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Los Alamos NATIONAL LABORATORY

Oppenheimer Science and Energy Leadership Program (OSELP)

National Security Life Sciences at LANL

Elizabeth Hong-Geller
Division Leader, Bioscience Division

Oct. 4, 2022

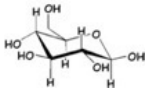
LANL contributions to biological science span decades

1945

Radiation health effect studies

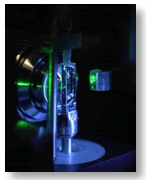
1970

LANL became an NIH Stable Isotope Resource



1980

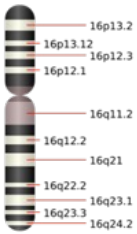
Flow cytometry invented. (1984: LANL-NIH Flow Cytometry Resource began).



National Laboratory Gene Library Project

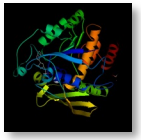
GenBank database created

1990



HGP mapping of Chromosome 16 & Joint Genome Institute founded

Human Genome Project begins



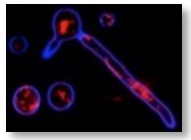
Tuberculosis Structural Genomics Consortium founded

2000

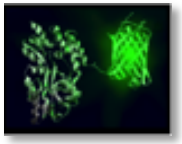
Established the SFAF meeting

2005

Finished 1000s of microbial genomes in JGI (many with biofuels & C cycling relevance)



Acoustic Flow Cytometer invented. R&D 100, spin-off acquired by Invitrogen



LANL-designed GFP and affinity reagents used worldwide

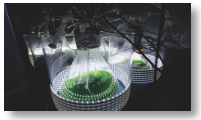
2010

Biofuels consortium founded

Science Focus Area (SFA) in Soil Metagenomics/Carbon Cycling established

Cooperative Threat Reduction programs for international genomics

2015



Collaboration in multiple consortia for biofuels & bioproducts

PuLMo R&D 100

Biosurveillance Gateway website launched

2020

Microbial Carbon Cycling SFA renewed & Bacterial-Fungal Interactions SFA begins

Retro Rx: R&D 100 Finalist & special recognition

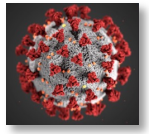
Los Alamos Medal for genomics contributions

EDGE bioinformatics R&D 100

Partnership in microbiome data collaborative

2021

SEDONA R&D 100



COVID-19 response honored by DOE Secretary

ADS Codex R&D 100

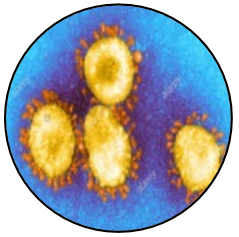
ERDE R&D 100 & Silver Award

National Security Life Sciences (NSLS) – Develop enduring capabilities to solve grand challenges in the biosciences

