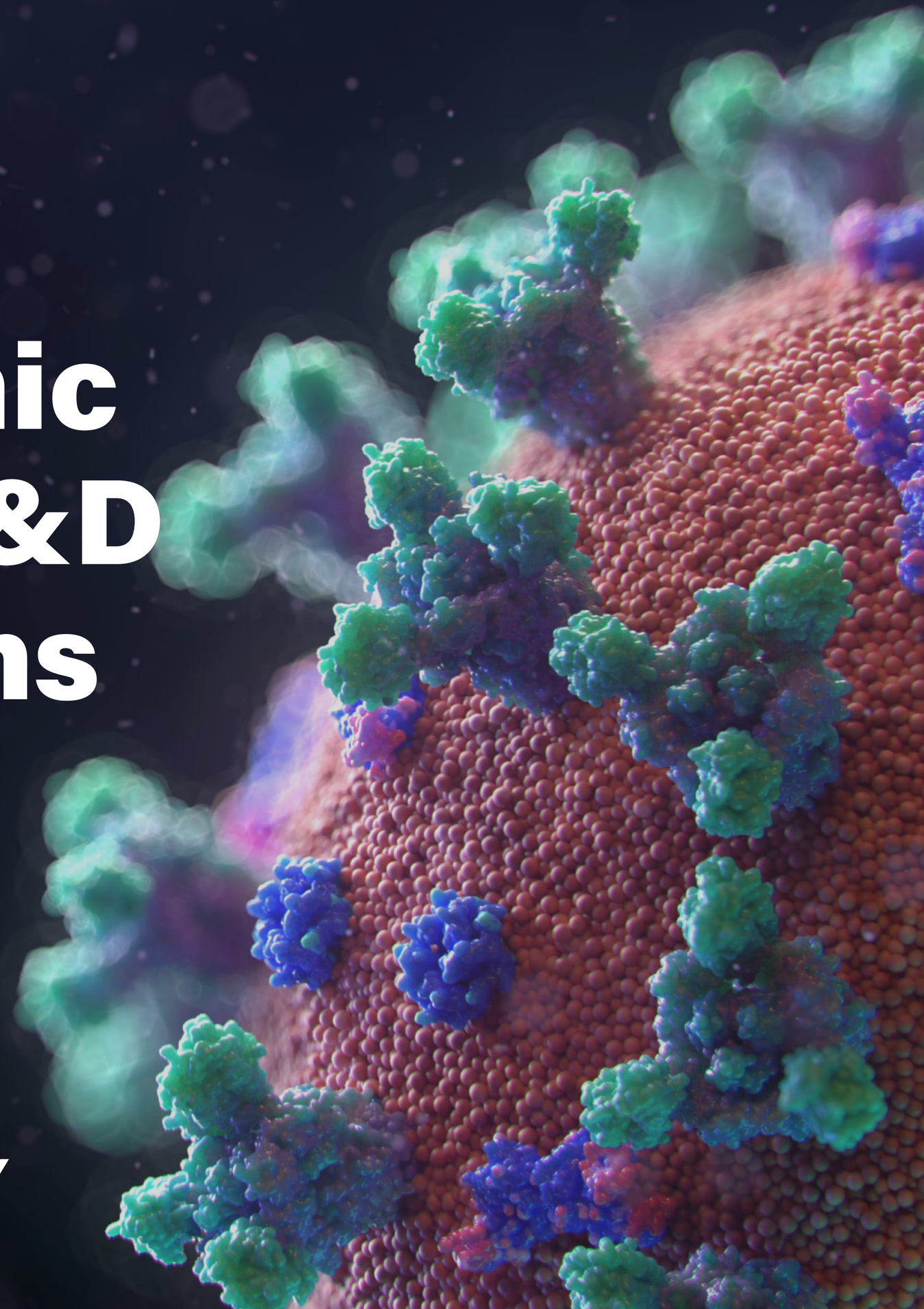
Key Pandemic Response R&D Contributions

by Los Alamos National Laboratory



Los Alamos NATIONAL LABORATORY

NNSA National Nuclear Security Administration

U.S. DEPARTMENT OF ENERGY

Contents

Rapid innovation

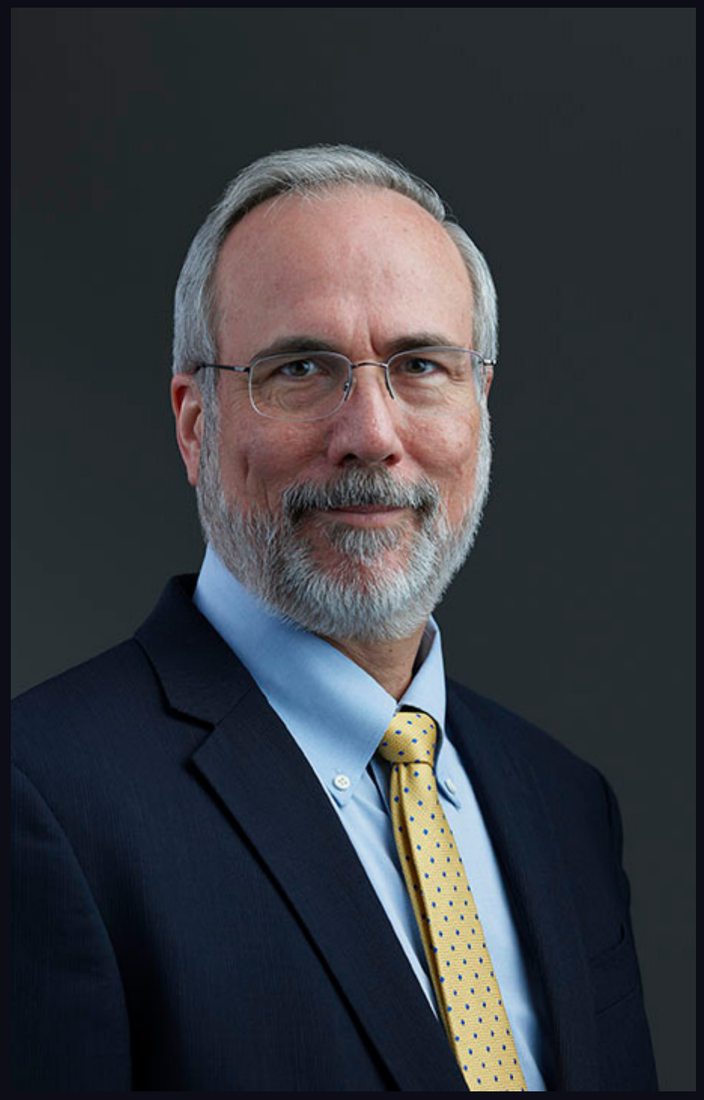
LANL'S R&D RESPONSE TO THE COVID PANDEMIC

New research goals, mitigation successes, and beneficial collaborations burgeoned from the early critical days of 2020 when LANL (Los Alamos National Laboratory) pivoted to help respond to the pandemic.

