioeconomy. The "bioeconomy," which encompasses a broad range of bio-based, bio-derived, and bio-inspired products and production processes, is a potential juggernaut of economic growth and has appropriately been recognized by the federal government, and governments around the world, as a key industry of the future.

Biology already plays an integral role in the U.S. economy. The foundation of every modern biomanufacturing effort is an important gene or suite of genes that were decoded and purposefully re-coded using genomics technologies such as those at the JGI as previously mentioned. According to a January 2020 National Academies of Sciences, Engineering, and Medicine report, the US bioeconomy is a set of economic activities valued at \$959B and is growing at a significant rate. Fueled by advances in life sciences, engineering, biotechnology, and computing and information sciences, the US bioeconomy is unique in the world. DOE, through BER and also through applied research programs within its Office of Energy Efficiency and Renewable Energy (EERE), is making incredible contributions to bio driven economic development.

EERE's Bioenergy Technologies Office (BETO), which funds research and development for industrially relevant transformative bioenergy technologies, is enabling economically and environmentally sustainable, domestically produced, biofuels, bioproducts, and biopower. BETO accomplishes this through a variety of mechanisms, including support for the national labs to address pre-competitive challenges where the solutions will be of broad benefit to industry. Some examples of applied biobased research at DOE include:

The Agile BioFoundry (ABF). The ABF, a collaboration project between seven national labs, is driving down the cost and time to develop new bioprocessing technologies through an integrated Design-Build-Test-Learn cycle using machine learning. Based on the design of electronic fabs, ABF provides state of the art biology tools and capabilities as a platform for industry -- from startups to large well-established companies.

The Advanced Biofuels and Bioproducts Process Development Unit (ABPDU). The ABPDU at Berkeley Lab was established in a previous time of crisis to de-risk and scale up early stage biofuels and bioproducts technologies for industry. Funded by the American Recovery and Reinvestment Act, the ABPDU staff have worked with over 60 partners to transition their early-stage technologies to commercialization ready, resulting in at least 12 products in the market today and over \$450M in follow-on investment for those partners.

Addressing the Coronavirus pandemic at the ABPDU. True to their mission to accelerate products to market, the ABPDU team assisted three new company partners in the fight against the SARS-CoV-2 virus and COVID-19 with development of new testing reagents, a possible treatment, and nutritional support for patients. The ABPDU stands ready as a resource for the biomanufacturing community and is poised to quickly adapt to any challenge.

First biotechnology-based jet fuel. BETO's investment in bioenergy research and PNNL's long-standing expertise in catalysis science has resulted in an ethanol-based jet fuel that has sustained transcontinental commercial flight. PNNL scientists and their industrial partner LanzaTech jointly developed the first jet fuel from industrial waste gas. This partnership will receive a 2020 Industrial Research Institute Interchange (IRI) Award for its breakthrough. The innovative conversion process fueled a Virgin Atlantic commercial passenger flight from Orlando to London in late 2018 and, in late 2019, an All Nippon Airways flight which flew from Seattle to Tokyo. Using a combination of biotechnology coupled with catalysis, the team proved carbon can be recycled and used for commercial flight.

Biology has the potential, however, to play an even larger role in enhancing U.S. international competitiveness if the nation undertakes a more sophisticated and integrated approach to strategic planning and collaboration that includes increasing targeted investments and developing clear goals and objectives. The international competition is moving fast and our nation's leadership is not assured.

Appointed by the U.S. Department of State, I serve as the US delegate to the Organisation of Economic Cooperation and Development's Biotechnology, Nanotechnology, and Converging Technologies Working Party. Serving in this role has given me a front row seat in the development of the bioeconomies of other nations. A number of countries have recognized the importance of undertaking a focused and concerted approach and have developed strategic plans and detailed roadmaps with clear goals, objectives and milestones. Once the lead country in embracing biotechnology as a driver of a bioeconomy strategy, the US now has considerable competition. Several other countries are evaluating the power of biotechnology as they consider updating their bioeconomy strategies from biomass-focused to include biotechnology in an effort to reboot economies ruined by the coronavirus pandemic.

An example of a plan with considerable investment behind it is China's 12th Five Year Plan, which calls for hundreds of billions of dollars in funding for research and development in biopharmaceutical, bioengineering, bio agriculture, and biomanufacturing R&D. The plan aims to strike the right balance between the seed corn of basic science and the technology development needed for commercial application.

The United Kingdom's (UK) roadmap, first issued in 2012, looks at the opportunities and challenges of biotechnologies from basic science to real world applications, regulatory considerations, and health, safety and environmental issues. Although funding allocated to these efforts in the UK is significantly lower than in China, their access to top talent, a focused approach and clear deliverables are helping to build a strong foundation of scientific leadership and entrepreneurial progress. The UK undertook a [major update](#) to their bioeconomy strategy in 2018 and doubled down on using biotechnology to solve societal problems, including addressing the plastics problem. Japan also renewed its plan in 2019 to feature biotechnology.

Again, demonstrating DOE's leadership and recognizing the importance of the nation's biosciences and biomanufacturing enterprises, Secretary of Energy Brouillette, Under Secretary for Science Paul Dabbar, and Office of Science Director Chris Fall tasked the national laboratories with organizing a BioManufacturing XLab, a summit, to highlight the national laboratories' biosciences and biomanufacturing capabilities for leading companies, large and small, from across the country. Organized and hosted by Berkeley Lab for DOE at the Cal football stadium, the Bio XLab attracted hundreds of attendees from companies across the biomanufacturing industry and featured talks from Emily LeProust, the CEO and co-founder of Twist Biosciences, a company that synthesizes DNA, Magalie Guilhabert, VP, Head of Microbial Research Technology at Bayer CropScience where they are developing new methods to improve our food crops; and Alta Charo, Professor of Law and Bioethics at University of Wisconsin-Madison, one of the foremost bioethicists working on issues of biotechnology. Speakers like Paul Dabbar, and Daniel Simmons, the Assistant Secretary for Energy Efficiency and Renewable Energy, emphasized DOE's commitment to discovery and development for new biomanufacturing technologies. Our national lab technology transfer experts devised a new innovation for this XLab event- bundles of available intellectual property across the national laboratories, organized by topic, for a "one-stop shop" for potential partners and licensees. This key innovation solves a crucial problem for industry. IP developed at the national labs is challenging to find, let alone coordinate. The XLab is still generating positive collaborations over six months after the event.

Importantly, it was at this January biomanufacturing XLab event that Director Chris Fall announced the concept of the NVBL. To prepare for future biological incidents, intentional or natural such as the current coronavirus pandemic, the DOE national laboratories have the bio-related core capabilities and are now more prepared to respond collaboratively in the event of a future biological crisis as a consequence of the establishment of the NVBL.

Conclusion

The need to develop novel energy and environmentally sustainable solutions, and to build the nation's bioeconomy, grows daily. Stressors, including the need to reduce and store carbon at humongous scales, develop crops for a changing climate and more resilient bio crops, and secure leadership of the global bioeconomy demand quick action and quick delivery to society of transformative technologies and processes. The nation or nations that are first to do so, and to do so responsibly, will reap the societal and economic benefits of being first. The United States must retain its lead.

Increased opportunities and greater expectations bring more complex challenges. And again, as in years past, BER's and the DOE national laboratories' ability to attract a diverse workforce of the best and brightest and to imagine, build, and maintain new sophisticated research tools, facilities, and expertise is keeping the Department and the nation at the vanguard of biosciences discovery.

Thank you, again, for inviting me to testify at this important hearing. And, thank you for your strong support for science and technology development, and for a diverse and inclusive STEM workforce.

Dr. Mary Maxon is the Associate Laboratory Director for Biosciences at Lawrence Berkeley National Laboratory. Berkeley Lab's Associate Laboratory Director for Biosciences (<http://biosciences.lbl.gov/>) oversees the Biological Systems & Engineering, Environmental Genomics & Systems Biology, and Molecular Biophysics & Integrated Bioimaging Divisions, as well as the DOE Joint Genome Institute. She has been integral to the strategic planning efforts and development of the Area for four years, most recently as the Biosciences Principal Deputy. She received a Ph.D. in molecular cell biology from the University of California, Berkeley. Prior to coming to Berkeley Lab, Maxon worked in the biotechnology and pharmaceutical industries, as well as the public sector; her tenure highlighted this service as the Assistant Director for Biological Research at the White House Office of Science and Technology Policy in the Executive Office of the President, where she developed the National Bioeconomy Blueprint (https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/national_bioeconomy_blueprint_april_2012.pdf). With her extensive background in industry, scientific foundations, and state and federal government, Maxon is a national leader in science and technology policy. She has helped Berkeley Lab develop important initiatives, including Microbes to Biomes, the National Microbiome Initiative, BRAIN, the Agile BioFoundry, and the California Initiative to Advance Precision Medicine.

Chairwoman FLETCHER. Thank you very much, Dr. Maxon. Dr. Mohnen, would you like to go next?

**TESTIMONY OF DR. DEBRA MOHNEN,
PROFESSOR, DEPARTMENT OF BIOCHEMISTRY
AND MOLECULAR BIOLOGY, UNIVERSITY OF GEORGIA**

Dr. MOHNEN. Certainly. Good afternoon, Chairwoman Fletcher, Ranking Member Lucas, and Members of the Subcommittee. It is my pleasure to respond to the three questions about the Biological and Environmental Research program, BER, within the DOE Office of Science.

First, why does the BER program have biological research and development activities and capabilities? That's a good question. One might ask what does energy have to do with biology. And the short answer would be a lot.

First, let's consider DOE's history. DOE was established in 1977 through a consolidation of more than 30 energy-related efforts in different government agencies, some of which were already doing viral science. Thus, even at the time of its establishment, DOE was involved in bioscience. The origin of the biological research within the U.S. energy effort began during and after World War II with the Manhattan Project and the postwar Atomic Energy Commission and the development of an advisory committee to study the effects of radiation on humans. And this was later expanded to studies on the effects of radioactive fallout on the atmosphere, terrestrial, and marine environments and organisms.

Thus, from the origin of DOE and the later-formed BER, they supported a combination of physical, chemical, and biological research. This was carried out by both DOE and academic scientists and facilities. And the goal was to meet the U.S. energy needs.

Importantly, due to a mandate for DOE at the time, there was a formal division between the basic and the applied research, and the Office of Energy Research, later named the Office of Science, was given the task to oversee the basic research programs. And since BER is a part of the Office of Science, it supports and fosters critical basic science to meet current and future energy needs.

In keeping with its historic roots, the current stated goal of the BER program is, and I quote, "to support scientific research and facilities to achieve a predicted understanding of complex biological Earth and environmental systems with the aim of advancing the Nation's energy and infrastructure."

It's relevant to today's hearing that the knowledge, tools, intellectual workforce, and facilities that BER has supported and developed over the last 30 years to meet the U.S. energy needs have provided cutting-edge scientific instrumentation, facilities, and expertise that can immediately be applied to national emergencies such as the development of COVID-19 pandemic. As mentioned already, these capabilities include DNA and RNA sequencing, including the initial mapping of the human genome, and to date, having fully sequenced genomes of over 12,000 bacterial species, 3,000 viral, and 93 plant species. This is an enormous accomplishment. Importantly, BER has also supported the development of a systems biology approach and, via the use of supercomputers and artificial intelligence, to help understand and model complex organisms.

Second, how are the BER-funded expertise and advanced research tools being leveraged to respond to the COVID-19 pandemic? The world-leading capabilities I've just mentioned, including the world's fastest computers, have enabled the BER-funded researchers to rapidly direct their attention to the national and global threat of COVID-19. The DOE capabilities being brought to bear include—I'll just mention two here—DOE structural biology resources, which have led, among others, to a new understanding of the three-dimensional structures and molecular actions of protein components of the SARS-CoV-2 virus, which helps us understand the disease.

Another example is the work by DOE Oak Ridge National Lab's Systems Biologist Dan Jacobson, who uses Oak Ridge supercomputers and systems biology to analyze the genome, the transcriptome, the RNA, the proteome, and evolutionary data from human lung samples of very ill people and also people—control samples, as well as taking advantage of the data across the world. His team has recently published and has continuing to work based on these holistic analyses a new proposed mechanism for COVID-19 infection, as well as multiple therapies using existing FDA (Food and Drug Administration) drugs discovered through this systems biology approach.

And finally, the future directions of the BER department, the importance of understanding and utilizing complex biological systems to meet our current and future energy needs is particularly evident when one considers that, each year, more than 100 billion tons of carbon dioxide are fixed by photosynthetic organisms into biomass, and this biomass is essential. It's an essential large-scale renewable resource for energy, chemical, and biomaterials production. And when one considers that fossil fuels, which represent 80 percent of our current U.S. energy needs, are simply ancient biomass that was converted over time and pressure to petroleum, natural gas, and coal. Thus, the importance of understanding plants and microbes that produce and can transform this biomass into materials and energy cannot be overstated.