Bioenergy

Climate

Environment



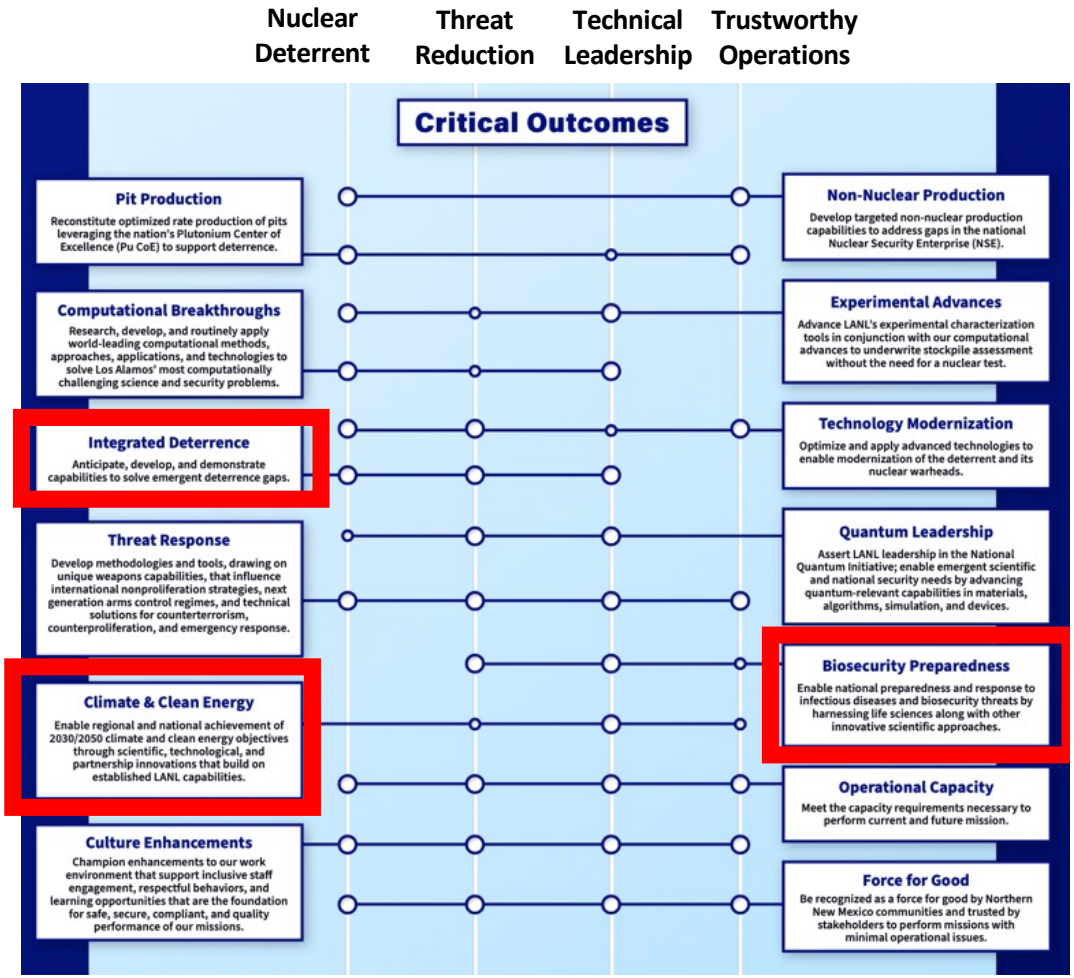
Infectious Disease

Bio/Chem Hazards

Regional Stability

LANL Lab Agenda maps our evolving mission

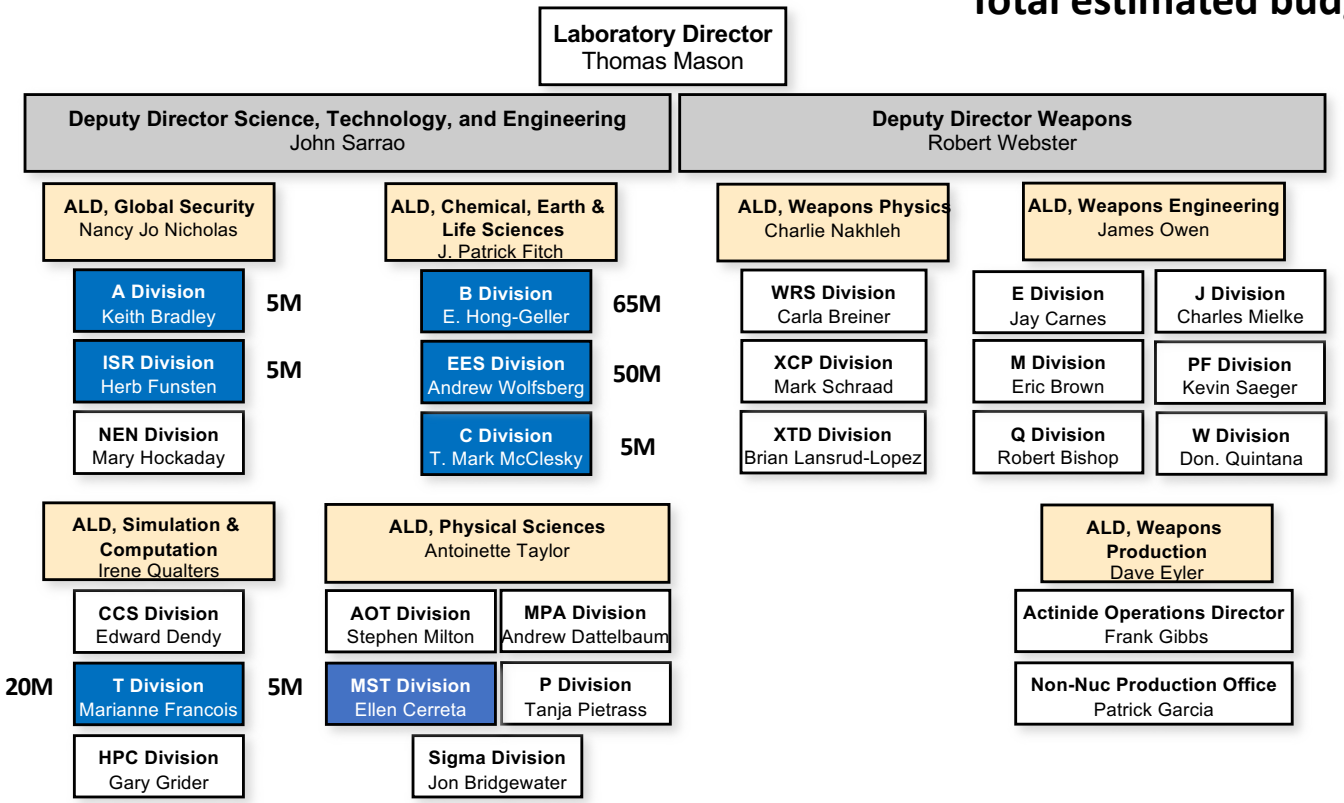
- **Four Strategic Objectives direct the Laboratory**
  - Nuclear deterrent, threat reduction, technical leadership, and trustworthy operations
- **The Agenda positions us to execute on 13 Critical Outcomes in 5–10 years**
- **Purpose is to integrate functions and maximize effectiveness across LANL**
  - Agenda provides a framework for the decision-making that occurs at all levels
- **Every employee has a role in executing this plan**



Los Alamos NATIONAL LABORATORY

Many Lab Divisions work in NSLS

Total estimated budget ~$150M



Sponsor base and LANL resources

Funding Profile

Science Program Offices
- Applied Energy – EERE, Fossil Energy
- Office of Science – BER