By applying its considerable capabilities in the fields of science, technology, and engineering (STE), LANL responded to the coronavirus infectious disease (COVID-19) pandemic. This report documents representative examples of that response. Through significant investments in COVID-19 mitigations and ongoing research and development (R&D), important advancements were made to address the pandemic that not only benefited the global population affected by the pandemic, but also protected our staff and collaborators as we executed our Lab's mission.

I extend special thanks to our dedicated team whose contributions were invaluable, including those contributions and contributors that could not be fully recognized in this document due to space limitations.

Pat Fitch, LANL Special Office for COVID-19



Los Alamos National Lab contributing organizations

Analytics, Intelligence, and Technology Division

Bioscience Division

Chemistry Division

Computer, Computational, and Statistical Sciences Division

Engineering Technology and Design Division

Materials Physics and Applications Division

National Security and Defense Program Office

Theoretical Division

Weapon Stockpile Modernization Division

Weapon Systems Engineering Division

Collaborating organizations

AMES LABORATORY U.S. DEPARTMENT OF ENERGY

Argonne NATIONAL LABORATORY

BERKELEY LAB Bringing Science Solutions to the World

CDC CENTERS FOR DISEASE CONTROL AND PREVENTION

CHRISTUS ST. VINCENT Health System

U.S. Department of Defense

U.S. DEPARTMENT OF ENERGY

Duke UNIVERSITY

FDA

FEMA

GISAID

HUMAN SERVICES DEPARTMENT

INL Idaho National Laboratory

NNSA National Nuclear Security Administration

La Jolla Institute FOR IMMUNOLOGY

Lawrence Livermore National Laboratory

NIH National Institutes of Health Turning Discovery Into Health

NMDOH NEW MEXICO DEPARTMENT OF HEALTH

OAK RIDGE National Laboratory

Pacific Northwest NATIONAL LABORATORY

PRESBYTERIAN

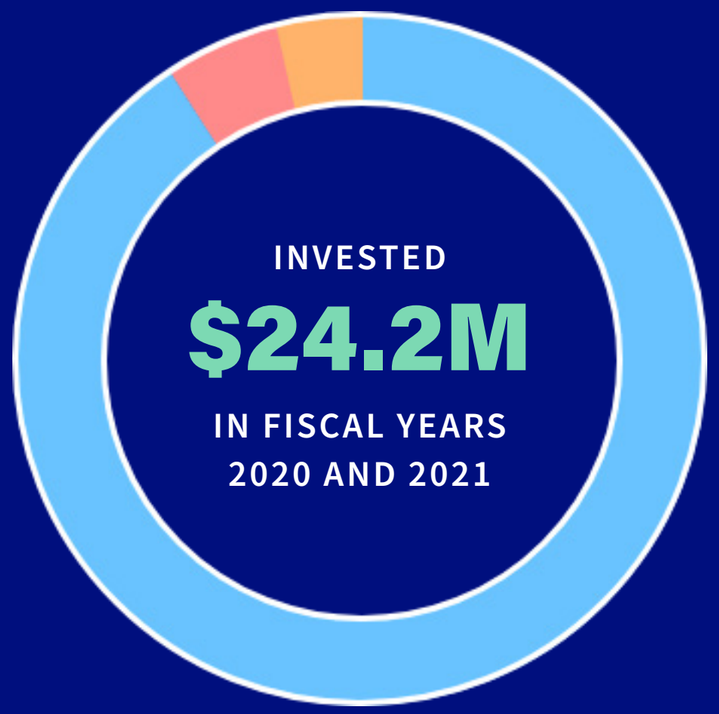
Sandia National Laboratories

SLAC NATIONAL ACCELERATOR LABORATORY

THE UNIVERSITY OF NEW MEXICO

The University Of Sheffield.

Pandemic response by the numbers



$20.4M

IN R&D PROJECTS

$3.0M

IN COVID TESTING AND PROCESSING

$0.8M

IN TECHNOLOGY EVALUATION AND DEMONSTRATION

Developed

Leads for diagnostics, vaccines, and therapeutics

COVID variant surveillance tools (**cov.lanl.gov**)

Models of virus evolution

A biosurveillance pipeline for future pandemics

Lung models and testbeds to support ventilator design and manufacture

Provided

Data to national-level regulators, impacting millions of tests

Sequencing, variant characterization, and data submission protocols used internationally