And, in conclusion, just as BER carried out biological research in the past to safely develop energy supplies, it's future must take the next step in understanding and utilizing biology and biological organisms to ensure a continuing and strong U.S. energy portfolio. Indeed, the United States should lead the world in these efforts, the results of which will drive a new national and world economy. Thank you.

[The prepared statement of Dr. Mohnen follows:]

Testimony of

Dr. Debra Mohnen

Professor of Biochemistry and Molecular Biology
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Before the United States Subcommittee on Energy, of the
House Committee on Science, Space, and Technology

Remote hearing on *“Biological research at the Department of Energy:
Leveraging DOE’s unique capabilities to respond to the COVID-19 pandemic”*

September 11, 2020

Introduction

Chairwoman Fletcher, Ranking Member Weber, and members of the Subcommittees, thank you for this opportunity to examine the biological research and development activities within the Department of Energy (DOE) Office of Science's Biological and Environmental Research Program (BER). I am familiar with the many strengths of the BER program, having been a researcher and a leadership team member since 2007 in two BER-funded large bioenergy research centers. Specifically, I was Focus Area Lead for Biomass Formation and Modification in the Bioenergy Science Center (BESC) from 2011 to 2017 and have been and continue to serve as Research Domain Lead for Integrative Analysis and Understanding in the Center for Bioenergy Innovation (CBI), since 2017. This statement addresses the following three areas as requested by the Subcommittee in the requested order:

- (1) historic reasons why the Department of Energy BER program has biological research and development activities and capabilities;
- (2) how this expertise and advanced research tools are being leveraged to respond to the COVID-19 pandemic
- (3) future directions for the Department's biological research activities.

Historic reasons why the Department of Energy BER program has biological research and development activities and capabilities

The Department of Energy was established in 1977 through a consolidation of more than 30 energy-related efforts located in different government agencies, some of which were already involved in bioscience research. Thus, even at the time of its establishment DOE, and more specifically what eventually became the BER program within DOE, was involved in bioscience. At the time of its establishment DOE's responsibilities were to *"advise the Secretary of Energy on DOE's R&D programs, identify gaps or duplication in DOE R&D programs, direct the Department's education activities, and manage grants and other forms of financial support for research activities"* (1). From its origin DOE and the later formed BER supported a combination of physical, chemical and biological research by both DOE and academic and research center scientists and facilities to meet the U.S. energy-related needs. There was a mandate from its inception that DOE have a formal division between its basic and applied research programs, leading to the formation of the Office of Energy Research to oversee basic research programs (name changed to Office of Science in 1998). The BER program lies within the Office of Science which targets basic research. Thus, the purview of the BER program is to support and foster critical basic science to meet current and future U.S. energy needs.

The origin of biological research within the U.S. energy efforts began during and immediately after World War II with the development of a medical advisory committee responsible for developing health and safety policy and research activities associated with and resulting from the Manhattan Project, as well as activities to oversee post-war related efforts by the Atomic Energy

Commission (AEC) (2). The early bioscience research included increasing understanding of the damaging effects of ionizing radiation on humans, gaining fundamental knowledge about the interactions between radiation and living matter, and ensuring distribution of isotopes for medical and biologic applications. It was the creation of a Division of Biology and Medicine in AEC on September 24, 1947, based in part on recommendations of the National Academy of Sciences, which may be considered as the origins of the BER program (2). Slightly thereafter in the early 1950s, multiple environmental science studies were initiated to investigate the spread of radioactive fallout in atmospheric, terrestrial and marine locations. These led to the creation of the Energy Research and Development Administration (ERDA) in 1974 to oversee *"environmental, physical, and safety research related to the development of energy sources and utilization technologies"* (2), a program which now lies within the DOE BER domain. From this brief overview of the history of DOE and the BER program it becomes clear that even at its origin the responsibilities of DOE and the BER program included increasing our basic understanding of biological and environmental phenomenon relating to U.S. energy-related efforts, including effects on human health.

In keeping with its historic roots, the current stated goal of the BER program is to support *"scientific research and facilities to achieve a predictive understanding of complex biological, earth, and environmental systems with the aim of advancing the nation's energy and infrastructure security"* (3).

It is relevant to today's hearing to recognize that the knowledgebase, tools, intellectual workforce and facilities that BER has supported and developed over the last 30 years to meet the U.S. energy needs and to move the nation forward towards the development of a sustainable energy system, have provided cutting edge scientific instrumentation and expertise that can be immediately applied to national emergency needs, such as the Covid-19 pandemic. These include leading developments in biological and Earth system science (4) and the sequencing of tens of thousands of genomes including the initial mapping of the human genome to today's more than 12,000 bacterial, 3000 viral and 93 plant sequenced genomes (5-7). Furthermore, BER's support has led to the development of foundational knowledge and biotechnological and systems biology approaches to advance the production of biofuels, biochemical and biomaterials from biomass, including advanced understanding of genetic and biochemical pathways that can be manipulated to increase productivity and fuel production in plants and microbes and the development of systems biology approaches to gain information from complex biological organisms (8-13).

Importantly, BER has funded research that was, and is, made possible due to the accessibility of DOE-supported supercomputers which enabled the development of predictive capabilities for understanding biosystems and ecosystems. This includes the development of global scale models through systems biology and artificial intelligence. The significance of these developments for tackling critical world problems cannot be overstated. Indeed, the development of such capabilities now enables BER-funded researchers to apply these technologies to the current

Covid-19 pandemic in order to understand the deadly SARS-Cov2 coronavirus and to develop strategies to protect ourselves against it.

How this expertise and advanced research tools are being leveraged to respond to the COVID-19 pandemic

As stated above, the development of world leading basic science knowledge, expertise, instrumentation and the world's fastest supercomputers has enabled DOE and BER-funded researchers to rapidly direct their attention to the national and global threat of the Covid-19 pandemic. Multiple DOE BER capabilities are being brought to bear on the Covid-19 pandemic, including DOE Structural Biology Resources which are leading to new understanding of the 3D structures and molecular actions of the protein components of the SARS-CoV2 virus (14), Light and Neutron Sources (15), the DOE Office of Science Environmental Molecular Sciences Laboratory (EMSL) and Joint Genome Institute (JGI) users facilities (7,16), and DOE supercomputers. To exemplify this, one example is given below to illustrate how DOE BER-supported scientific expertise and experimental facilities combined with the use of Oak Ridge National laboratory's (ORNL's) supercomputers have enabled a scientific team led by DOE ORNL systems biologist Dan Jacobsen to propose a novel mechanism for Covid-19 as well as multiple therapies using existing FDA-approved pharmaceuticals.

With the use of high power nucleic acid sequencing, Jacobson and the team were able to determine the sequence of RNA transcripts (RNASeq) of lung wash (bronchoalveolar lavage) samples from nine Covid-19 patients with severe disease symptoms (17). Armed with the ORNL supercomputer and taking a holistic systems biology approach they analyzed over 160,000 transcripts from the 9 patients and 40 controls and discovered that Covid-19 appears to enter host cells in the nasal passage, migrate to the throat, pass through the stomach and then to the intestines (18). The authors suggest that initial infection may not occur in the lungs, but rather result from travel of the virus from the intestinal system. The authors also propose that a so-called bradykinin-driven storm along with an inactivation of host viral defenses drives Covid-19 symptoms, resulting in part from a series of elevated and inhibited proteins whose misregulation may be contained by known-FDA-approved medications.

Extending this ground breaking work, Jacobson and the team (18) (Prates et al., 2020) took a broad systems biology approach that integrated genomic, transcriptomic, proteomic and molecular evolution data from host cells infected with the SARS-CoV2 virus. These data were analyzed via high-resolution structural models and atomistic molecular dynamics simulations using the Summit supercomputer at the ORNL. The results indicate that the corona virus may use two different receptors to enter cells, effectively eliminate macrophages and cytokine activation and thereby drastically reduce an immune response in the host, and also eliminate that host's interferon-based antiviral response. These BER-supported studies, which were empowered by years of prior energy and bioscience-driven research, enabled the DOE-funded researchers to use artificial intelligence combined with available globally distributed data to propose that a

reevaluation of the current view of how the Covid-19 infection occurs is warranted, a result that will likely increase the rate at which we are able to overcome this pandemic.

Future directions for the Department's biological research activities

I would like to end by restating the current goal of the BER program: to support *"scientific research and facilities to achieve a predictive understanding of complex biological, earth, and environmental systems with the aim of advancing the nation's energy and infrastructure security"* (3).

The importance of understanding and utilizing complex biological systems to meet current and future energy needs is abundantly evident when one considers that each year more than 100 billion tons of carbon dioxide are fixed by photosynthetic organisms into carbon-rich biomass. This biomass is an essential, large scale, renewable resource for energy, chemical and materials production. Indeed, since fossil fuels which account for ~80% of current U.S. energy needs (19), are ancient biomass that was converted by time and pressure into energy rich petroleum, natural gas and coal, the importance of understanding the plants and organisms that produce and transform the carbon-rich biomass into materials and energy for human needs cannot be overstated.

Through its leadership and directed focus to seek out and support the best science and scientific facilities, BER-funded research has had significant and long-lasting impacts that directly address its goal to *"discover the underlying biology of plants and microbes as they respond to and modify their environments"* (3). This understanding is already enabling their goal of *"reengineering of microbes and plants for energy and other applications"* (3). Therefore, just as BER carried out bioscience research in the past to safely and effectively develop novel energy supplies, its future must be to take the next step in understanding and utilizing biology and biological organisms to ensure a continuing and strong U.S. energy portfolio in the years ahead.

These efforts must also continue with support of research that *"advances understanding of the dynamic processes needed to model the Earth system, including atmospheric, land masses, ocean, sea ice, and subsurface processes"* (3). The different goals of BER come together in the realization that the long standing geochemical, atmospheric and biological balance that organisms, including ourselves, on earth have enjoyed for the past 400,000 millions of years is currently destabilized, as indicated by multiple measurements and data points including temperature extremes and fluctuations, atmospheric gas levels, and sea level rises.

Thus, while it is appropriate and wise to make use of some of BER's expertise, instrumentation and computer resources to work to overcome the current Covid-19 crisis, its future must continue to emphasize the development of long term sustainable energy solutions and the production of biomaterials and biochemicals from our rich biomass reserves. Indeed, the U.S. should be leading the world in these efforts, the results of which will drive a new sustainable national and world economy. These efforts should include and indeed increase DOE support of academic and national lab research, as well as continue to build strong academic and DOE lab

basic and fundamental research collaborative and partnerships including the bioenergy research centers and DOE user facilities. The continuation of support for DOE-government-academic-research center collaborative efforts, and of individual researchers and their research programs, will ensure continuing novel research discoveries that will serve as foundations for future industries while also guaranteeing a talented scientific work force, a cutting edge instrumentation and computing infrastructure, and a scientific enterprise ready to meet national challenges as they arise.

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Debra Mohnen is Professor of Biochemistry and Molecular Biology at the Complex Carbohydrate Research Center, University of Georgia (UGA). She has studied plant cell wall synthesis, structure, and function for over 30 years with emphasis on the non-cellulosic cell wall polysaccharides. In 2008 she was awarded the Bruce Stone Award for research in pectin synthesis and in 2013 elected as a fellow of the American Association for the Advancement of Science. She was bestowed the Inaugural Georgia Athletic Association Professorship in Complex Carbohydrate Research at UGA in 2018. Since 2007 she has concentrated a large part of her research on improving plant biomass yield, sustainability and composition for improved biofuel and biomaterials production. She was Focus Area Lead of Plant Biomass Formation and Modification in the DOE-funded BioEnergy Science Center (BESC) where she was responsible for the direction of a team of ~ 100 researchers aimed at understanding and overcoming biomass recalcitrance to deconstruction. Since 2017 she serves as Research Domain Lead for Integrative Analysis and Understanding in the DOE-funded Center for Bioenergy Innovation (CBI) with responsibilities of working with the Deconstruction Fundamentals, Computational Biology, and Economics and Sustainability Teams to ensure integrated and successful research within the teams and across CBI. She is also a principal investigator of RG-I biosynthesis in the DOE-funded Center for Plant and Microbial Complex Carbohydrates at the University of Georgia Complex Carbohydrate Research Center.

Chairwoman FLETCHER. Thank you, Dr. Mohnen. Next, we'll hear from Dr. Randall.