Global Security
- Intelligence and Emerging Threats – IC
- Nuclear Non-proliferation - DOS
- National Security and Defense – DTRA, DHS

Feynman Center for Innovation
- HHS – NIH
- Business Development, CRADAs

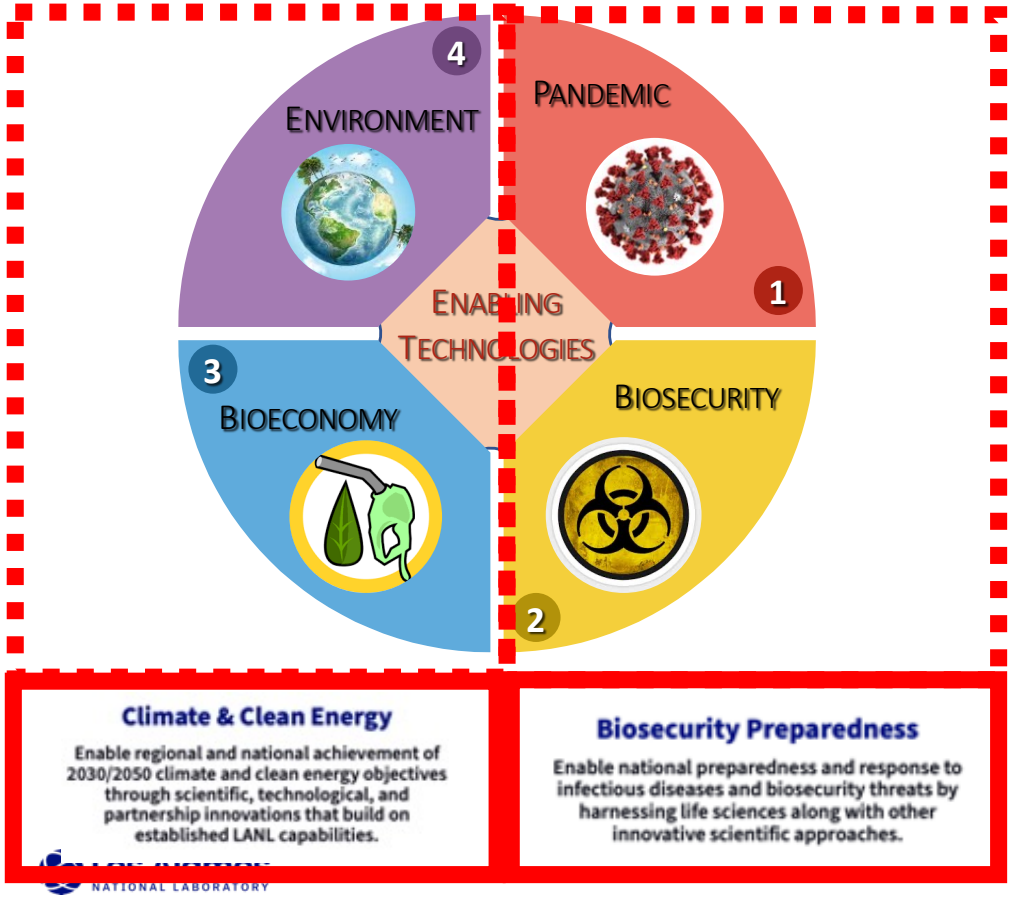
Laboratory Directed Research and Development (LDRD)