Thousands of onsite tests

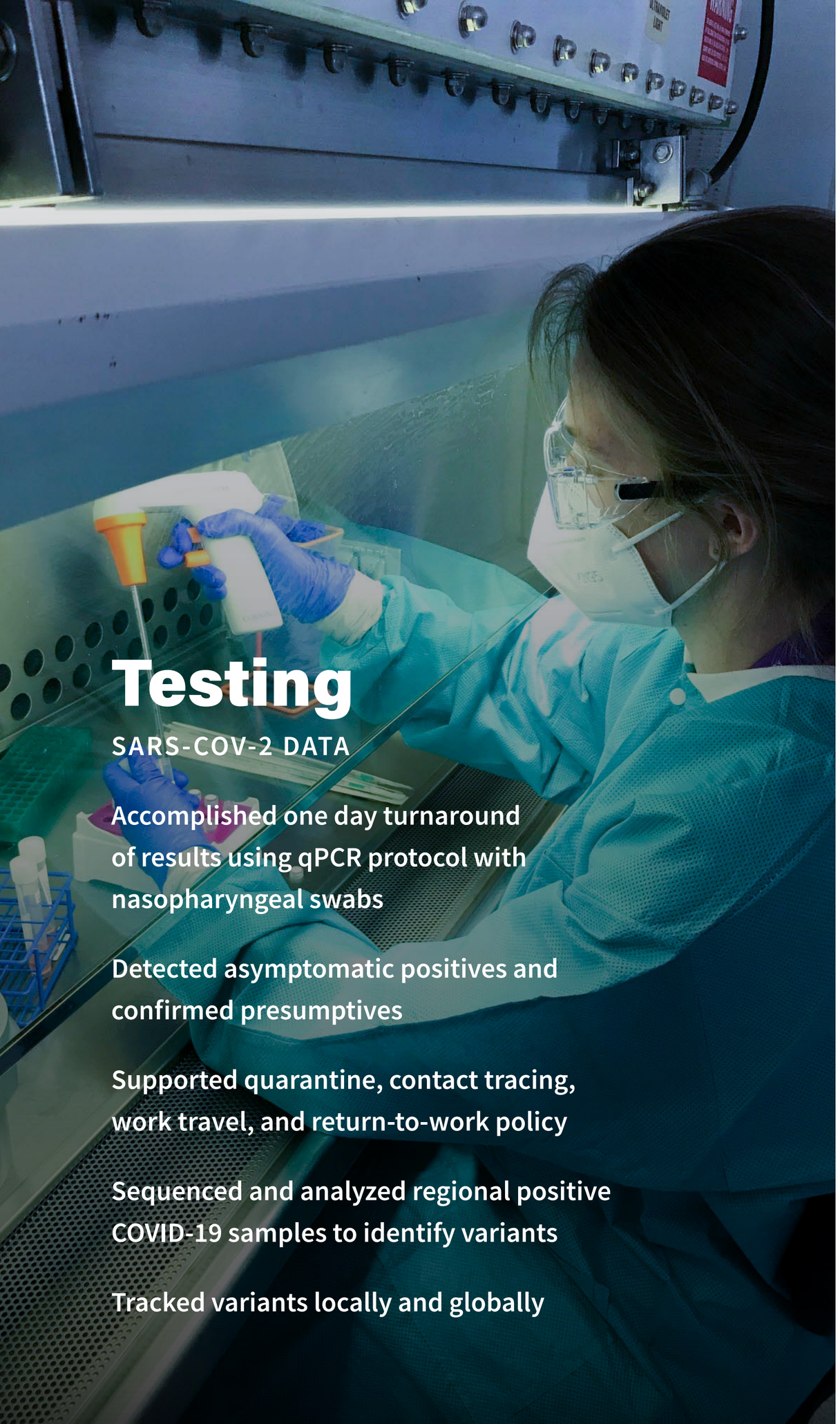
Web-based, publicly-available genome analytics to rapidly validate assays

Web-based tools for assessing the impact of virus evolution on public health, diagnostics, and vaccines

Expertise for vaccine design

Experimental biosciences

Biosciences at LANL comprise a diverse group of experimentalists and computer scientists that developed science and technology to understand and reduce the threat of COVID-19.



Testing

SARS-COV-2 DATA

Accomplished one day turnaround of results using qPCR protocol with nasopharyngeal swabs

Detected asymptomatic positives and confirmed presumptives

Supported quarantine, contact tracing, work travel, and return-to-work policy

Sequenced and analyzed regional positive COVID-19 samples to identify variants

Tracked variants locally and globally

Regulatory support

IMPACTED MILLIONS OF TESTS

Identified and assessed PCR test kit contamination

Developed antigen test kit evaluations

Optimized viral transport media and protocol assessments

Enhanced clinical sample stability assessments

Systematized sample pooling strategies and experiments

Molecular design

FOR DIAGNOSTICS, VACCINES, AND THERAPEUTICS

Inhibited viral-host interactions through predictive molecular synthesis

Developed high affinity SARS-CoV-2 targeting antibodies

Collaborated with other national labs to identify small molecules for therapeutic and in-vitro testing

Impact

1,000 tests per week capacity

performed by CLIA-certified laboratory

Millions

of tests impacted by LANL support of regulatory organizations

Tens of thousands

of tests performed for LANL staff

Over 80 compounds

for diagnostic, vaccine, and therapeutic leads developed and *de novo* synthesized