**TESTIMONY OF DR. GLENN C. RANDALL,
CHAIR, COMMITTEE ON MICROBIOLOGY,
THE UNIVERSITY OF CHICAGO**

Dr. RANDALL. Chairwoman Fletcher, Ranking Member Lucas, and Members of the Subcommittee, I thank you for the opportunity to participate in today's discussion about biological research at the Department of Energy.

As was mentioned, I am currently directing COVID-19 research at one of our country's 13 regional biocontainment laboratories, and so I will focus my remarks as to how DOE is responding to COVID-19.

So, earlier this year, we established a SARS-CoV-2 research core, and the idea behind this is that very few of these high biocontainment biosafety level III facilities exist, and there are many people with good ideas who don't have access to high containment. And so we provide collaborations where we provide both the facilities and the expertise to work directly with SARS-CoV-2. And this is primarily focused on evaluating treatments and vaccines, a little bit on the biology of the virus but mostly translational.

It's in this capacity that I've gained a real appreciation for the value of the COVID-19 research performed in the Department of Energy. In particular, I've enjoyed multiple productive COVID-19-related collaborations with scientists at the DOE's Argonne National Laboratory that I would be happy to discuss in further detail. But suffice it to say we have identified dozens of therapeutics, both FDA-approved and novel, that are active against the virus, at least in vitro.

The DOE's Office of Science's Biological and Environmental Research or BER program, as has already been discussed, has a storied history integrating biologists, physicists, computer scientists, and engineers to address some of the important questions of today and tomorrow. Many of the extraordinary capabilities that BER has nurtured have been foundational to a specific response to COVID-19, which is the virtual biotechnology library. This is a consortium of all 17 DOE national laboratories, each with core capabilities that are relevant to the threats posed by COVID-19. They leverage expertise in technology that synergistically interact with each other, academia, and industry to advance our fight against COVID-19.

This effort capitalizes on long-held expertise in BER in unequaled strengths, particularly solving structures of proteins, what they look like, and how to target them with drugs or neutralizing antibodies and supercomputing to stimulate billions of potential drug target interactions. This amplifies our current pharmaceutical capabilities by orders of magnitude.

It is in these two areas that I have collaborated with the DOE scientists and am most knowledgeable. I have worked together, as I said, to identify multiple drug candidates with DOE scientists. Other areas of NVBL emphasis include genome sequencing to track SARS-CoV-2 evolution and potential development of resistance to treatments, epidemiological and logistical support, protected data

bases that would host patient health data for research and analysis, manufacturing capabilities to address supply chain bottlenecks in areas such as PPE and ventilators, testing of clinical and nonclinical samples, and, more recently, a project designed to address open questions about the mechanisms of SARS-CoV-2 transmission that will help inform approaches to interrupt chain infections and inform strategies that will guide our resumption to normal activities.

The coordinated response of the NVBL to COVID-19 addresses critical needs in developing effective cures and vaccines that will help end the pandemic and, as applies to the future, will help provide a framework with how to more—be more responsive to the coming pandemics because this won't be the last one. Thank you for your time.

[The prepared statement of Dr. Randall follows:]

Testimony of Glenn Randall, PhD.
Professor of Microbiology
The University of Chicago

Before the
Subcommittee on Energy
Committee on Science, Space and Technology
U.S. House of Representatives

“Biological Research at the Department of Energy: Leveraging DOE’s Unique
Capabilities to Respond to the COVID-19 Pandemic”

September 11, 2020

Chairman Fletcher, Ranking Member Weber, and Members of the Subcommittee, thank you for the opportunity to participate in today’s discussion about Biological Research at the Department of Energy: Leveraging DOE’s Unique Capabilities to Respond to the COVID-19 Pandemic.

I am Glenn Randall, a Professor of Microbiology and Chair of the Committee on Microbiology at The University of Chicago, where I have studied emerging RNA viruses for the past 15 years. I am also the Director of Emerging Infections at the Howard Taylor Ricketts Regional Biocontainment Laboratory. This is one of thirteen National Institutes of Health-funded Regional Biocontainment Laboratories built to sustain research with pathogens that require enhanced biosafety (Biosafety Level 3), such as SARS-CoV-2, the causative agent of the COVID-19 pandemic. This facility is operated by the University of Chicago. There are a limited number of Biosafety Level 3 facilities in the United States. I direct a COVID-19 research core at this facility. The purpose of this core is to facilitate the COVID-19 research of other scientists, who need us to do experiments with live virus under enhanced safety conditions that they cannot do themselves due to a lack of expertise or facilities. This research is primarily focused on evaluating potential treatments and vaccines for SARS-CoV-2. It is in this capacity that I have gained an appreciation of the value of COVID-19 research performed in the Department of Energy. In particular, I have enjoyed multiple productive COVID-19-related collaborations with scientists at the DOE Argonne National Laboratory.

The U.S. Department of Energy Office of Science’s Biological and Environmental Research (BER) program has a storied history. Decades ahead of the curve, it embraced inter-disciplinary science. It integrated biologists, physicists, computer scientists and engineers to address some of the most important questions of today and tomorrow. It is specifically designed to answer questions larger than one field can answer, such as our current pandemic. The needs are vast: effective drugs (both against the virus and to treat

the symptoms), a vaccine (both effective initially and likely better generations of vaccines in the future that provide long-lasting protection), and drugs and vaccines that will also protect against coronaviruses that will emerge in the future. Additional issues include more and better personal protective equipment (PPE) for our front-line health care workers. Moreover, coronaviruses are not our only pandemic threat. Influenza virus, as one example, will almost certainly cause a new pandemic in the not too distant future.

Many of the extraordinary capabilities that BER has nurtured have been foundational to a specific response to COVID-19: The U.S. Department of Energy National Virtual Biotechnology Laboratory (NVBL), which is a consortium of all 17 DOE National laboratories, each with core capabilities relevant to the threats posed by COVID-19. They leverage expertise and technology that synergistically interact with each other, academia and industry to advance our fight against COVID-19. This effort capitalizes on long-held expertise in unequaled strengths, such as discovering the structure of proteins (what they look like and how to target them) and supercomputing to simulate billions of potential drug-target interactions that amplify our current pharmaceutical capabilities by orders of magnitude.

The NVBL effort focuses on the following areas: <https://science.osti.gov/nvbl>¹

Molecular structural determination: X-ray sources and neutron sources at DOE user facilities provide protein crystal structures needed for both computational modeling and experimental studies related to drug and vaccine development. These include the Advanced Photon Source (APS) at Argonne, Advanced Light Source (ALS) at Lawrence Berkeley, Stanford Synchrotron Radiation Light Source (SSRL) at SLAC, the Linac Coherent Light Source at SLAC, National Synchrotron Light Source II (NSLS II) at Brookhaven, and Spallation Neutron Source (SNS) at Oak Ridge National Laboratories. In addition, cryo-electron microscopes can be used to provide high resolution structures of virus particles and their interactions with antibodies and other drugs. DOE's Nanoscale Research Science Centers provide additional capabilities for imaging and characterization, as well as materials synthesis and nanofabrication capabilities to support study of biomolecules.

The DOE X-ray and neutron sources are a long-held treasure for the biological sciences, in addition to many other disciplines. We mostly study proteins blindly, not knowing what they look like or how to target them with drugs. These groups provide us with a detailed picture of the target. Many structures of SARS-CoV-2's 30 proteins have been solved at these facilities, many by DOE staff. These protein structures allow predictions as to what types of drugs may be effective against SARS-CoV-2. Structures of SARS-CoV-2 proteins bound by drugs are also being solved to give us important clues as to how we can modify the drugs to be more effective. Similarly, the structure of antibodies bound to the viral Spike protein are solved to better understand how they neutralize infection. Every submitted SARS-CoV-2 manuscript thus far involving my group relies on this invaluable capability.

Computational modeling and simulation: High performance computing resources at DOE user facilities, employing artificial intelligence, molecular dynamics simulations, and

modeling tools, combined with input from protein structure data, provide information to support research related to rapid survey of existing drugs and development of anti-viral agents and vaccines.

Most pharmaceutical companies have a library of 1-3 million compounds to screen against a disease target of interest. The supercomputers of multiple DOE National Laboratories have collaborated to generate a virtual library of every known chemical (~5 billion) and then screen them by molecular docking computer simulations of potential drugs bound to the SARS-CoV-2 protein structures described above. This is done over multiple iterations using artificial intelligence and machine learning to identify the best drug candidates. Now that candidates have been identified computationally, we are currently helping this consortium experimentally screen ~1000 potential drugs for anti-SARS-CoV-2 activity.

Genomic sequencing: Genomic resources at DOE's Joint Genome Institute and other facilities can sequence large numbers of patient samples to identify constrained regions, compare COVID-19 with other genomes to identify candidate regions for immunotargeting, and construct models of individual susceptibility.

This capability is important for tracking how SARS-CoV-2 evolves. We have already witnessed an example where a SARS-CoV-2 variant emerged in Europe and overtook most of the world, including the United States (D614G in Spike). This capability will prove more valuable as we track drug and vaccine resistant emergence in the months to come.

The NVBL also works in areas that don't currently involve me, but are no less important such as:

Epidemiological and logistics support: Proven capabilities based on data analytics, artificial intelligence, and other decision tools have previously supported many national emergencies including oil spills, hurricanes, DOD supply chains and epidemiology. These capabilities have been deployed for government agencies, such as DOE, FEMA, and DOD. Such tools can yield information for health care providers and government groups on modeling disease spread, collecting/analyzing information and data from open sources world-wide, and providing tools for real-time decision making, risk analysis and prioritization for patient care and supply chain logistics.

Knowledge Discovery Infrastructure / Scalable Protected Data (KDI/SPD): Specialized facilities consisting of a multi-tier architecture facilitating a private cloud environment are available to host protected health data for research and analysis. These facilities meet NIST 800.66 and 800.53 control sets that meet Federal Information System Management Act (FISMA) requirements for a classification of moderate with enhanced controls. These capabilities are currently being used by Veteran's Affairs, Center for Medicare & Medicaid Services, and the National Cancer Institute's Surveillance, Epidemiology, and End Results programs.

Supply Chain Bottlenecks: Extensive manufacturing capabilities across the DOE laboratory complex are addressing supply chain bottlenecks associated with COVID-19.

Guided by input from both public and private stakeholders (government, health care providers), three health care supply chain bottlenecks have been identified: surgical masks and face shields, ventilator systems, and consumables (swabs, test kits components) used in COVID testing. These DOE teams have capabilities to rapidly reverse engineer/design and manufacture prototype parts, dies, and molds for industrial scaling.

Testing of clinical and non-clinical samples: DOE laboratories have established deep capabilities in high throughput preparation and analysis of biological samples using PCR-based protocols. While currently used to support DOE's mission in energy science, these facilities and trained personnel can be deployed to help address the rising surge in clinical samples. In addition, many labs have expertise in sampling and analysis of surfaces for biological materials developed in support of DOE programs.

NVBL has also recently started a new project on understanding *SARS-CoV-2 viral fate and transport*. This research effort leverages capabilities in computational modeling, data science, chemistry, environmental science, material science, aerosol chemistry and modeling, indoor air quality science and bioaerosol facilities, genomics and biodefense and makes extensive use of DOE user facilities, biosafety level 3 (BSL 3) facilities, environment research facilities, and the computational infrastructure across the national laboratory complex, to address the open questions around mechanisms of SARS-CoV-2 transmission. Enhancing the potential to predict SARS-CoV-2 viability and transmission in built and natural environments will help inform approaches to interrupt the chain infections, as well as inform strategies that guide society's resumption of normal activities.

I thought the best way for me to discuss DOE's impact on COVID-19 is to describe four of my personal experiences working with them. The first two studies I will describe used the strategy of drug repurposing, which was the topic of a prior subcommittee hearing. The basic idea is that drug development is a lengthy process, beginning with biochemistry, virology, animal studies, and finally clinical trials. By repurposing already approved drugs, you can greatly accelerate this process. In the first study², DOE scientists at Argonne National Lab first described the structure of the SARS-CoV-2 protein Nsp15. They then developed biochemical assays to assess the activity of the protein. Based on structural similarities, they predicted that the FDA-approved drug Tipiracil would inhibit the activity of the protein, which it did. Although Tipiracil had limited antiviral activity in our assays, co-structures of the drug bound to Nsp15 suggest modifications to improve its antiviral activity.