People ~300 staff
Scientists
Technologists
Post-docs
Students

Center for Space and Earth Sciences
Center for Non-linear Studies

Partnerships
National Labs –NNSA and Office of Science
Academia
Industry

The four National Security Life Sciences (NSLS) Grand Challenges



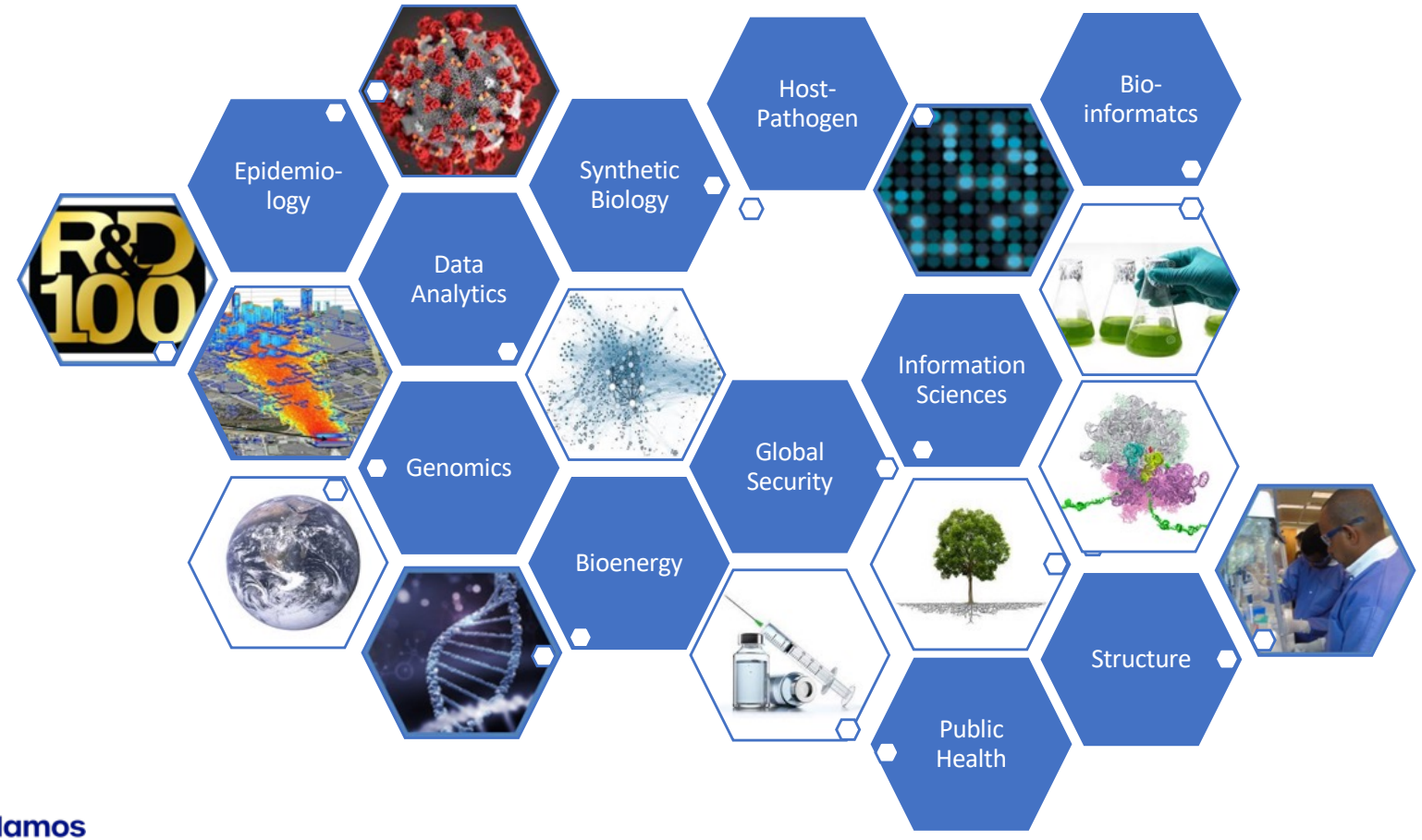
1 PREPARING FOR THE NEXT PANDEMIC
- EPIDEMIOLOGICAL MODELING
- GLOBAL BIOSURVEILLANCE
- DATA INTEGRATION AND RISK COMMUNICATION

2 BUILDING OUR BIOSECURITY FUTURE
- BIOTHREAT IMPACT TO HUMANS
- DIAGNOSTICS AND COUNTERMEASURES
- CLASSIFIED ANALYSES

3 GROWING A ROBUST BIOECONOMY
- RENEWABLE BIOENERGY AND BIOFUELS
- BIOMANUFACTURING
- ALGAL BIOTECHNOLOGY

4 CLIMATE CHANGE, ENVIRONMENT AND HUMAN HEALTH
- CLIMATE IMPACTS AND NATIONAL SECURITY
- ECOLOGICAL HEALTH SECURITY
- FOOD SECURITY

LANL capabilities that contribute to NSLS mission



❶ Preparing for the Next Pandemic

LANL COVID-19 R&D Response

DOE National Virtual Biotechnology Laboratory (NVBL) – one stop shop to bring all DOE National Labs capabilities to bear on COVID-19 response and mitigation