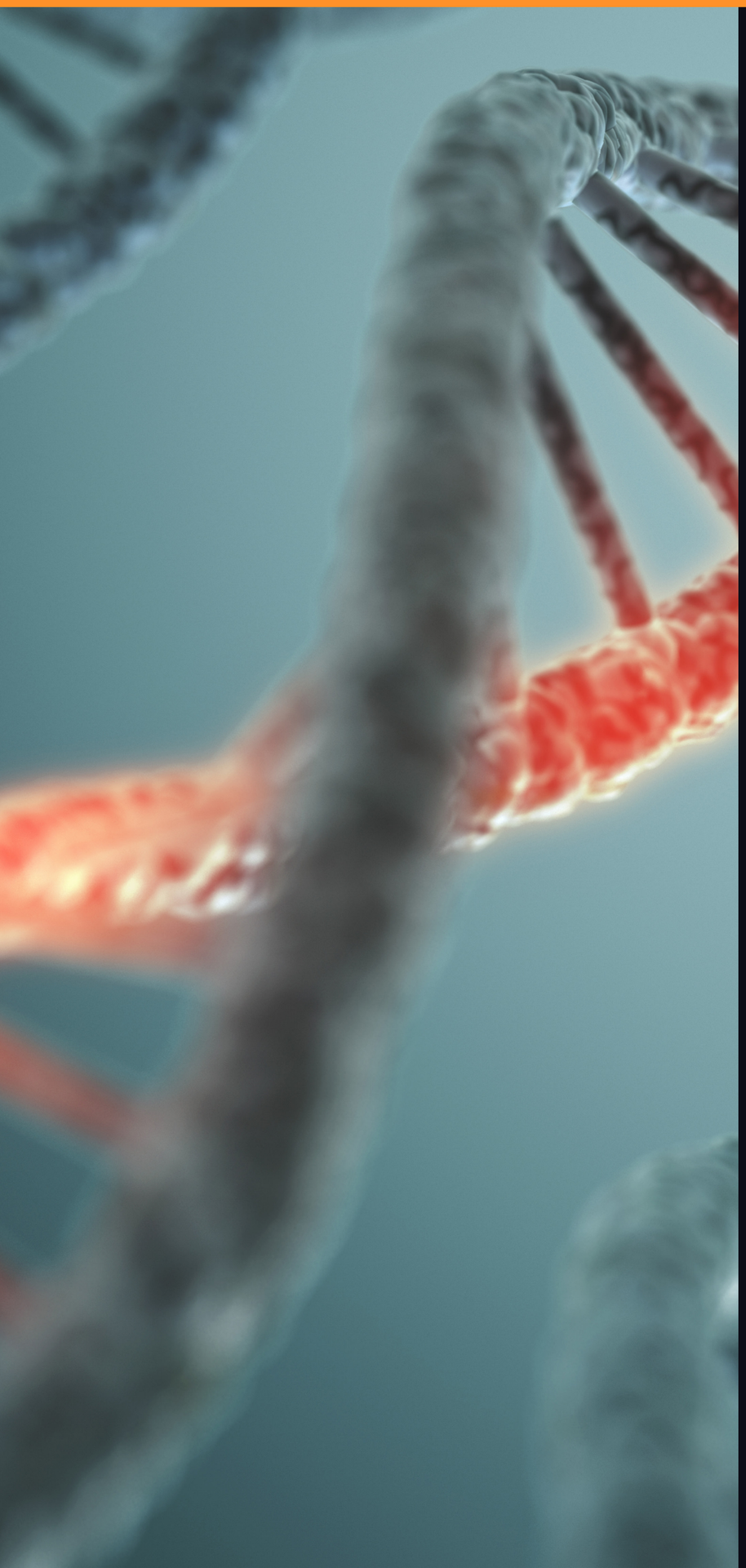
Vigorous COVID-19 biosurveillance

Performed by regional collaborative network among research communities

LANL TEAM

Elizabeth Hong-Geller, Samantha Adikari, Emily Alipio, Marc Alvarez, Elizabeth Anaya, Patrick Chain, Karen Davenport, Alina Deshpande, Armand Dichosa, Jason Gans, Cheryl Gleasner, Jennifer Harris, Andrew Hatch, Attelia Hollander, Ramesh Jha, Antonietta Lillo, Ryszard Michalczyk, Hau Nguyen, Jurgen Schmidt, Nileena Velappan, Geoff Waldo, Robert Williams, and Ruilian Wu

For more information contact
Elizabeth Hong-Geller



Genomics and bioinformatics

Recognized as a leader in genomic sequencing and analysis for decades, LANL pooled its extensive infrastructure, considerable genomics research expertise, and novel bioinformatics development to rapidly analyze the novel coronavirus.

Analytics

SARS-COV-2 SEQUENCE DATA

Provided standardized sequence analysis for variant characterization and data submission protocols

Provided web-based, publicly-available genome analytics

Analyzed COVID-19 lineage-defining sequence mutations to identify variants

Created bioinformatics tools to assess diagnostic efficiency of PCR assays based on sequencing of viral variants over time

Biosurveillance

MONITORING POPULATIONS THROUGH WASTEWATER PIPELINES

Monitored wastewater at LANL, Los Alamos townsites, and beyond for SARS-CoV-2

Utilized wastewater as a proof of concept and established a process to accommodate other sample types

Demonstrated that wastewater testing monitors whole populations, not just individuals tested, and captures asymptomatic and presymptomatic cases

Established a genomic and bioinformatics resource

Impact

Developed easy-to-use website

for COVID-19 sequence analysis

Contributed to global and national

sequencing working groups (e.g., SPHERES, SIG, and ACTIV TRACE) for public health emergency response, epidemiology, surveillance, and international standards

Genomics-based biosurveillance pipeline

developed for future pandemics

Established workflows

for environmental surveillance and genomic detection of SARS-CoV-2 and other infectious agents in the population

LANL TEAM

Patrick Chain, Karen Davenport, Mark Flynn, Jason Gans, Bin Hu, Elais Player Jackson, Julia Kelliher, Po-E Li, Chien Chi Lo, Adan Myers y Gutierrez, Migun Shakya, Yan Xu

For more information contact
Alina Deshpande

Multi-scale modeling

LANL's integration of data science, algorithms, and diverse approaches to computing accelerated its capability in discovery-to-prediction of emerging COVID-19 variants.

Predicting impact

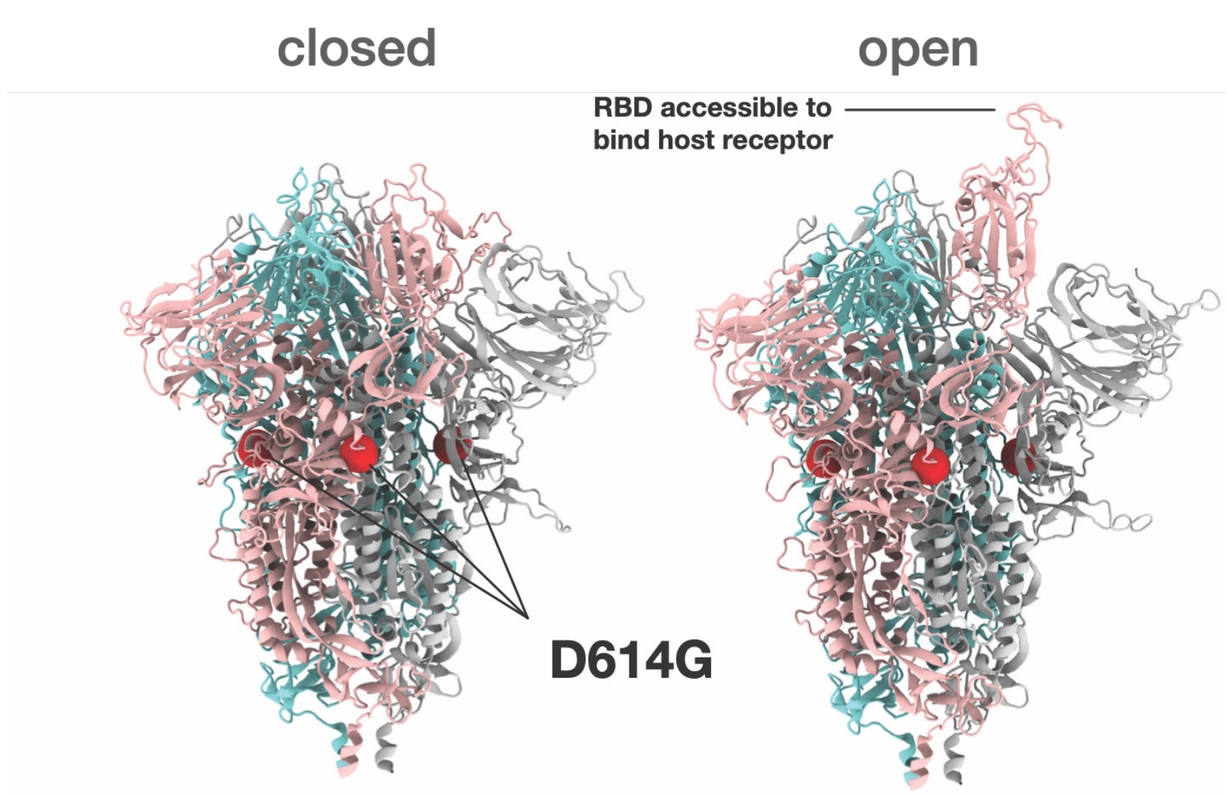
TRACKING THE D614G MUTATION

The LANL team began tracking persistent changes in the SARS-CoV-2 genome in February 2020, zeroing in on the spike protein (Spike) that mediates virus entry.

