Testimony of

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

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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 coronvirus 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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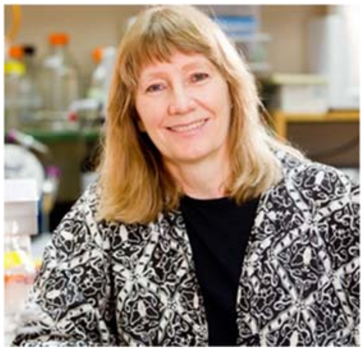

Debra Mohnen is Professor of Biochemistry and Molecular Biology at the Complex Carbohydrate Research Center, University of Georgia (UGA). She has studied plant cell wall synthesis, structure, and function for over 30 years with emphasis on the non-cellulosic cell wall polysaccharides. In 2008 she was 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.