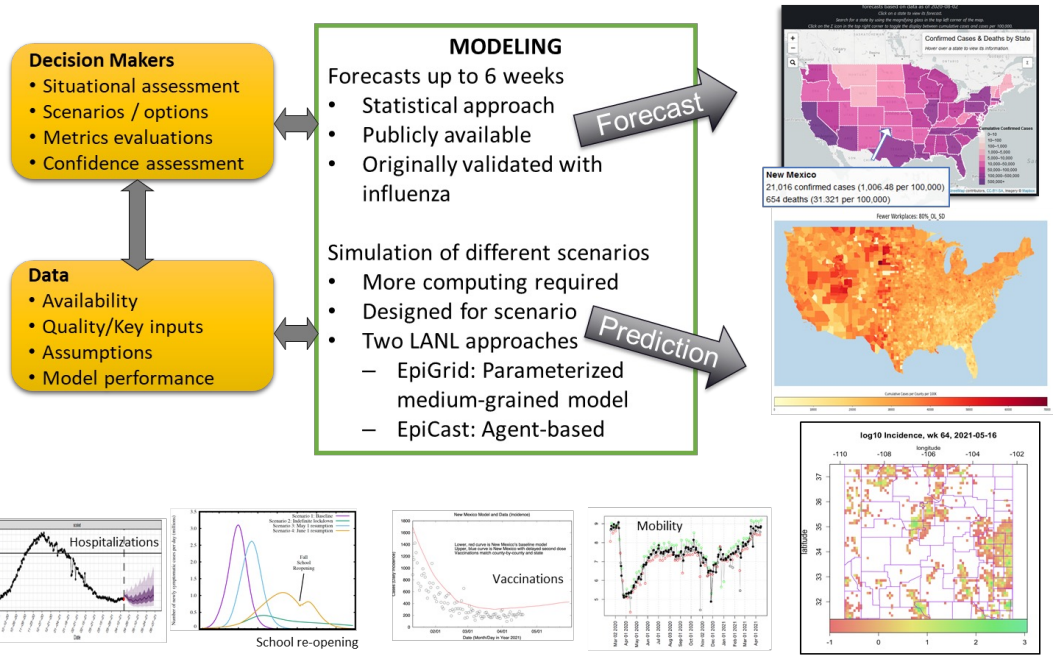
•LANL Special Office for COVID-19 R&D

•LDRD Rapid Response call ~$2.5M for 17 R&D projects

- Support to Operations feeds our R&D:
  - Epidemiological modeling - LANL, NM state, FEMA, HHS, NA-43, DoD
  - Laboratory testing - CLIA Lab, NVBL, National Task Force (CDC, DoD)
  - Manufacturing – ventilator design
  - Medical Countermeasures – therapeutics and countermeasure design and synthesis

GLOBAL DISEASE MODELING & FORECASTING CENTER

Multi-scale modeling to provide decision support: evaluate forecasts, potential actions, and specific scenarios.



Global biosurveillance pipeline

Samples

- Wastewater
- Clinical
- Air filters
- Zoonotic (wild, domestic)

Diagnostic lab

Sequencing lab

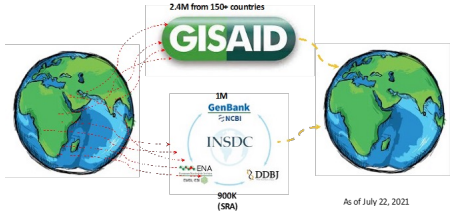
Genomes

Raw reads

NCBI

SRA ~3.1M*
Genbank ~4.2M*

9M*



Data Repositories

***As of 3/2/22**

Decision Support

World Health Organization

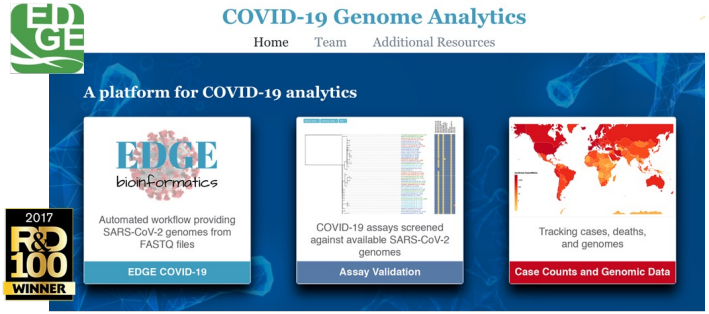
CDC Centers for Disease Control and Prevention

2M funding for developing SARS-CoV-2 sequence analysis pipelines to ensure high-quality data quality

- What organisms are co-occurring in the samples?
- What lineages are they (like SARS variants of concern)?
- Do they harbor mutations of interest or antibiotic resistance genes?

LDRD Laboratory Directed Research & Development

LDRD Director's Initiative:
Scalable digital biosurveillance to advance pandemic science and preparedness



https://covid19.edgebioinformatics.org/#/home

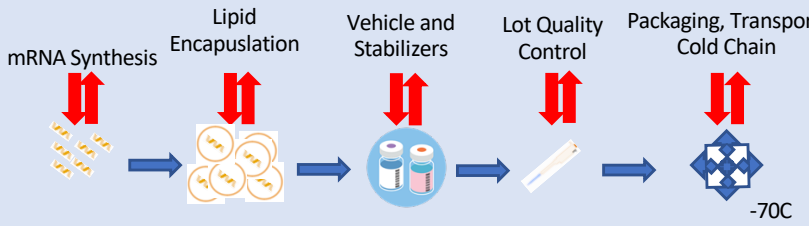
Analytic Capabilities

Los Alamos National Laboratory

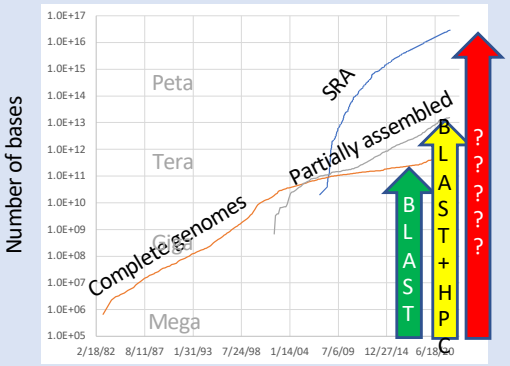
2 Building our Biosecurity Future

Digital biosecurity – a new threat at the intersection of biosecurity and cybersecurity

Security of vaccine manufacturing process



- Process is not linear, with hundreds of inputs and outputs
- Develop ontology of entire vaccine manufacturing process from inputs to outputs of each step
- Consequences of failure in each node



Safeguarding Integrity of Sequence Read Archive (SRA)

- Passive biosurveillance
- Convert individual SRA records into much smaller "thumbnail" sketches using Bloom filters