The LANL team identified a mutation in Spike, called D614G. LANL predicted and collaborators verified that the G-form:

- Replicates readily in the upper respiratory tract
- Is more infectious
- Is better neutralized by host antibodies

As D614G became the dominant circulating virus variant, the LANL prediction that it did not lead to increased hospitalizations was confirmed.



Innovating design

VACCINES AND THERAPEUTICS

LANL scientists utilized existing expertise developed for the ongoing HIV pandemic in their COVID-19 response.

Molecular dynamics simulations increased the understanding of virus-host interactions through comparisons of SARS-CoV and MERS-CoV with the new SARS-CoV-2.

Application of “mosaic” design increased the diversity of targets in a single drug, reducing the probability of vaccine breakthrough.

Impact

Developed bioinformatics

for viral evolution surveillance, informing vaccine design, public health, and diagnostics (cov.lanl.gov)

Modeled molecular dynamics

of virus mutations to assess mutation impact

Modeled temporal dynamics of pathogen resiliency

for room air filtration with virus deactivation capabilities

Evaluated modifications

by quantifying selection strengths of new and emerging variants

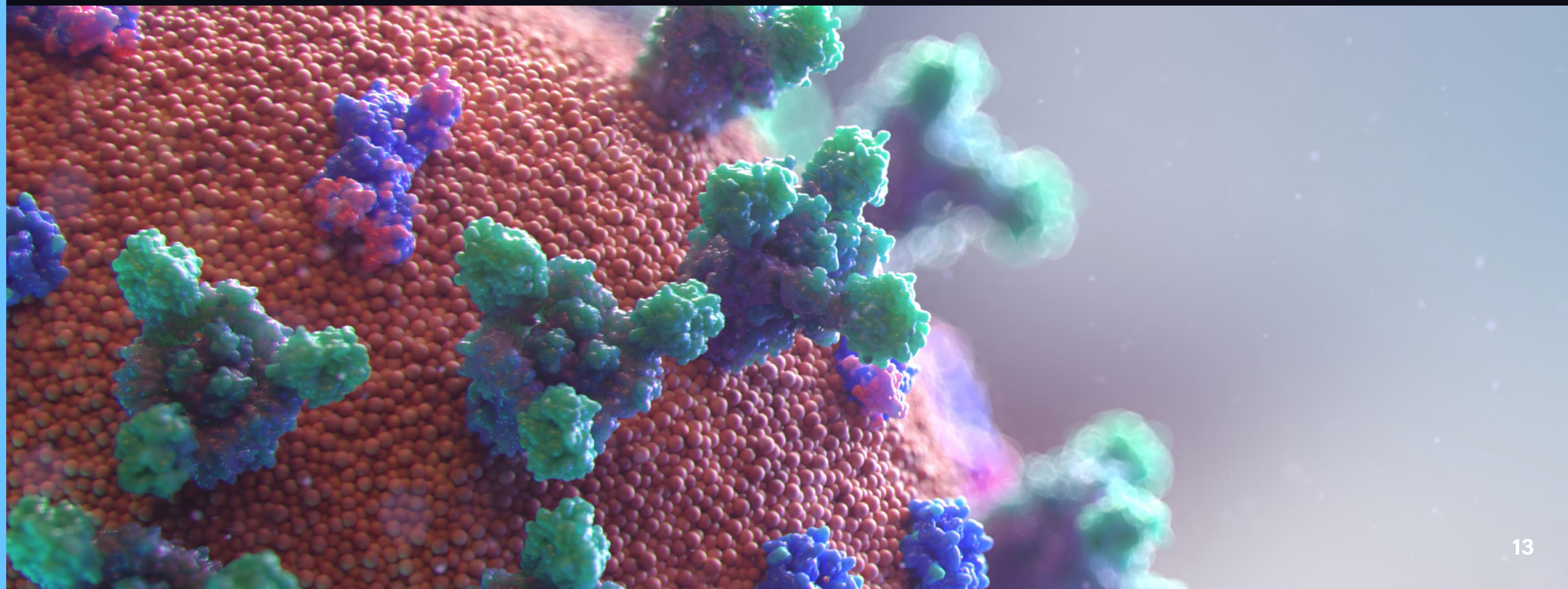
LANL TEAM

Werner Abfalterer, Srirupa Chakraborty, Will Fischer, Brian Foley, Gnana Gnanakaran, Emma Goldberg, Nick Hengartner, Ruian Ke, Bette Korber, Rachel Mansback, Kien Nguyen, Ethan Romero-Severson, James Theiler, Christiaan van Dorp, Kshitij Wagh, and Hyejin Yoon

For more information contact
Nick Hengartner

Epidemiological modeling and predictive analytics

LANL pivoted multidisciplinary areas of scientific and technical strength to support COVID-19 response with pandemic-customized simulations, predictions, data-driven insight, and information integrity management.