In the second study³, colleagues of ours at The University of Chicago screened a library of ~1900 FDA-approved drugs against the related coronavirus OC43, a cause of the common cold that can be worked with under standard biosafety conditions (BSL 2). We then tested the top 30 hits in their screen for anti-SARS-CoV-2 activity and identified 20 drugs, ~ half of which were not previously identified in the literature. Collaborators at The University of Chicago and Duke University tested the 20 drugs for activity against the major viral protease, 3CLpro. One drug in particular, Masitinib completely blocked 3CLpro and virus replication. Our colleagues at Argonne solved the structure of Masitinib bound to the active site of 3CLpro. You can think of it as a key that perfectly fits in a lock, inactivating the

protein and preventing infection. Two potential clinical trials have emerged from this study. One involves the manufacturer of Masitinib (AB Science). The second trial would be run out of the University of Chicago and examine the potential use of a nasal spray Azelastine as a preventative against COVID-19. As these drugs show activity against multiple coronaviruses, there is potential for stock-piling them for future pandemics.

The third study⁴ included many of the same collaborators. A major drug target of SARS-CoV-2 is another protease called PLpro. Proteases are attractive, in part, because they have been successfully targeted by drugs to treat HIV and hepatitis C virus. Our collaborators at Argonne solved the structure of PLpro, while colleagues at The University of Chicago designed inhibitors against the protein and biochemical assays to test the potential drugs. They confirmed activity against PLpro and for some of the compounds, we showed activity against the virus. Finally, our Argonne colleagues solved structures of the drugs bound to PLpro, suggesting strategies to further improve them.

I have already described the final study, which is testing potential drugs identified by the NVBL Molecular Design for Medical Therapeutics project. The work is a little less developed on the biology side, as we have begun testing compounds in the past two weeks (it is quite advanced on the computing side). There are already clearly potential antiviral compounds in this group.

In the past few months, I have enjoyed my collaborations with the DOE labs at Argonne. The unique skill sets that they bring to COVID-19 research are valuable and impressive. My interactions have been with just a fraction of the capabilities that DOE brings to combat COVID-19. DOE work in epidemiology, patient databases, manufacturing to address supply chain bottlenecks in PPE and ventilators, and clinical sample testing address important complementary challenges present by the pandemic.

Thank you for the invitation to testify to the Subcommittee on Energy. I would be happy to answer any questions you or other members of the committee may have.

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Glenn Randall Bio

Glenn received his B.S. with distinction in Microbiology from the University of Illinois, Urbana-Champaign. After an internship at Abbott Laboratories, he pursued graduate studies at The University of Chicago in the laboratory of Bernard Roizman. His doctoral thesis describes mechanisms by which herpes simplex virus I establishes a latent infection. He then joined the Laboratory of Virology and Infectious Disease at Rockefeller University in New York. His American Cancer Society postdoctoral fellowship was under the mentorship of Charles Rice. His research focused on hepatitis C virus (HCV)-host interactions with an emphasis on the interaction between HCV and cellular RNA interference (RNAi) pathways. He joined the Department of Microbiology at the University of Chicago in August of 2005. Since joining The University of Chicago, Glenn has received numerous awards, including the Schweppe Fellowship, the American Liver Foundation Heman Lopata Hepatitis C Scholar, The University of Chicago DDRCC Outstanding New Investigator, a Career Development Award from the Great Lakes Center for Excellence (NIH/NAIAD) and an American Cancer Society Research Scholar Award. In 2019 he was promoted to Professor and in 2020 appointed Chair of the Committee on Microbiology. In 2020 he was also appointed as the Director of Emerging Infection Research at the Howard Taylor Ricketts Regional Biocontainment Laboratory where he leads COVID-19 research.

Glenn's laboratory investigates the roles of virus-host interactions in replication and pathogenesis. They study emerging RNA viruses, including hepatitis C virus, dengue virus, norovirus, and SARS-CoV-2. They now study the importance of cellular genes in diverse steps of the viral life cycle, including entry, the regulation of viral protein translation and RNA replication, modulation of cellular lipid metabolism, the establishment of viral replication complexes, the secretion of infectious virus, and control of infection by the innate immune system.

Chairwoman FLETCHER. Thank you very much, Dr. Randall. We'll now hear from Dr. Wrighton.

**TESTIMONY OF DR. KELLY C. WRIGHTON,
ASSOCIATE PROFESSOR, DEPARTMENT OF SOIL
AND CROP SCIENCE, COLORADO STATE UNIVERSITY**

Dr. WRIGHTON. Chairwoman Fletcher, Ranking Member Lucas, and the rest of the Committee, thank you for inviting me today. As you've heard about DOE's history of biological research, I'm here to tell you about how this history of pioneering biological research is active today and is perhaps best manifested by ongoing DOE investments in user facilities, including those of the Joint Genome Institute or the JGI and the Environmental Molecular Sciences Laboratory or EMSL, amongst more than 20 other facilities. Although I am not directly affiliated with these facilities, I represent the experience of a self-titled superuser.

Since my laboratory's inception in 2014, I have managed nine different projects and awards with EMSL and JGI. From my narrative, I want you to take away a key message. These user facilities propel science in this country and especially can benefit those like myself at the earliest stages of their independent research programs.

Starting your research program at a university is much like starting your own small business. Essentially, your job is to take the university's investment in you called startup funding and use it to finance innovative science. The goal is the short-term investment by the university will enable one to obtain data and recognition to compete for external research dollars that fuel independent scientific endeavors.

User facilities played a vital role in my early career by allowing me to maximize my startup investment. First, they allowed me to scale my scientific scope beyond what was possible in my new laboratory with a small nascent workforce. Second, they provided me access to equipment beyond what was located in my building or even on my campus. Third, they networked me with experts who are at the cutting edge of their fields.

My early collaborations with DOE user facilities led to scientific publications that developed me as a research leader in a few short years. More important, we generated data that facilitated my future fiscal independence, forging projects sponsored by U.S. industry and the National Science Foundation. This symbiotic relationship between individual researchers and user facilities benefits the entire scientific community because what it enables us to do is collect diverse data streams and then this content is subsequently populated in data bases that's shared with the community. In summary, DOE investments and user facilities are invaluable resources that amplify innovation and extend the research dollars of our scientific enterprise.

I know today when we talk about biology we must address the dominant issue of public health, COVID-19. While DOE's direct contributions to COVID-19 research will be articulated and were very well-articulated by other members of my panel, an area that I can speak to is this idea of translational investment. Essentially, how is investment in one scientific arena energize or cross-pollinate

other parallel scientific discovery? You don't have to know biology or envision—that detangling invisible microbes from wetland soils or shale rock is not the cleanest or easiest of work. On the environmental side, we have a long history of developing methods for isolating DNA and RNA from these complex matrices, technologies that are used by my colleagues doing SARS-CoV-2 surveillance research in wastewater and other systems.

Moreover, even prior to the pandemic, DOE was leading investments in viral mechanistic ecology from every habitat we explored from deep below the Earth's surface to our soils, to our rivers, and even our own guts, research for my group and others has recovered new viruses and demonstrated key roles for these viruses in modulating nutrient cycles.

Currently fueled by DOE's support, teams I am part of are devising new software for rapidly detecting viral genomic signatures and environmental data, as well as defining the biochemistry enigmatic within these poorly understood viruses. In summary, DOE has developed the foundational expertise in technology and genomic sciences that can lead and be translated to epidemiological solutions for today and future public health challenges.

Lastly, despite the advanced capabilities user facilities shepherd, looking to the future, there are areas to reinforce our Nation's capabilities. Currently, genomics information is being generated faster than the corresponding capabilities can keep up with, and more so than our computational infrastructure can mine. This means we have thousands to tens of thousands of genes that lack any known function or, said more positively, this means there is a huge reservoir of biotechnological applications awaiting discovery.

But what three areas are needed to expedite the speed in which researchers can translate genomics information into actual knowledge? We—first, we need a coordinated, organized computational infrastructure that enables computer-aided pattern recognition of this deluge of genomics and microbiome data. Second, we need research automation and scale that extend beyond the resources of any one lab and even those of our user facilities as they're designed today. And last, the heart of future discovery lies in creating this multidisciplinary higher-risk collaborative space.

In summary, this streamlined and cross-disciplinary scientific vision will allow us to embark on a new era of decoding biological information that heavily leverages DOE's genomic infrastructure. This trailblazing will result in new biotechnological innovations to environmental, engineering, and health-related challenges that will be faced by mine and subsequent generations. I thank you for your time.

[The prepared statement of Dr. Wrighton follows:]

Kelly C. Wrighton, PhD

Written Testimony

TO: Committee on Science, Space, and Technology
 FROM: Kelly C Wrighton, PhD
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 RE: Written Testimony, "Biological research at the Department of Energy: Leveraging DOE's unique capabilities to respond to the COVID-19 pandemic"

Below I provide my written testimony to the three main questions I was asked to address in response to the U.S. Department of Energy Office of Science's (DOE) Biological and Environmental Research (BER) program.

(i) What are benefits of the Department's Bioscience Research Capabilities?

As you have heard from our other panelists, the DOE has a long history of biological research. This tradition of pioneering scientific innovation continues today and is manifested by ongoing DOE investments in The Joint Genome Institute (JGI) and Environmental Molecular Sciences Laboratory (EMSL). Although I am not directly affiliated with these facilities, I am a self-proclaimed super-user, meaning that since my laboratory's inception, I have 9 different project and awards with EMSL and JGI that I have led (this does not account for other collaborative efforts). In sharing my narrative with you, I want you to take away how these facilities propel science innovation in this country, and especially benefit those like myself at the earliest stages of their independent research programs. Simply, these user facilities provide foundational biological resources that support scientific advances across environmental, energy and human health sectors for the United States.

Starting a research program at a R1 university is much like starting your own small business. Essentially your job is to take the universities investment in you, called start-up funding, to finance a research program doing impactful, innovative science. The goal is that short term investment from the University can enable one to compete for federal research grant dollars that sustain, and further fuel expanded scientific endeavors by your research program.

User facilities play a vital role in that transitional phase of early career scientists. The facilities allow scientific researchers like myself to maximize their investment by (1) scaling the scope of their science to levels unachievable by a single, academic laboratory, (2) providing accessibility [minimizing privilege] to technical resources located beyond the walls of any building or campus, and (3) networking motivated, early career scientists with trained experts who are at the very frontier of this technology. In return, the user facilities create large amounts of environmental data for databases and develop expertise beyond that retained within the DOE national laboratory systems. This is a symbiotic relationship between individual researchers and the user facility that benefits the entire scientific community.

To better articulate this value, let us use a single example (of many) from my research portfolio. The year is 2014 and I have just started my brand-new research program at The Ohio State University. Due to my geographic proximity to the emerging shale oil and gas industry in the Appalachian Basin, I became interested in interrogating the microorganisms that colonize hydraulically fractured shale wells. These contaminating microbes from the earth's surface can prosper 2,500 meters below the surface in shale energy wells. Here this unexpected microbial growth can sour the valuable hydrocarbon commodity, corrode the well infrastructure, and maybe, alternatively if managed in a different fashion, can be harnessed for greener, energy efficiency or yield.

My university start-up funds allowed me to hire the personnel and collect and process 10 or so samples from a single well collected over a year period. At the same time, I competed and was awarded EMSL and JGI resources to further advance this research. This collateral resource investment by the Biological arm of DOE allowed me to scale my research enterprise from this handful of samples in a single West Virginian

well, to over 50 wells across North America, with sample collection occurring over thousands of days. Moreover, through my collaboration with DOE user facilities, I was exposed to new, higher resolution analytical chemical methods that had not been applied to these systems and were not readily accessible at my institution. This technology led to new insights about how and what these microbes were living off in the deep subsurface in this new, engineered system. Moreover, EMSL and JGI scientists became my collaborators, providing invaluable insights into the project from their multi-disciplinary perspectives.

Those early investments by DOE user facilities led to scientific publications that helped develop me as a research leader in this domain in a few short years, with my laboratory's findings awarded the top 100 discoveries by Discovery magazine in 2016. More important, this collaboration generated data that facilitated my future fiscal support from applied projects supported by US industry, as well as more foundational scientific efforts by the National Sciences Foundation. Research collaborations provided by user facilities like JGI and EMSL catalyzed impactful biological science, with recognition culminating in my PECASE (the presidential early career award for scientists and engineers) award that represents the highest honor bestowed by the US government to scientists in the early stages of their independent research careers. In summary, DOE investments in user facilities amplify the innovation and discoveries of our US scientific enterprise.

(ii) How has BER expertise and their advanced tools been leveraged to respond to the COVID-19 pandemic?

A quick scan of others in this panel led me to believe the direct contributions of the DOE to COVID-19 research will be better covered by others like my esteemed colleague Dr. Mary Maxon. An area that I am uniquely qualified to speak to is the translational value of DOE investment in environmental research. Essentially, how does investment in one scientific arena energize or cross-pollinate other parallel scientific discovery?