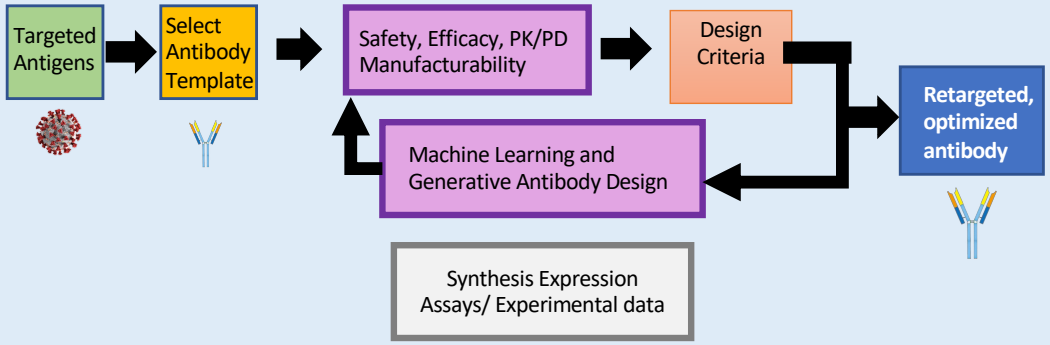
Goal is 100-fold size reduction (15 PB → 150 TB)

LDRD LABORATORY DIRECTED RESEARCH & DEVELOPMENT

Next generation countermeasure design

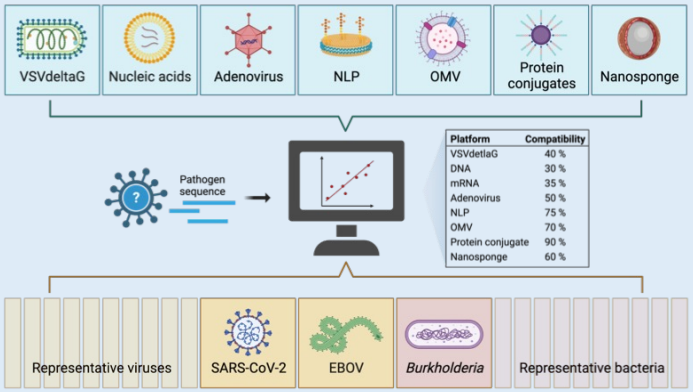
Generative Unconstrained Intelligent Drug Engineering (GUIDE)

Computationally "re-target" existing antibodies to address variants, related species, and engineered threats.



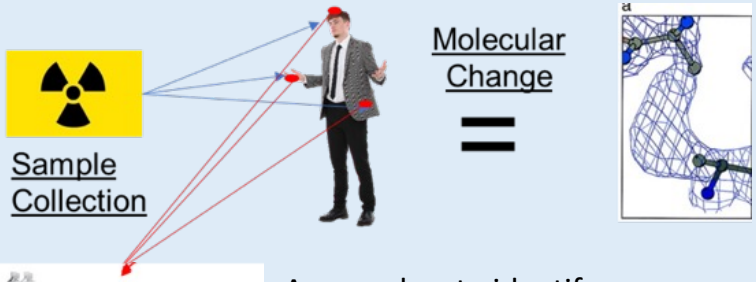
Rapid Assessment of Platform Technologies to Expedite Response (RAPTER)

Develop processes that predict the compatibility of vaccine platforms with a pathogen in order to rapidly combat any biological threat



Next-generation biodosimetry for radiation threats

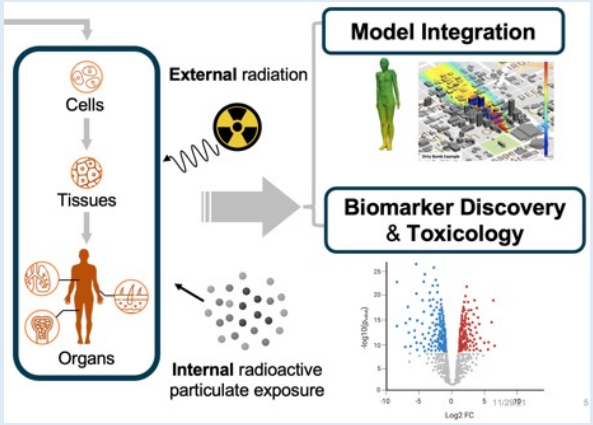
TEI-REX -Targeted Evaluation of Ionizing Radiation Exposure



Approaches to identify radiological activities and/or exposures in people and the environment

IARPA

HEROS - Human exposure of radiation using organ systems



Actionable strategies for measuring low-dose human radiation exposure and identifying real risks of accidents and incidents

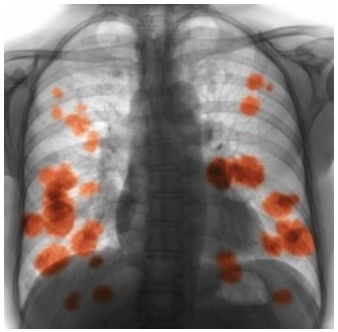
LDRD LABORATORY DIRECTED RESEARCH & DEVELOPMENT

Enabling technologies - Data analytics

Trinity supercomputer (>900,000 cores)

First ***billion*** atom simulation - entire gene locus GATA4

National Cancer Institute collaboration with DOE



Development of algorithms and informatics tools for scalable, and cost-effective national cancer surveillance program