Modeling COVID-19

EFFORTS BEGAN MARCH 2020

Integrated publicly available data for situational awareness

Developed statistical tools to forecast hospital resource requirements

Developed statistical tools to identify new 'waves' of infection

Developed mechanistic understanding of transmissibility and fatality rates by age and gender

Integrated cell phone-based mobility measurements to predict transmission

Developed visual communication tools for decision makers

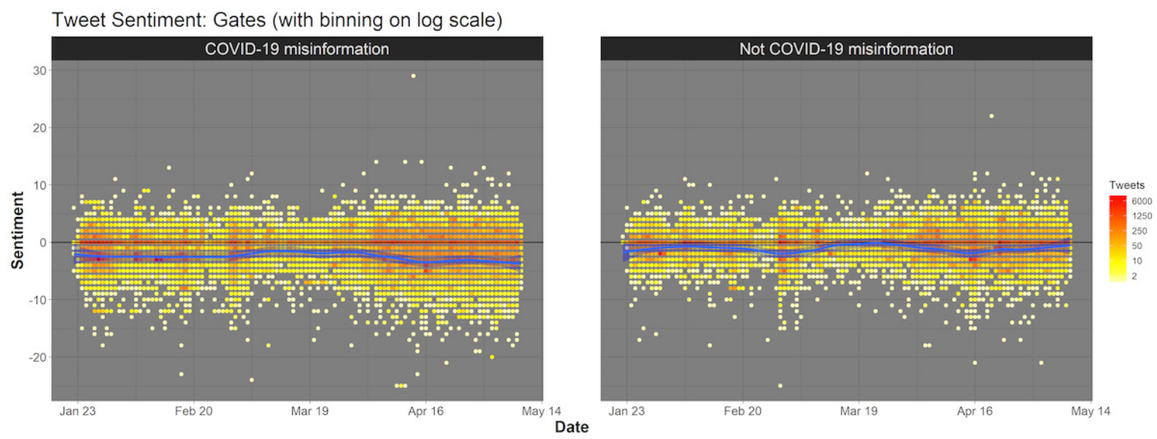
Developed detailed formats and presentations to improve decision support processes

Projected case counts and subsequent resource requirements for housing and behavioral health needs

Quantified the relationship between real-world testing and mitigation efforts

Created detailed predictions of school reopening and vaccine rollout strategies

Characterized relevance of studies on ventilation, mask usage, and contact tracing



Innovative response

DATA MINING TO MEASURE HUMAN BEHAVIOR

By combining machine learning and language processing, the team analyzed geospatial trends over time.

Impact

Linked science and policy

by providing early warning through the Global Disease Modeling and Forecasting Center team (covid19.bsvgateway.org)

Provided 6-week global forecasts

with weekly web updates via covid-19.bsvgateway.org

Assessed hundreds

of potential scenarios for national, regional, and Lab decision makers

Provided early estimates

of epidemic parameters by combining travel pattern data and epidemic growth models

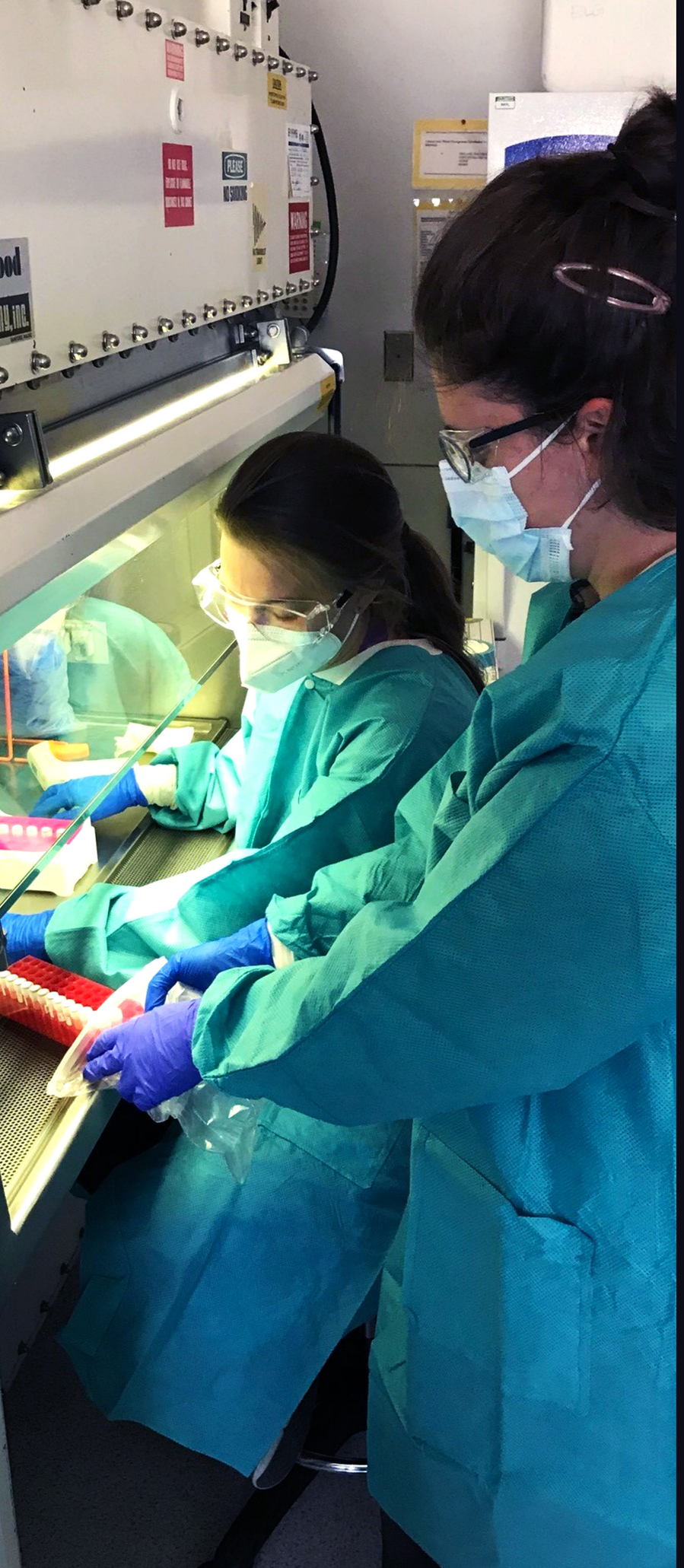
Evaluated the effectiveness of lockdowns

by combining human mobility patterns and excess mortality models

LANL TEAM

Leticia Cuellar, Ashlynn Daughton, Sara Del Valle, Jeanne Fair, Paul Fenimore, Nick Hengartner, Ruian Ke, Riya Mahesh, Carrie Manore, Kirsten McCabe, Ben McMahon, Judy Mourant, Nathaniel Ortega, David Osthus, Sara Pungitore, Ethan Romero-Severson, and Steven Sanche