Let me contextualize this quickly. The hydraulic fracturing example that I described, where we gained insights into the chemical diet that enabled microbes to adapt and persist to life thousands of meters below the surface, has direct applications to the microbes living in your gut. In fact, leveraging our newly developed technologies for working with complex samples, and our newfound understanding of the microbial reactions catalyzed, it turns out those same processes predict why one person is more susceptible to cardiovascular disease than another person. The microbes in your gut use the same enzymes and produce the waste products as those in shale rock. As such I was able to take my DOE and NSF supported research and compete and earn support from the National Institutes of Health for research in medicine. Biological discovery is seamless and transcends disciplinary boundaries.

You don't have to know much about biology to know that extracting microbes from shale rock and human feces is not the cleanest or easiest of work. Work by myself and others in environmental sciences involving extraction of DNA and RNA from complex matrices has yielded knowledge that is leveraged by my colleagues working with RNA viruses in wastewater for Sars-CoV-2 research. Moreover, even prior to Covid pandemic, DOE BER was leading investments in viral mechanistic ecology - advancing research into how and where viruses establish and function. Through their funding calls that academics like myself compete for, a critical area of research has been dedicated to understanding viral roles in the environment. Recent discoveries by my group and others have uncovered how critical viruses are to maintain the functional balance in our soils, our rivers, our own guts, and even the deep subsurface. As such, DOE investments have led research for development of viral genomic tools that enable insights ranging from identifying and categorizing the viral world, to elucidating the biochemistry contained within it. For example, earlier this year I was funded through the DOE Genomic Sciences program to participate in a multi-disciplinary research team containing microbiologists, chemical engineers, and computer scientists. Here we are devising new genomic algorithms for defining the chemical reactions encoded, but currently enigmatic with viral genomes. This new software will yield translational content facilitating viral

environment and health research avenues. Beyond direct investments and repurposing of DOE infrastructure for virtual interaction as discussed earlier, DOE enabled biological platforms and technological insights support this pandemic. In summary, BER supported expertise and tools are immediately transferable to solutions of existing and emerging environmental, energy, and health challenges.

(iii) What are my perceptions of possible future directions for the Departments biological research activities?

Despite the advanced capabilities the User Facilities shepherd there are gaps in our nations capabilities to ensure we remain as the world's premier scientific enterprise. We need to address the increasingly complex challenges residing in the biological systems of present. Currently genomics information is being generated faster than the corresponding proteomics, metabolomics and structural imaging capabilities can keep up, and more so that our computational infrastructure can mine.

The result is a list of 10's or 100's of thousands of proteins that have potentially critical yet unresolved function. Our recent DOE-supported discovery in *Science*, a premier research journal, last week demonstrated how even within fairly well characterized bacterium, we identified a mis-annotated pathway that can generate ethylene without using oxygen. While this discovery has important ramifications for industry, as it represents a non-combustible pathway for generation of this industrial precursor, it also directly explains many environmental phenomena such as the observation that ethylene accumulates in soils after rain events with toxic outcomes for crops. Given that this process is catalyzed by less than 5 genes in a pathway, and bacteria encode several thousands more genes that have this same unresolved content, think of how much discovery is awaiting us.

What is needed to expedite the speed in which researchers can translate genomics information into actionable knowledge?

- (1) A coordinated, organized computational infrastructure that enables computer aided pattern recognition of this deluge of environmental genomics/microbiome data. Efforts led by DOE supported national microbiome data collective (NMDC) are paving this way. The NMDC is a first of its kind microbiome central repository that links the environmental context, the genomics, and the environmental chemistry across a range of ecosystems that DOE supports. This indexing and cross-linking of data will allow for machine learning and artificial intelligence data mining of content that can steer new experimentation.
- (2) Research automation and scale that extend beyond the resources of any one laboratory. Imagine a future, where you can be shipped modular labs to your workspace or ship your samples and login to a command center and run samples through robotic systems. This virtual, shared lab allows for resource use efficiency, data generation that is customized, reproducible, productive. The same could be said of computational resources. While shared computational resources are supported by DOE and NSF, they aren't readily accessible for common workflows, timelines and data storage to enable efficient genomics research. The future of science extends beyond 4 walls and personalized compute power. There is redundant investment being made with federal dollars, and perhaps the future will be streamlined workspaces needed to advance and capitalize on our genomic investment.
- (3) More so, the heart of future innovation lies in multi-disciplinary collaborative nexus. Examples like you have heard from my other colleagues today, where new teams and resources rapidly emerged to address knowledge gaps for COVID19 research. Research incentives that drive this cross-agency, multi-disciplinary, higher risk innovation are needed, and ideally prior to, not in spite of, the next global challenge.

This streamlined and cross-disciplinary scientific space will allow us to embark on a new era for scientific discovery, leveraging the recently developed foundational genomics infrastructure. Human, physical, and computational capital is required to position the US to lead breakthrough applications in biological sciences in the next decade.

Dr. Kelly Wrighton's research focuses on the chemical reactions catalyzed by microorganisms- to identify microbial solutions to today's environmental and health challenges. Using a genomic tool kit, her research queries wild microbial content from the environment to generate hypotheses that are evaluated using model-system approaches in the laboratory. Prior to becoming an Associate Professor of Soil and Crop Sciences and Microbiome Science at Colorado State University, Dr. Wrighton was an Assistant Professor of Microbiology at The Ohio State University. She received her PhD training in Microbiology, and post-doctoral training in Computational Biology, both from the University of California Berkeley. Her research program is supported by funding from the Department of Energy, the National Institutes of Health, the National Sciences Foundation, as well as industry. She currently supports a team of 6 graduate students, 3 post-doctoral researchers, 3 staff scientists, and numerous undergraduate researchers. She is an active member of science advisory panels associated with industry and the Department of Energy. Dr. Wrighton has given over 60 invited talks in the past five years and contributed to research resulting in more than 80 publications, with over 5,000 citations. In the past two years, Dr. Wrighton has received career research honors from the American Geophysical Union, The International Society of Microbial Ecology, the Geobiology Society, and was recently awarded the Presidential Early Career Award for Science and Engineering (PECASE), one of the highest honors bestowed by the U.S. government for outstanding scientists.

Chairwoman FLETCHER. Thank you, Dr. Wrighton. We will now proceed with our first round of questions, and I will recognize myself for 5 minutes.

This question that I have is really a broad question directed at all of the witnesses, so happy for you all to take this in any order you choose and to kind of share with us between each other a question about what has happened basically in response to the pandemic. DOE launched the National Virtual Biotechnology Laboratory, NVBL, which is charged to mobilize the resources of the Department's 17 national labs to engage in COVID-19 research.

I would like to hear from you all whether you think the NVBL should continue its work even in the future when we are not actively responding to a global pandemic, and if so, why? And if you could touch on in your responses maybe in what ways could the activities of the NVBL help accelerate [inaudible] pandemic and how has the creation of the NVBL influenced operations or changed the partnerships between the national laboratories or with academia and the private sector?

So I'd love to turn it back to the panel for your thoughts on that question, and maybe if we'll go back in order, we could start again with Dr. Maxon.

Dr. MAXON. Thank you for the question. I'll tackle a couple of parts of it, the first being do I think the NVBL should continue? I think there are a number of good reasons why the NVBL should continue, and a primary one being that it's likely that this will not be the only pandemic that we'll see, and it would be a missed opportunity not to have an NVBL poised and ready to tackle the next one.

You also asked about how has the creation of the NVBL and the response of the coronavirus pandemic influenced partnerships. I can say having been at a national lab for a number of years now, I've never seen more collaboration across the national labs working synergistically on a common problem with different pieces of it in ways that we are now doing as a consequence of the NVBL.

Chairwoman FLETCHER. Terrific. Thank you, Dr. Maxon. Dr. Mohnen?

Dr. MOHNEN. If I could be the last one to speak—

Chairwoman FLETCHER. Sure.

Dr. MOHNEN. —I'm not directly influenced—I want to read up just a little bit.

Chairwoman FLETCHER. Oh, absolutely. I will come back to you. Maybe Ms. Wrighton?

Dr. WRIGHTON. Sure. I actually am not directly affiliated with NVBL as well, but I think when I was talking about this future of discovery and how we can catalyze and build around kind of a central unit and a theme, I think NVBL embodies that. And so really it was a problem that we were faced with as a research community, and it took new disciplinary teams and it brought together people that hadn't worked together before. And I really think that that's the heart and soul of this future kind of innovation is building these kinds of teams to address real-time problems. So I really think that NVBL and others like it should continue.

Chairwoman FLETCHER. Terrific. Thank you, Dr. Wrighton. And Dr. Randall?

Dr. RANDALL. Yes, I'd like to first amplify what Dr. Maxon said, which is that there will be future pandemics. And I think there's a history of investing briefly in an emergency and then sort of forgetting, and so the anthrax attacks are an example of where we had biodefense apparatus that was heavily invested in for 10 years and then was no longer supported. And really, as we look at what works and doesn't work and have a response to the current pandemic, that can really help through the framework of how we respond to the next one.

From my personal interactions, the advantages are teamwork, collaboration, and really bringing forward a multipronged attack to address multiple disparate issues with this pandemic. In terms of immediate needs—I can talk about my own experience. We've talked a lot about the capabilities of the labs to solve protein structures. I benefited in that by the time we got SARS-CoV up and running here, our colleagues a few blocks away at Argonne had already solved structures of some of the most important proteins that are drug targets. Now, we screen with them, give them the drugs, and within a week they can show where the drug has bind to that protein, how to make the drug better, and how the drug works. It's spectacular.

And the other aspect I would highlight is the supercomputing. So, the typical drug company has compound libraries of 1 to 3 million compounds that they'll physically screen, and so there's a consortium of supercomputing that basically put together a virtual library of every chemical on earth, 5 billion. So you're talking three orders of magnitude more and can basically do machine learning and artificial intelligence to look at how these compounds bind to these drug targets and then whittle that down to the top thousand or so and then bring them over to my lab where we can test if they work. And quite a few do. And really, you know, there hasn't been drug screening thought of this way, this is going to go way beyond COVID to any disease model, cancer, et cetera. So there's really a lot that can be leveraged not only for COVID but for future advancement.

Chairwoman FLETCHER. Thank you so much, Dr. Randall. And 5 minutes goes very fast, so I will thank all of you for your answers. Unfortunately, my time has expired, so I will now recognize Mr. Lucas for 5 minutes.

Mr. LUCAS. Thank you, Chairwoman.

Dr. Wrighton, in your research you leverage expertise from the Joint Genomic Institute and the computational capacities of the Environmental Molecular Sciences Laboratory. Can you talk about your experiences in working with both user facilities?

Dr. WRIGHTON. Sure. I don't know how familiar everyone is, but if and when you want to access user facility resources, basically, you write a grant. That grant gets reviewed by a board or a review panel of other scientists. And so basically the DOE gives you a charge. So this year, the theme is—and then they actually look at goodness of fit. So I've written grants and I've basically been awarded many by JGI, the Joint Genome Institute, as well as at EMSL. I actually don't use their computational resources. I use more of their molecular resources.

So they are innovators. I mean, they have access both at Ohio State and Colorado State we did not have the FTICR mass capabilities, this mass spec capabilities that EMSL had. And so it was a great example of where I didn't have resources on my campus, nor did we have trained experts that could use that environmental data, but I could collaborate with EMSL and I could get detailed information on the molecular structural of the soils that I was working in. And so they serve that role for many in the scientific community. And so it really is a way to enhance accessibility and to really expand your science beyond any boundaries that you may have on your campus or in your department.

The same goes for JGI. I mean, the sequencing capabilities they have, I could maybe sequence 10 samples. With them, I've had hundreds to thousands of samples sequenced in a rapid turnaround time.

Mr. LUCAS. Speaking of accessing facilities, could you touch on for a moment about how the COVID-19 pandemic has affected your access to these facilities?

Dr. WRIGHTON. Yes, you know, I have not—it has not changed my access to these facilities per se. I mean, obviously, when there's lab shutdowns, these facilities were also shut down, but only in that sense. And I think that the facilities are really just trying to make good faith to turn around and get samples processed as rapidly as they can. So I have not seen a change in my science in collaboration with those facilities due to COVID-19.

Mr. LUCAS. Dr. Maxon, can you give us your perspective from the laboratory side of how COVID has impacted access to user facilities at the Berkeley Lab?

Dr. MAXON. Yes, thank you for that question. Many of the facilities at the lab have remote capability, the supercomputing facilities, the Joint Genome Institute. Several of the data handling things obviously happen remotely. The advanced light source has remote activities.