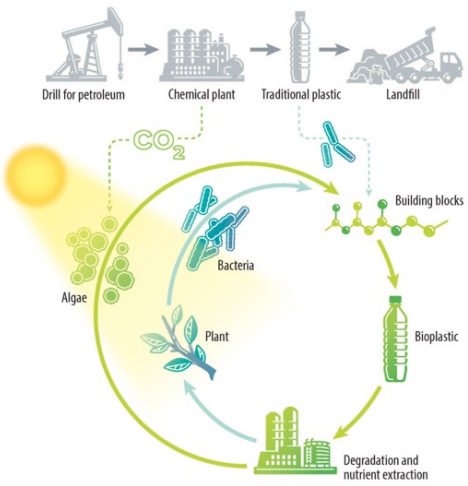
LDRD
LABORATORY DIRECTED RESEARCH & DEVELOPMENT

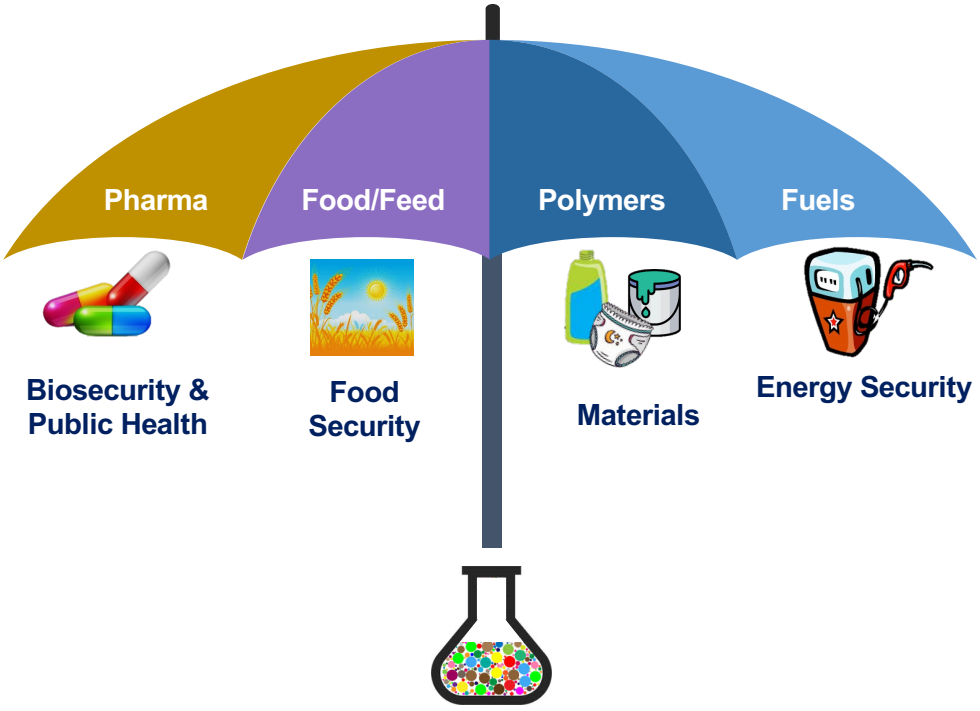
Analytics of health datasets from Veterans Affairs

A deeper understanding of disease and promise for better outcomes using data science

❸ Growing a Robust Bioeconomy

Moving towards a circular bioeconomy





Advanced Algae Systems: Algae as a bio-feedstock for fuels and bioproducts; molecular tools to improve growth and productivity

Conversion: Technologies for conversion into biofuels, bioproducts, and biopower

Advanced Development and Optimization: Integrating individual technologies into a system/process