For more information contact
Kirsten McCabe



Solution-driven integration

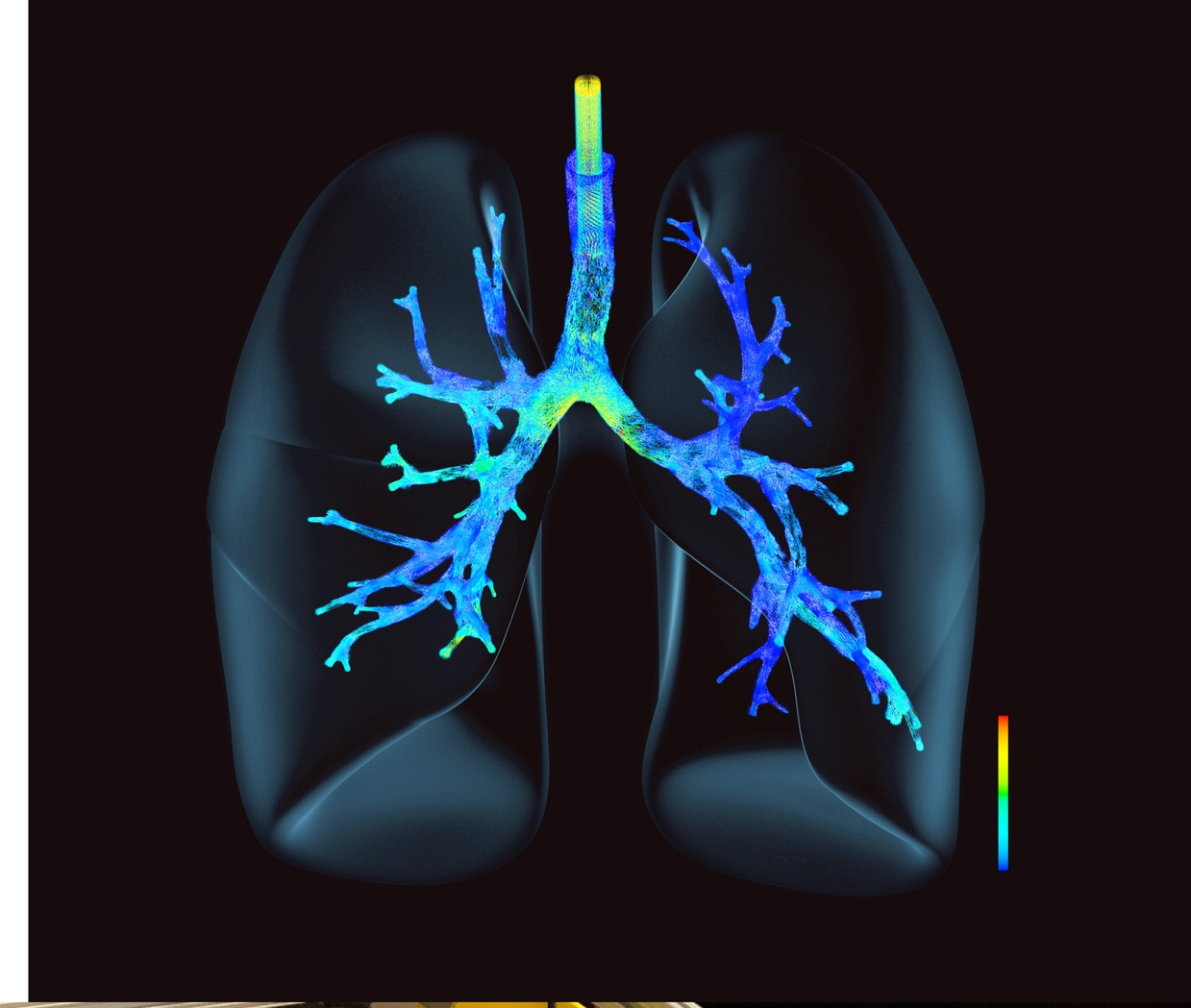
LANL applied its world leading multi-disciplinary approach to the COVID-19 pandemic response and created solutions through scientific and technical innovation that integrated across experiment, theory, modeling, and simulation.

Transforming IPV

IMPROVING PATIENT OUTCOMES

By merging numerical and experimental research with machine-learning, the LANL team formed predictive models of lung behavior under Intrapulmonary Percussive Ventilation (IPV) therapy.

Ventilation alone is not enough to save a patient. Combining IPV with traditional ventilation delivers aerosol medication in mucus-clogged passages and improves the odds for air flow and oxygen exchange.



Harnessing ultraviolet light

UV-C AIR DECONTAMINATION SYSTEM

A prototype UV-C (254nm) aerosol decontamination system was designed, built, and tested, delivering an intended flow rate of 1,000 to 1,700 cubic feet per minute and two logs (99%) deactivation of the SARS-CoV-2 virus.

Impact

Facilitated ventilator design

through lung modeling and device testing

Reduced risk of virus exposure

through additive manufacturing expertise and prototypes of urgently needed personal protective equipment (PPE)

Developed prototypes

for room air filtration with virus deactivation capabilities

Evaluated modifications

to commercial equipment for cold chain transport and storage of vaccine vials

LANL TEAM

John Bernardin, Beth Boardman, Andres Cortez, Jeremy Danielson, Nitin Daphalapurkar, Kumkum Ganguly, John Greenhall, Michael Ham, Jennifer Harris, Todd Jankowski, Gary Krugger, Matthew Lee, Leah Lujan, Therese Lujan, Adam Martinez, Marwan Mohamed, Arvind Mohan, Murray Moore, Robert Morgan, Cristian Pantea, Jeremy Payton, Martin Perraglio, Jacob Riglin, Alexander Rose, Denver Smith, Dusan Spernjak, Mike Steinzig, Toni Taylor, and Nina Weiss-Bernstein

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John Bernardin

Capability stewardship

LANL PILLARS SUPPORTING COVID-19 R&D

Throughout this document, we identified capabilities from across LANL that that were brought together to respond to the COVID-19 pandemic. The capabilities and assembly of multidisciplinary teams were key.

Because our capabilities often reside in multiple organizations, LANL utilizes an institution-wide “Pillar” framework to support capability stewardship. A Capability Pillar is a broad, multidisciplinary infrastructure of technical strength ($100 million or more of R&D activity) for the execution of programs where the Laboratory needs to maintain national and international leadership. Pillars facilitated a rapid pivot of LANL capabilities to help address the pandemic crisis.

Four of LANL’s six Capability Pillars enabled the Laboratory’s impactful response to the COVID-19 pandemic.

Complex Natural and Engineered Systems

Leveraged an on-going strategic goal for non-nuclear human-natural systems interactions; an initiative in national security life sciences; and approaches that integrate experiment, theory, and modeling.