However, there are things that need to get done by humans, and we are working very hard now to understand with safe what we call COVID controls, face coverings and distance working to protect the workers and shiftwork actually, which we never did before. We're trying to bring the full strength of the user facilities back online because we know the users depend on them. So we're doing our best to do that now, and we're not quite up to full speed, certainly not at the JGI yet, but we are definitely trying.

Mr. LUCAS. From your position now looking forward, what do you expect in terms of the requests from researchers from this point on?

Dr. MAXON. I think it will largely depend on what researchers can do with respect to collecting field samples. In the case of the JGI, we're looking at DNA that comes—nucleic acids that come from field samples. And if researchers are able to do the fieldwork that generates the samples that then gets sent to the user facilities, then I think it will be a good response. I think we'll be fine. We'll be able to have a lot of users' needs met. If, however, the pandemic limits the ability of people to travel to go to their field sites, I think there will be a reduced demand.

Mr. LUCAS. Absolutely. Dr. Wrighton, one more question. On top of being a frequent facility user, you also sit on the JGI advisory board. What would it mean for your researchers or others you hear from if BER's user facilities are not updated? Would the facilities simply become obsolete?

Dr. WRIGHTON. Yes. Yes. I mean, absolutely. I think especially JGI does a really nice job and they have a call for early investigators, so you're not competing with people who have 20 years of experience. You're competing in a much smaller group, and they really train you in how to analyze the data and how to work with your data. So if those investments weren't made, I think that the biggest impact would actually be on the next generation of science and early career scientists especially because they do a really good job of kind of corralling scientists into learning how to use the data and the technology, as well as giving access.

So one of the neatest things about JGI is that they're always on the cutting edge. I mean, they're using the newest technology. And so I think that's what keeps them so competitive and makes them a place that really people want to come and bring their data and be part of because of the benefit of the cutting-edge technology they offer.

Mr. LUCAS. Thanks, Doc. And Chair, my time's expired. I yield back.

Chairwoman FLETCHER. Thank you, Mr. Lucas. I'll now recognize Chairwoman Johnson for 5 minutes.

Chairwoman JOHNSON. Thank you very much. I'd like to start with Dr. Mohnen. As you noted in your testimony, much of the COVID-19 research BER has carried out and has built upon years of previous research. Can you speak to the importance of consistent and robust long-term investments in the BER program as a tool to fight future health and environmental crises?

Dr. MOHNEN. Yes, absolutely. I've been working now in the capacity of the bioenergy research centers with DOE and many BER-funded researchers for over 13 years. And it's very interesting to compare just briefly academic researchers versus DOE. DOE researchers are very much mission-driven. Academic, as was mentioned, you decide on the field or fields you're going to develop, and you do a very deep dive. And so what the DOE labs have been able to do is they take a mission-oriented long-term approach on developing capabilities and then proving them and do multiple things at once. They will attack critical questions that are mission-important.

And one of these, for example, with the bioenergy research centers, has been to understand both on the microbial side and on the plant side the complex array of genes on the plant side that make the biomass and modify it. This has led to understandings that have allowed us to manipulate plants to get them to grow six times more biomass in the field. This has led to understandings of microbes that can produce chemicals. This has led to the development of systems biology capabilities and artificial intelligence to look at huge gene networks. And this research has both a fundamental and a potentially applied portion of it. And it develops a long-term commitment to build on the foundations that are established.

So even though we've made, for example, great strides in understanding how to utilize biomass, deconstruct it so to speak, convert it into various types of biofuels, we're still at a point where there is, again, as much that needs to be learned to make the kind of fuels that are needed for the future, to understand the involvement of the microbes in the field to biomass growth to be able to respond to climate change.

I'm not sure. Did I answer your question well? I could continue.

Chairwoman JOHNSON. Yes. Are there other witnesses who would like to comment on that?

OK. Well, Dr. Maxon, DOE has a long history of supporting a variety of user facilities used by researchers all over the world. In particular, DOE holds several x-ray light sources that allow in-depth studies of materials at the atomic and molecular levels. Could you expand on how these light sources have been used to better understand COVID-19, as well as diagnostic and treatment options?

Dr. MAXON. Thank you for the question. Yes, the x-ray light sources have been critically important. One of my colleagues on the panel mentioned that the x-ray light sources are being used to study in detail the specific proteins of the SARS-CoV-2 virus, how those proteins interact with the host, that's critically important, and so that's one simple example.

Yesterday, I saw a fascinating presentation by a researcher using the Advanced Light Source with soft x-ray tomography to look inside cells that are infected with SARS-CoV-2. What does it look like when they're not infected, what does it look like when they're infected, and how can we understand how the virus can hijack the internal machinery of the cell to make more and more viruses? And so I would say the light sources have very quickly responded to help not only identify the critical pieces of the viral proteins but understand how the virus does what it does inside the host cells to make advances toward new therapeutics.

Chairwoman JOHNSON. Thank you very much. I think my time is about to expire, so I yield back.

Chairwoman FLETCHER. Thank you very much, Chairwoman Johnson. I will now recognize Mr. Biggs for 5 minutes. Is Mr. Biggs still with us?

Mr. LUCAS. I believe he's departed.

Chairwoman FLETCHER. I believe he has, in which case I will recognize Mr. Cloud for 5 minutes.

Mr. CLOUD. Can you pass on me for the moment?

Chairwoman FLETCHER. Yes, I can. I will now recognize Dr. Baird for 5 minutes.

Mr. BAIRD. Thank you. I really appreciate the opportunity to sit in on this session, and it's fantastic, the work that these researchers are doing.

Dr. Maxon, you just finished discussing how the proteins in the coronavirus, what they do in infected cells. And would you care to elaborate on that? I find that very interesting, how those proteins, you know, DNA, RNA, the genome, and so on. I really would be interested in how the proteins in this coronavirus impact cells, lung tissue, for example.

Dr. MAXON. Thank you for that question. So what I was able to learn yesterday in the study of the infected cells, it's still early days, so the experiments need to be worked out and they are developing some results now. It looks like when the virus infects the cell, it then goes through a process of creating what's called a replication center. That replication center does what it sounds like it should do, and that is it begins to use the machinery of the host cell to replicate more and more and more pieces of the virus to create more viruses to then be released and infect other cells.

It's really early, though, to be able to detect what the actual form of infection is that causes sickness. At least from these x-ray studies from the user facility we're just a few ways off from understanding that. But understanding at the cellular level, the creation of a replication complex center and the fact that there are cells that can fuse together to have two nuclei in the cell, that was found by these x-ray tomography studies, very interesting and still very early days. We're not sure what it means yet, but getting closer to understanding it for sure. Thank you for the question.

Mr. BAIRD. Can I continue on with one more question then? So these new proteins, how do they escape the original cell? Do you have a feel for that?

Dr. MAXON. Yes, so thank you. There's a process by which the cellular machinery is hijacked if you will not only to make more virus but to extrude the virus out of the cell. For decades we've understood how cells are infected with other types of viruses to then release the virus particles into other cells.

Mr. BAIRD. Very good. Dr. Wrighton, you mentioned your work and getting a lot of sequencing done in a very short period of time, but my question to you is what happens to the coronavirus as it comes in contact with soil?

Dr. WRIGHTON. You know, I think that we're still in very early days in terms of surveillance of the coronavirus and other viruses like the coronavirus and their distribution across different ecosystems, soils, rivers, wastewater streams. I think a very active and exciting research that's led by some colleagues at JGI that I was actually just speaking to this morning about this was we're basically trying to figure out ways that we can survey the diversity of these types of viruses so we get a sense for the reservoirs of these viruses. Also, we're trying to develop new tools so we can look at the variation within these viruses so that we can maybe start seeing those different populations and these changes and we could maybe better track these viruses using their genome tags over time and space beyond just the human host but have a better, broader environmental context. So I think that's a place where JGI will really play an important role moving forward.

Mr. BAIRD. So I got about 1 minute left, and I would ask you and Dr. Maxon both, so the BER in your opinion plays an important role in finding the answers you just both discussed.

Dr. MAXON. Yes.

Mr. BAIRD. I see you nodding your head.

Dr. WRIGHTON. Yes, without a doubt. And I just think, too, it's this parallel investment. I mean, I think anytime you get discovery in one end, it transcends and fuels another side and back and

forth. And I think that's what we really need to be armed and ready for this pandemic and the next pandemic.

Mr. BAIRD. Well, I think that kind of cooperation and collaboration is absolutely essential. And I think this basic research is really critical, especially in times like this pandemic.

So I see my time is about up, and so, Madam Chair, I yield back the balance of my time. Thank you.

Chairwoman FLETCHER. Thank you, Dr. Baird. I'll now recognize Ms. Horn for 5 minutes.

Ms. HORN. Thank you very much, Chairwoman, and thank you to all of our witnesses for this insightful and incredibly helpful hearing today.

My first question is for Dr. Maxon and Dr. Randall. And specifically around DOE's laboratories and their involvement in past pandemic responses such as HIV, Ebola, and influenza, and I'm wondering how the existing research has been adapted or reoriented for COVID-19 research purposes right now.

Dr. RANDALL. Yes, I can say, you know, in particular two past coronavirus pandemics, SARS-CoV-1 and not as big but Middle Eastern coronavirus, we're talking about how these proteins look, their structures, and they're similar and they have similar biochemical properties, so knowing how we could make and purify them and what they look like really expedited how fast we could learn the structures of the current coronavirus, SARS-CoV-2. So that's certainly one example of where past research really had us prepared and ready to move very quickly with the current pandemic.

Ms. HORN. Thank you very much. Dr. Maxon?

Dr. MAXON. Thank you. I will offer one example. I know that from the time of the Ebola virus pandemic, the Advanced Light Source researchers again used the x-rays to understand the viral structure and how the proteins of the virus do what they do. So I do know that at least in the case of the Ebola, the Department of Energy was in fact involved.

Ms. HORN. Following up on that a little bit more, Dr. Maxon, how is the COVID-19 pandemic different from outbreaks of other infectious diseases in terms of impact on DOE's research efforts or the way that DOE has approached disease-specific research?

Dr. MAXON. Impacts, there's a couple of ways. I think, first, I would be remiss if I didn't say that a major impact of the COVID-19 pandemic is on the cost of doing research. That has been a significant challenge for us to deal with. So that's one.

I think in terms of impacts of disease research specifically around this pandemic, as I said, bringing together the labs to pull all parts of what we have as core capabilities toward this problem, we have people working with the parts of the lab that do biomanufacturing process development, never before working on a treatment for an antiviral but definitely doing that now and working with companies to do it.

Ms. HORN. Thank you very much. And I want to turn slightly different focus for just a moment. And, Dr. Maxon, continuing on with you. In your testimony you mentioned that DOE research has drastically reduced the predicted cost of new biofuels. And as we are looking at not only addressing the next pandemic and DOE's role

in research, we also have to take into account so many other factors, environment and related factors. And biofuels are going to be a critical component of, I think, next generation energy. So I'm curious about what advances—or how these advances are transferred to industry and what additional resources may be needed by DOE to help enable the commercial adaptation and adoption of biofuels?

Dr. MAXON. Thank you. Biofuels, so the way that these advances are translated to industry include from the Bioenergy Research Centers' proactive engagements with industry to make clear that there are new technologies available in the biofuels space for licensing, frankly. And I think what's required now, there's still a gap, as I mentioned. The costs have come down, but the gap in being able to make these commodity products, these biofuels at scale is missing, and that piece, being able to take a small-scale laboratory proof-of-concept and make it commercially scaled, that's the gap that I think is seriously missing and we could use some help.

Ms. HORN. I have very little time left, but thank you for that, and I think filling that gap is critically important, so thank you. And Madam Chair, I yield back.

Chairwoman FLETCHER. Thank you, Ms. Horn. I'll now recognize Mr. Cloud for 5 minutes.

Mr. CLOUD. Thank you. And thank you all for being here today. We certainly appreciate the work you do to keep us on the forefront of science, especially when we consider the competitive global environment that we're in, how important it is for the United States to stay on the cutting edge of these technologies and these advancements in science. I really appreciate it.

Kind of continuing on with the questioning Ms. Horn had, just talking about some of the lessons learned from previous pandemics and such, not only are we learning a lot about the science when it comes to COVID, but it seems to me we're doing things a lot differently, not only coming up with new discoveries but also new best practices. Could you compare maybe some of the lessons we're learning from an operational standpoint, from a best-practice standpoint compared to how we approached the work of research compared to previous pandemics?

Dr. MOHNEN. With people that use systems biology and computational modeling on plant systems where we don't have as much information as we do on human systems because on plants there are many, many species, humans we've got a lot more money concentrated on humans and model mice, et cetera. So the data that you have for human systems is incredible, whereas a systems biology approach is always limited by the data set.