Science of Signatures

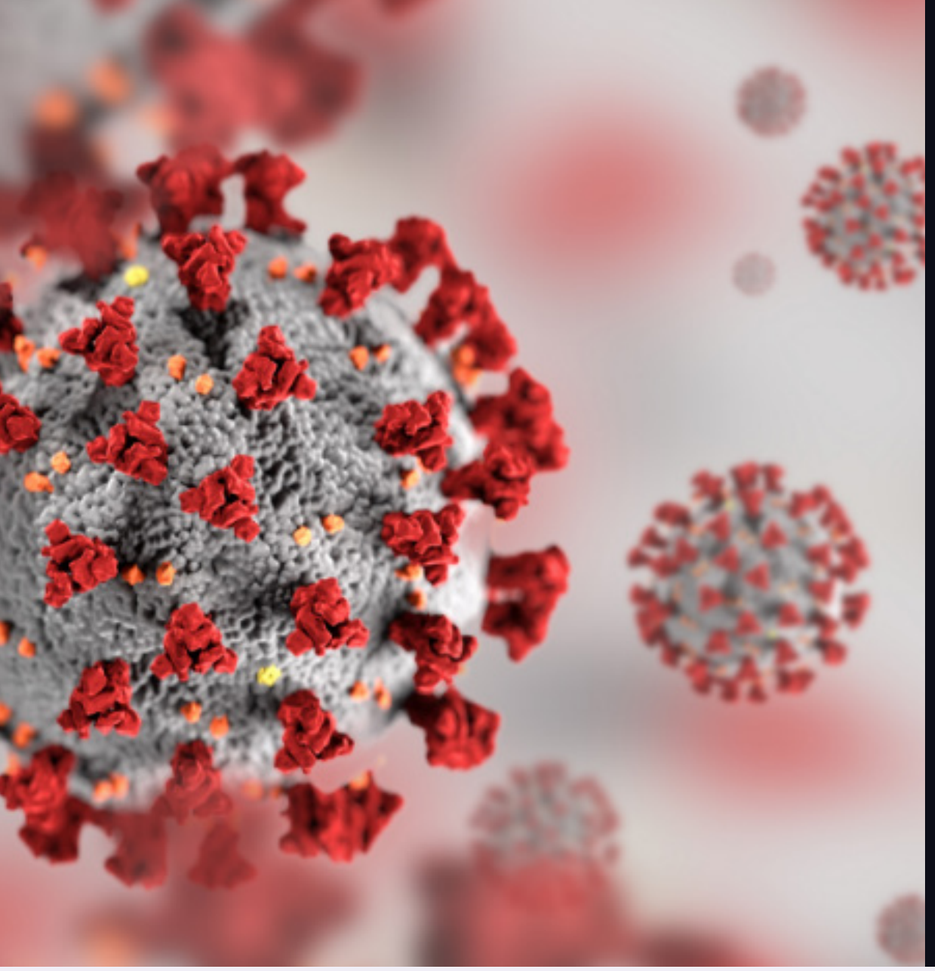
Leveraged an on-going strategic goal in natural and anthropogenic phenomena.

Integrating Information, Science, and Technology for Prediction

Leveraged on-going strategic goals in data science, computational methods, and computing platforms.

Materials for the Future

Leveraged materials design, characterization, and manufacturing



Looking forward

IMPROVING FUTURE RAPID RESPONSE

The DOE and its laboratories continue to provide the nation with multidisciplinary scientific and technical capabilities. One recommendation for improvement is to strengthen investments at DOE and at the labs to position them for rapid response to future pandemics and other national emergencies. This could be accomplished by using the National Virtual Biotechnology Laboratory approach for other challenges and by re-establishing an NNSA biological national security program.

Outstanding support

ORGANIZATIONS INTEGRAL TO COLLABORATIONS

Our COVID-19 R&D projects required efficient connections to outside organizations for information sharing and to ensure that LANL efforts were targeted to new solutions. This effort required agility and urgency for executing agreements, protecting intellectual property, and expediting work reviews and material transfers with outside partners.

Many supporting organizations at LANL provided staff or expedited action. LANL demonstrated a commitment to DOE fairness of opportunity requirements while enabling quick selection of collaboration partners, with a framework for rapid filing and non-exclusive licensing of any COVID-19 inventions.

Other agreements (non-disclosure, material transfer, CRADA, etc.) were expedited on a case-by-case basis with the partner best positioned for rapid engagement with LANL, especially during the early months when connections to New Mexico state government, private sector supply chains, and medical providers were needed for vital operations while supporting the exceptional needs of the communities around the Laboratory.

Capabilities leveraged

EXPERIMENTAL BIOSCIENCES

GENOMICS AND BIOINFORMATICS

MULTI-SCALE MODELING

EPIDEMIOLOGICAL MODELING AND PREDICTIVE ANALYTICS

SOLUTION-DRIVEN MULTI-DISCIPLINARY INTEGRATION

Laboratory team

VITAL CONTRIBUTORS TO PANDEMIC RESPONSE

Formation of the Special Office for COVID-19 (SOC-19) helped with communication, coordination, and prioritization. The SOC-19 minimized administrative burdens for LANL principal investigators and their teams.

The SOC-19 points of contact were:

Artificial Intelligence and Machine Learning:
Aric Hagberg

Computing:
Irene Qualters and Paul Dotson

Consumables:
Marc Witkowski and Matthew Lee

Decontamination and Personal Protective Equipment:
George Goff

Industry Outreach:
Duncan McBranch

Laboratory Testing:
Elizabeth Hong-Geller

Manufacturing:
Toni Taylor

Medical Countermeasures R&D:
Srinivas Iyer

Modeling:
Kirsten Taylor-Mccabe and Ben McMahon

NVBL and SOC-19:
Pat Fitch

Ventilators:
John Bernardin

Administrative support for SOC-19, NVBL, and this report was skillfully provided by Rhiana Knope.

A special Fiscal Year 2020 LANL LDRD call was executed within a few weeks in early 2020. Many thanks to the LDRD Office led by Bill Priedhorsky and Laura Stonehill and our lead for technical and programmatic reviews, Kirsten Taylor-Mccabe.

Research was supported by the DOE Office of Science through the National Virtual Biotechnology Laboratory, a consortium of DOE national laboratories focused on response to COVID-19, with funding provided by the Coronavirus CARES Act.

Publications, presentations, and patents

LANL COVID-19 R&D efforts were productive. Due to space limitations, please download the LA-UR-21-32130 document (PDF) below for a list of publications, presentations, and patents.

DOWNLOAD PDF

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LA-UR-22-20276