When you get to humans, what I've seen now with what Dan Jacobson and others can do with these supercomputers that DOE funds, we've got the second-fastest in the world and the amount of data out there, both published and in-house from the DNA sequencing, RNA sequencing, et cetera, they are now at a point I actually didn't believe a couple years ago we would be at. They can make predictions by running supercomputers and integrating all the data from metabolomics, from proteomics, genomics, evolution, and they can come up with hypotheses that have a very strong potential of being correct, that can direct our thinking. We've gone

over, I think, an edge to where now you're not going to get definitive answers from this but you're going to get answers that are highly probable and then can inform the people that go in the lab into the experiments. I think this is a turning point that only has become possible with these supercomputing abilities and the ability to do the systems biology.

And, finally, the fact that you've got this national lab set up where you interact with a bunch of specialists, whether they be academic or in the labs to inform the information as the results are interpreted. I'll stop.

Mr. CLOUD. Well, thank you.

Dr. RANDALL. Yes, I was just going to follow that up and say I agree completely. And also the speed of sequencing and so forth has ramped up so fast that within discovery of the virus we had sequenced within, you know, a week and all the companies that are rushing out their vaccines and knew how to synthesize spike to get it in their vaccine platforms to where we're getting these vaccine candidates years before we traditionally have.

And these platforms were all developed, you know, for things that were not SARS-CoV-2. The only thing SARS-CoV-2-related in them is the spike protein. And so really there's a lot of platforms and best practices in place. I know the pandemic seems long, but the response historically is very fast.

Mr. CLOUD. Yes. Well, thank you. Dr. Maxon, I was wondering from your experience in Berkeley National Lab, you know, we can appreciate the research going on, but then we also know that our research has been under attack in a sense from other nation-states, specifically China. Can you speak to what the DOE has been doing to ensure that our research continues to be safe and secure?

Dr. MAXON. I can speak from the perspective of an employee at Lawrence Berkeley National Lab.

Mr. CLOUD. Right. Right.

Dr. MAXON. We definitely take very seriously the export controls. We follow those controls very clearly to make sure that our research stays our research. We are looking very carefully at our foreign visitors' processes to make sure that we know who's coming onto the lab and we know what they're there to do. And so we're taking the precautions to make sure that our research stays our research. We've actually in the last couple of years updated some of our badge-in systems so that we can keep track of who came in and when. And so I think we are at least at our national lab and I'm sure others are very, very concerned about keeping things and all of the data that we have in our labs secure from attack.

Mr. CLOUD. Well, especially with teleworking, I guess that's one of the concerns I have. Can you speak to that at all or—

Dr. MAXON. I understand—thank you. Teleworking does present some new concerns, especially many of the computing people don't have home systems that can handle the big scales of data that they need to use. But as it relates to the security of the data, I understand that the IT (Information technology) infrastructures at the labs are working hard to make sure that we have all the right up-to-date tools. We talked about updating facilities earlier, updating the cyber aspects of the labs are important, too, just for that reason.

Mr. CLOUD. Thank you very much. I appreciate it. My time is expired. Thank you for being you today, all of you.

Chairwoman FLETCHER. Thank you, Mr. Cloud. I'll now recognize Mr. McNerney for 5 minutes.

Mr. MCNERNEY. Well, I thank the Chairwoman and Ranking Member and I thank the panelists. I have to say it is exciting hearing about what's going on in the labs.

And my first question is for Dr. Maxon, and it'll be a softball. And it's good to see you here, Dr. Maxon. You noted that societal challenges such as the need to store carbon at massive scale and produce crops and develop crops for changing climate demand quick action and quick response. How important is it for the United States to maintain its lead in these areas?

Dr. MAXON. Thank you for the question, Doctor. It's critically important that the Nation maintain our leadership. We have the capability to produce a billion tons of sustainable biomass in the United States. It's a strategic natural reserve of sorts. And to be able to convert that biomass into the bioeconomy's products, including transportation fuels and chemicals and reduce greenhouse gas emissions, it's critically important that we maintain that lead. We're the only country that has a lead like that.

Mr. MCNERNEY. Is the current Federal investment adequate to ensure that we do maintain the lead?

Dr. MAXON. Well, that's a challenging question to answer. I would offer from my own perspective that more resources would be very helpful in allowing us to understand how to take diverse feedstocks such as agricultural waste and forest waste. In California, as you know, we have a lot of forests that are overgrown.

Mr. MCNERNEY. Yes.

Dr. MAXON. If we could turn that forest waste in—that woody biomass into biomanufactured products, fuels and chemicals used regionally, for example, like microbreweries, I think that would be a very good investment to make, more about how to change the feedstock capabilities of the United States.

Mr. MCNERNEY. Well, thank you. The pandemic has been with us since February or March, and we hear about the capabilities of the lab complex to address national crises such as the pandemic. Can anyone on the panel point to specific achievements in this effort that is now helping the Nation fight the pandemic?

Dr. MOHNEN. Well, Mr. McNerney, as I mentioned more so in the written statement, I was actually very surprised when I read Dan Jacobson's work because I worked on the plant microsite, so I had to catch up. That systems biology approach identified 11 FDA-approved medications that should be able to, if the analyses are correct, improve some of the effects of the COVID infection. And I assume those are being looked at immediately in small clinical trials. There are other people on the panel who are more experts in the COVID themselves. But even that—and his work's made quite a splash. It's been covered in *Forbes* and many medical journals. And that's just one example.

Then the other example was the work—and I've forgotten the researcher's name now. It comes out of a laboratory where they used the modeling capabilities and the 3-D protein structure prediction. These researchers determined the first structure of one or more of

the COVID proteins at a temperature that might exist and the temperature of the body actually. And that gave information on slightly different structures that could be important in understanding how medications or cell proteins or metabolites interact with them. So the results are completely new, up-to-date, and informative. But I yield now to people with more expertise with COVID-19.

Mr. MCNERNEY. Well, I'm going to move on to my next question, though. The lab consortium or collaboration have been working with the pharmaceutical companies to develop vaccines. You just mentioned, Dr. Mohnen, about therapeutics. Is anyone able to give an example of collaboration between the BER and private companies? And what are the ownership issues involved?

No one's going to bite on that one? OK.

Well, my last question, on Wednesday, 78 Stanford researchers and physicians issued a letter about the falsehood and misrepresentations of science that have been spread by Dr. Scott Atlas, who was appointed to the White House Coronavirus Task Force last month. This is only one example of the Administration's attack on science. What impact do these disregards for science have on our ability to fight COVID? Whoever wants to step up.

Dr. RANDALL. I'm not going to speak specifically to that, but what I will say is that public trust in science is critical to get people to take the vaccine when we get it, and that is a concern.

Mr. MCNERNEY. All right. Thank you. I yield back, Madam Chair.

Chairwoman FLETCHER. Thank you, Mr. McNerney. I'll now recognize Mr. Foster for 5 minutes.

Mr. FOSTER. Thank you, Madam Chairman and to our witnesses.

So I have one very specific question and then one much more general one. The specific one is that there is this theory of very severe cases of COVID that goes by the name of the bradykinin storm hypothesis. And this apparently was discovered or verified using the Oak Ridge supercomputers where they analyzed the fluid coming from people's lungs who were very sick with COVID and looking for genes that were massively overexpressed and saw that the genes involved in—what do they call it, the RAS system which is local and inflammatory response and blood pressure regulation.

And so apparently, this hypothesis, which was verified on the Oak Ridge supercomputers, explains everything from COVID toe to the fact that the virus gets in through the blood-brain barrier to the fact that vitamin D is a very promising therapeutic and prophylactic. I was just wondering, is that on any of your radar screens? Is that a real result coming from the DOE supercomputers? Anyone familiar with that?

Dr. MOHNEN. Yes, it absolutely is a real result. It comes from Dan Jacobson's work. And he's got multiple papers, and I've been reading a couple of them. He is top-notch world-class systems biologist. I spoke to him personally for this panel. I know him. He works in the bioenergy center. Because he's so good at what he does—and he's done two—it's either the largest or the fastest computational predictions using computers anywhere in the world. He really is outstanding.

I talked to him about this because I couldn't understand how he did it. And he told me—because he had to keep up his other work, which was on microbes and plants—as this hits—and he knew the systems biology approach and the computers because this is what he does. He takes multiple pieces of data, uses the computers, looks for connections, then reads the literature deeply. He was working 21 hours a day for weeks and weeks on end. And he brought in multiple medical people from multiple institutions.

Now, what we have to say is when you do this kind of systems biology approach—and—the data looked very compelling, and he will say in his paper now it has to be tested. These have to be tested in clinical trials. But the data are incredibly robust. And I believe it's all being followed up, but I know there are many more papers, so this—

Mr. FOSTER. Yes, his paper—

Dr. MOHNEN [continuing]. Is top-notch.

Mr. FOSTER [continuing]. Identified a number of therapeutic targets. And I presume those are being followed up in clinical trials, though I'm not familiar with that.

Dr. MOHNEN. I'm not sure, but I believe so, too.

Mr. FOSTER. Yes. All right. And my more general question is one of the trends that people mentioned in biology is this business of what's sometimes called cloud-based biology. And that's where you have large farms of robots that will do biological experiments. And so this is something where potentially, you know, a scientist at a university can sit down on their computer, define the experiment we want to, you know, get this cell line and modify it genetically this way, expose it to this, wait 18 days, and then, you know, section it up and send me the photos. And so without actually ever touching or owning or taking possession of the biological samples, you could perform experiments.

And it strikes me this is something where there may be a role for national labs to actually engage in gigantic purchases of initial systems the same way we engage in new generations of supercomputers, the new generations of experiments and then open it up, you know, in a way very similar to supercomputers where different university groups can sort of bid for time on these things.

And I was wondering is that a sort of model that makes sense to seed investments that can be immediately used by universities? And this seems to relate to Dr. Wrighton's comments earlier.

Dr. WRIGHTON. Yes, I am so excited, Congressman Foster, to hear you say this because this is exactly up my alley. I mean, I think that what we're finding at the user facilities is they're very successful, and many of the key resources are becoming fairly inundated, so the turnaround time or the lifecycle of actually processing samples is somewhat delayed just because of the demand, and so we really have to rethink scalability in terms of maybe not one building but maybe like—and there's a—there are some companies that you may be familiar with, Emerald Cloud Labs and others where you can basically—you know, they have these robotic facilities, and you can log in and kind of high throughput with more reproducibility and greater efficiency.

And so that will really allow us to run little pilot studies, look at the data in real time, and then do bigger experiments. And so

it creates a much more dynamic and efficient working environment than having to collect 400 samples and send them all in because that's the allocated time you get.

So I think the future—if we're really going to talk about how we can innovate and do more with what we have or even just extend our resources in new ways, I think that's a very exciting future.

Mr. FOSTER. Yes. And it would allow, you know, smaller university-based researchers to compete at the very top level, as well as dealing with the reproducibility crisis—

Dr. WRIGHTON. Absolutely.

Mr. FOSTER [continuing]. Some fraction of it at least in biology that you publish the specifications that could reproduce that at any robotic facility anywhere. I see my time is up and yield back.

Chairwoman FLETCHER. Thank you, Mr. Foster. I will now recognize Mr. Casten for 5 minutes.

Mr. CASTEN. Thank you, Chairwoman Fletcher, and thanks to our panel. This is going to surprise all of my colleagues, but my questions are about climate change, not COVID.

I have—and, No. 1, we—you know, just [inaudible] conclusions, we have got to get to zero net carbon emissions, and we've got to get there yesterday. I am somewhat sanguine about our path to get there in terms of our energy use because I can identify technologies to make electricity and transportation fuels, heat, the things we need for energy. I have real concerns about what we are going to do in those places where we use fossil fuels as a chemical input typically to reduce organic compounds. How do we make fertilizer? How do we make steel? How do we make silicon? How do we make magnesium? And biology has a way to do that, right, with photosynthesis is a way to reduce compounds with sunlight input, some of the weird archaeobacteria that live on volcanic [inaudible].

And it strikes me that there are interesting research projects that are scattered. I introduced a bill that's passed through this Committee, H.R. 4320, the *Clean Industrial Technology Act*, which has a purpose to bring all of the DOE research around how do we decarbonize those hard-to-decarbonize industries and bring it's one place?

And I guess I want to start with you, Dr. Maxon. Can you give us any oversight of what if any programs you are aware of that DOE is doing in that vein around how do we use biological solutions to reduce inorganic materials? And what if anything can we do to help accelerate that research?

Dr. MAXON. Thank you for that question. Biomanufacturing, yes, in fact, the Department of Energy in January hosted an InnovationXLab biomanufacturing summit directed on this very topic and invited hundreds of companies to come in and see the technologies, the assets, and the programs that the Department of Energy has at its national labs to do just this, to reduce the energy intensity of manufacturing and to use petroleum to reduce petroleum feedstocks.

I mentioned a little while ago the billion-ton bioeconomy, the billion tons of sustainable biomass. We're making big progress in being able to convert that biomass into useful things but can't do it cheaply yet.

There are a number of other programs. The Agile BioFoundry is a Department of Energy program that is looking to speed for industry and for academic partners the ability to design biological systems to do just this, to harness them to do by a manufacturing. So the Agile BioFoundry is a new one. The Bioenergy Research Centers are focused on conversion of lignocellulosic products, woody biomass, for example, into fuels and bioproducts. So there are a number of them that exist, but I would say that given the crisis, we could use a lot more help in this regard, more of these and more pilot fermentation facilities, steel, if you will, fermentation to get us to that next scalable leap.

Mr. CASTEN. So if I could—and maybe others—I'm not sure I've asked my question very well. The lignocellulosic materials, making building materials, making products like—I get that. What I—and I don't even understand the thermodynamics well enough, but if we're going to take, you know, nitrogen and make it into ammonia, I know how to do that with natural gas. If we're going to take quartz silicon dioxide, make it into silicone, I know how to do that with coal or to reduce iron oxides into steel. Are there biological pathways that we could imagine to use biological systems' ability to reduce those compounds? And is there potential to scale that up, or is there some reason why those are just—is there something about, you know, the way that life has put together the thermodynamics that makes that impossible?

Dr. WRIGHTON. I think, Congressman Casten, there's two parts to this answer. One is the biological discovery, and I think, you know, just two weeks ago it came out in the paper looking at how you can produce ethylene with microbes using enzymes that we never knew about until just this year. And do it independent of oxygen, so do it independent of combustion. So I think that there is this discovery aspect and there's that basic science aspect, but the scalability part I think is the yet-to-be-seen part for me in terms of harnessing these new biological pathways and overcoming the thermodynamics within an organism and then thinking about how we actually can develop these precursors with, you know, more neutral carbon economy.

But I think that we're at the point now where we're able to now mine and scratch the surface into the biology, and the next phase of our discovery is going to be scaling, again, to do these technologies—at least in these really new spaces, not some of those like plant deconstruction and they're, you know, 10 or 15 years ahead of some of the more new discoveries we're fighting about, microbial pathways for these compounds.

Mr. CASTEN. OK. Well, I'm out of time and yield back but will maybe follow up with you offline because I'd like to get some overview of where these programs are and what we could do to accelerate because I do think we're out of time and we need to—

Dr. WRIGHTON. OK. I look—

Mr. CASTEN. But 5 minutes, we're out of like—our species is running out of time. But we'll continue that offline. Thank you.

Chairwoman FLETCHER. You are correct, Mr. Casten. Your 5 minutes has expired, and we will now recognize Mr. Beyer for 5 minutes.

Mr. BEYER. Thank you, Madam Chairman, very much. And thank you, panelists, for an amazing amount of information. I'd like to start with Dr. Mohnen, and thanks for your comments about Dr. Jacobson and the work done at Oak Ridge. And I want to thank Bill Foster for sending that article of that, which I thought was just remarkable, the notion of crunching data, 40,000 genes, sending in a thousand genetic samples, two and a half billion genetic combinations. And the articles themselves really lead to some interesting thoughts about treatment. If this thing is bradykinin storm thing is real, we could be in a very different place in a couple weeks from now.

But, Dr. Mohnen, you're also the historian, so I want to thank you for letting us know that the Human Genome Project started through BER. And I wonder because I've always thought, you know, Francis Collins, Frank Venter, George Church, how now does JGI interact with NIH and with the other folks doing human genomes?

Dr. MOHNEN. Well, thank you for the question. I think it's a very interesting one. But I think that there are other panelists who probably have better information on that interaction, so I think I will pass that off to someone who knows more about that particularly.

Mr. BEYER. Dr. Wrighton?

Dr. WRIGHTON. So the question—sorry, could you repeat your question?

Mr. BEYER. Well, so you have the Joint Genome Institute, but then you also have NIH and Francis Collins, nebula genomics, all the work being done at Harvard, MIT (Massachusetts Institute of Technology). How do all those work together?

Dr. WRIGHTON. Yes, and so I think—so to my knowledge—and others may be able to have a broader perspective—is that the Joint Genome Institute generally focuses on the nonhuman aspects of the biology. That does not mean that they're decoupled from NIH, and I want to stress that because there are themes that you can do in one system like understand enzymes and pathways and make discoveries, and then you can take those to the NIH—and I've done this in my own career—and apply for funding in the NIH and site those same processes in the human data.

So it's not that they're—but the research focus of the JGI is typically on nonhuman, you know, research, but it doesn't mean the discoveries that are made at JGI by JGI researchers or their collaborators do not then go and advance through the NIH angle. So they're just kind of different themes, but you can take ideas from one area and bring it to the other and vice versa. Does that make sense?

Mr. BEYER. It does. And you set up my next question, which I think is for Dr. Maxon because you're the Federal lab person. Just reading your testimony and listening to it, I came up with the CABBI (Center for Advanced Bioenergy and Bioproducts Innovation), the CBI, the GLBRC (Great Lakes Bioenergy Research Center), the JREI, the JGI, the ERC (Engineering Research Centers), the NMDC (National Microbiome Data Collaborative), the APPBD, the EMSL, the KBase (Systems Biology Knowledgebase), the ADF, and others. Is this the idea that we have micro-focused so many

different places or is this empire-building or why do we have such an incredible proliferation of separate institutes within the Department of Energy just on biology?

Dr. MAXON. Thank you for the question. The biological challenges are enormous, and they are complex. And each one of those four Bioenergy Research Centers that you mentioned is working on a different way to attack the similar problem. And so it's a way to have nonredundant maximum shots on goal to achieve the solution rather than putting all your money in one basket.

Going back to your question about NIH for a second, I'd like to weigh in on that as well for just a minute to say that the National Microbiome Data Collaborative is a brand new DOE program that is intended to take all microbiome data, as Dr. Wrighton was just talking about, and make that data fair, findable, accessible, interoperable, and reusable, meaning it doesn't matter whether the microbiome data came from an NIH researcher or a DOE researcher or a USDA (United States Department of Agriculture) researcher. All those data based on the vision, should be able to be findable, interoperable, and used together to develop all new theories and hypotheses and experimentation programs. So that new thing is helping to bridge the gap.

Mr. BEYER. That's terrific. And one last question, Dr. Maxon. We have at least three prominent women scientists on our panel today. Does this mean that women are finally assuming their rightful place in science?

Dr. MAXON. Wow. I'll say yes.

Mr. BEYER. OK, great. Madam Chair, I yield back.

Chairwoman FLETCHER. Thank you.

Mr. BEYER. Madam Chairwoman, yield back.

Chairwoman FLETCHER. Thank you, Mr. Beyer, great last question. And it is wonderful to see the expertise assembled on this panel, the incredible women here, but really the efforts of everybody at our national labs, the work you have done in response to the coronavirus pandemic and more broadly, so it's really wonderful for us to hear from you this afternoon. So I thank you all very much for your participation, for your insights, and for your work for our country right now. We need you, and we are so lucky to have you. So thank you so much for your testimony here today.

Before I bring the hearing to a close, I just want to let my colleagues know that the record will remain open for 2 weeks for additional statements from Members and for any additional questions that the Committee may ask of the witnesses.

With that, the witnesses are excused, and I'm going to use my gavel here so you can all hear. The witnesses are excused, and the hearing is adjourned.

[Whereupon, at 3:01 p.m., the Subcommittee was adjourned.]

Appendix

ANSWERS TO POST-HEARING QUESTIONS

ANSWERS TO POST-HEARING QUESTIONS

Responses by Dr. Mary Maxon

10/27/20

House Committee on Science, Space, and Technology
 “Biological Research at the Department of Energy: Leveraging DOE’s unique capabilities to respond to the COVID-19 pandemic”

Hearing September 11, 2020

Dr. Mary Maxon, Associate Laboratory Director for Biosciences
 Lawrence Berkeley National Laboratory

Question submitted by Chairwoman Haley Stevens:

What are the research needs for developing future capabilities and tools, like pandemic forecasting, to help the U.S. more effectively plan for and manage future pandemics, and what is DOE’s role in supporting research in these areas?

Answer:

Following the SARS epidemic in 2003/2004, researchers began to predict future coronavirus epidemics as early as 2007. Amidst increasing worldwide cases of covid-19 today, researchers continue to assess the probability of future coronavirus threats and call for new therapeutic and prophylactic strategies to combat and prevent them. The Department of Energy has an opportunity to leverage its considerable biological and computational research capabilities to prepare for and respond to future pandemics by developing new capabilities and tools such as the ones described below. New investments in these areas would also enhance the national labs’ abilities to address DOE’s core mission objectives in energy and environmental sustainability. The following are examples of critical areas in which new investments would have significant impact on the nation’s ability to respond to pandemic and other biological emergencies.

Invest more in the development and utilization of advanced imaging technologies to study pathogen interactions with human cells, tissues, and organs.

Building novel imaging capabilities, such as advanced cryo-EM and new tools and methods for x-ray and neutron imaging, will drive DOE-relevant discoveries and also aid scientists in the investigation of the molecular mechanisms by which pathogens interact with humans to understand how diseases progress, and to design interventions that disrupt these mechanisms. Further, integrating novel imaging technologies in multimodal systems will enable the safe and dynamic, real-time imaging of living systems including cells, tissues, and organs leveraging workflows that include data processing, analysis, and sharing for different modalities and data types.

Develop high throughput automated biological laboratory systems to accelerate discovery and reduce human exposure to pathogens.

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Accelerated development of robotic and automated laboratory systems, new microsystems for experimentation, and “self-driving labs” can speed solutions to address emergencies such as pandemics and to meet core DOE mission needs. These technologies quickly undertake multiple assays, using machine learning to refine experimentation in cycles, minimizing use of reagents and consumables while allowing humans to perform the necessary knowledge work to validate hypotheses, design new approaches, and identify the breakthroughs in vaccines and treatments for new pandemics. Development and deployment of such technologies would also enable remote laboratory research, reducing laboratory worker exposure to pathogens and support the continuation of research during quarantines, sheltering in place, and reduced staff density in a pandemic.

Additionally, high-throughput (HTP) protein production and characterization capabilities for complex biological systems would allow scientists to more effectively execute on many types of studies where protein production is central to enabling scientific advancements such as rapidly understanding protein structures from pathogens and their hosts, allowing researchers to design new drugs to combat infection and disease.

Build next generation animal facilities to enable expanded pandemic response throughout the National Laboratory complex.

Expanded federal support for Biosafety Level 3 facilities at DOE national laboratories, outside of the NIH and DOD, would provide surge capacity during pandemics or for other diseases that require the quick and urgent study of organisms that are harmful to humans and animals.

Invest in the development of tools for design and synthesis of novel materials with anti-infective properties.

The high-throughput discovery, design, and characterization of new materials with properties that prevent the spread of pathogens, including viruses, bacteria, and fungi, are critical parts of a holistic approach to pandemic response. These materials could be employed for HTP testing procedures that can protect health care workers, including new sample collection materials and enhanced PPE. New materials could also be used to signal when PPE surfaces have become exposed to pathogens and used in building ventilation systems to capture and kill pathogens, preventing their spread indoors.

Improve and expand modeling approaches to enable prediction and mitigation strategies.

Epidemiological modeling is central to any informed pandemic response, and a strategic federally coordinated multi agency effort would greatly benefit any future pandemic response. Among federal agencies, DOE leads in the use of large-scale modeling and should partner with the NIH, NSF, and CDC in epidemiological modeling. DOE and NIH are mission-driven agencies that can immediately execute on urgent priorities, and with its national laboratory complex and long history of expertise in and support for supercomputing it could be argued that DOE has the

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most powerful public sector supercomputing response capability anywhere in the world. The ultimate translation of models to operational impact would require that DOE be prepared for and involved in the provisioning of computing and data resources to meet needs of the NIH, NSF, and DOE pandemic response research communities as well as operational needs of relevant agencies such as the CDC and the FDA.

On a more granular level, more work needs to be done to develop integrated and validated modeling frameworks that link population mobility and disease transmission, enabling targeted research to prevent transmission and providing evidence that can be used to make informed decisions for public transit and other methods of transportation. DOE's expertise in modeling and simulation, high performance computing, and uncertainty quantification could be brought together with complementary assets at research universities to develop a framework for collecting, protecting, and integrating observational data on disease characteristics and spread.