Programs at LANL that advance the bioeconomy

BETO Bioenergy Consortia
Annual Operating Plan Program

bottle

Agile BioFoundry

DISCOVR

fcic FEEDSTOCK-CONVERSION INTERFACE CONSORTIUM

Co-Optimization of Fuels & Engines

ChemCatBio Chemical Catalysis for Bioenergy

BIOPROCESSING SEPARATIONS CONSORTIUM

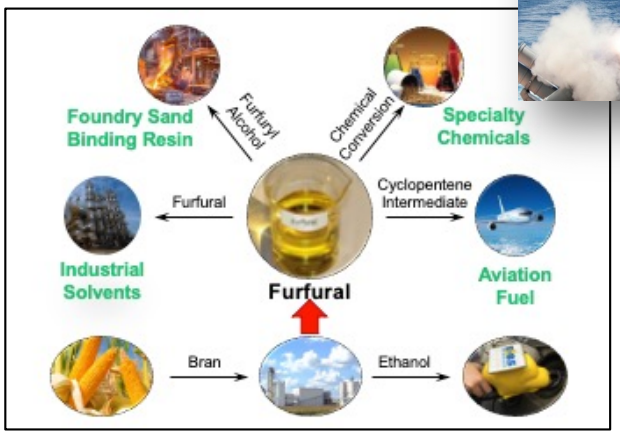
AOPs

U.S. DEPARTMENT OF ENERGY | Energy Efficiency & Renewable Energy

BIOENERGY TECHNOLOGIES OFFICE

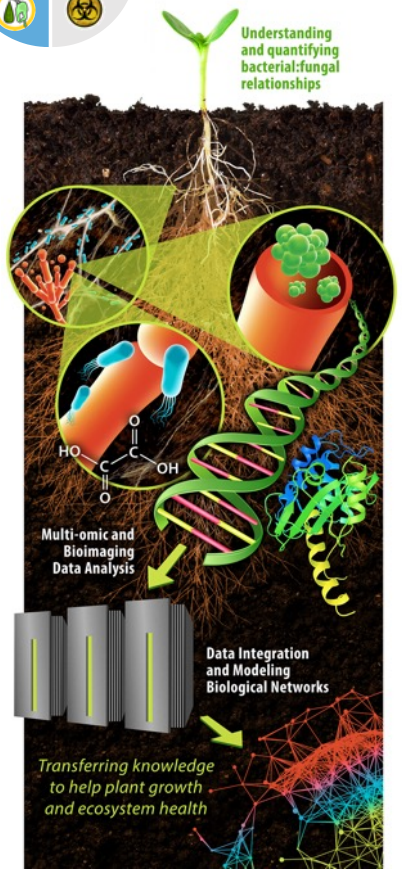
Optimizing algae growth for biofuels and bioproduct development

Next-gen jet fuel



Develop alternative route to produce JP-10 from biomass at or below current costs from petroleum feedstocks

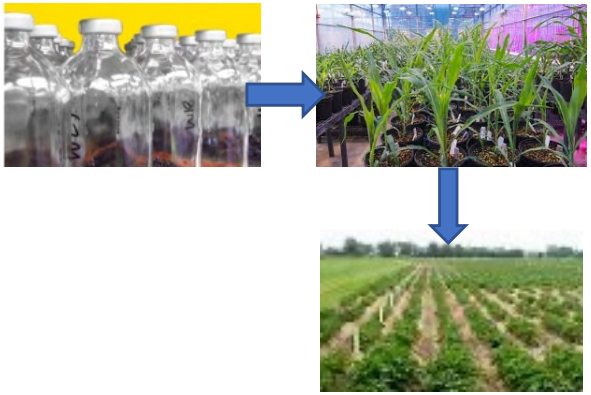
The role of the soil microbiome in food and climate



Two DOE Office of Science BER Science Focus Areas (SFAs)

- Soil Metagenomics and Microbial Carbon Cycling in Terrestrial Ecosystems
- Bacterial:Fungal Interactions and Their Role in Soil Functioning

Microcosm **Greenhouse**

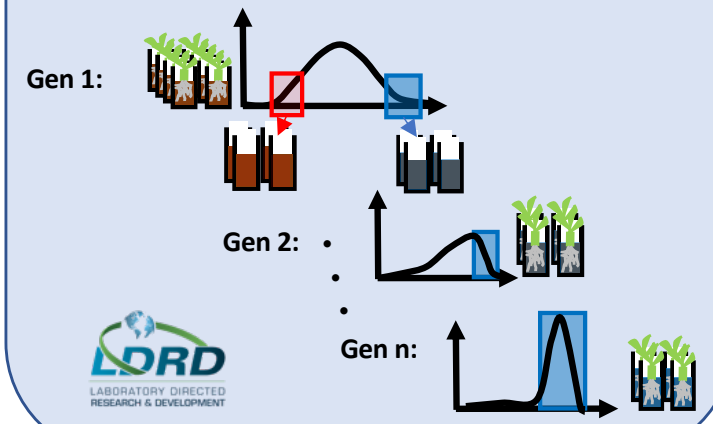


Fieldwork

nmdc National Microbiome Data Collaborative

An initiative to empower the research community to harness microbiome data exploration and discovery through a collaborative integrative data science ecosystem.

Food security:
Evolving the soil microbiome to enhance plant growth



LDRD LABORATORY DIRECTED RESEARCH & DEVELOPMENT

Los Alamos NATIONAL LABORATORY

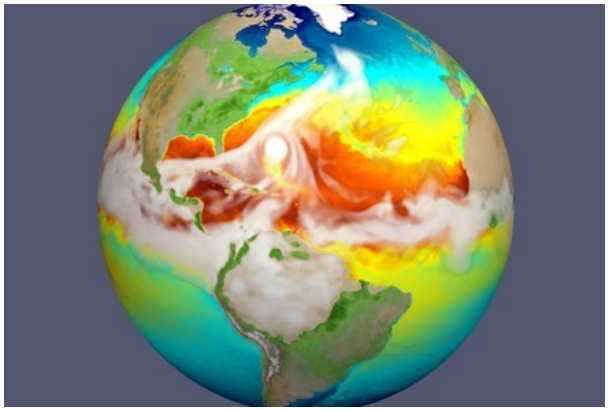
4 Climate change, environment and human health

Climate impacts and national security

MOSAiC Campaign - Multidisciplinary Drifting Observatory for the Study of Arctic Climate

E3SM: Energy Exascale Earth System Model

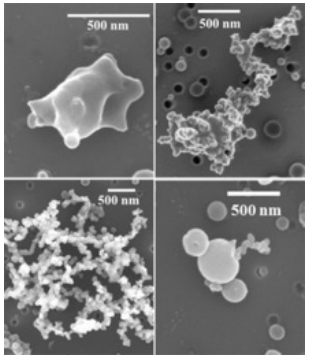
Computationally advanced coupled model, that bridges weather to climate temporal projections, at spatial scales relevant to national security needs.



This simulation from E3SM represents how sea surface temperature changes evolve as a hurricane moves across the Atlantic

Impacts of climate on fire and infectious disease

2011 Las Conchas fire in NM

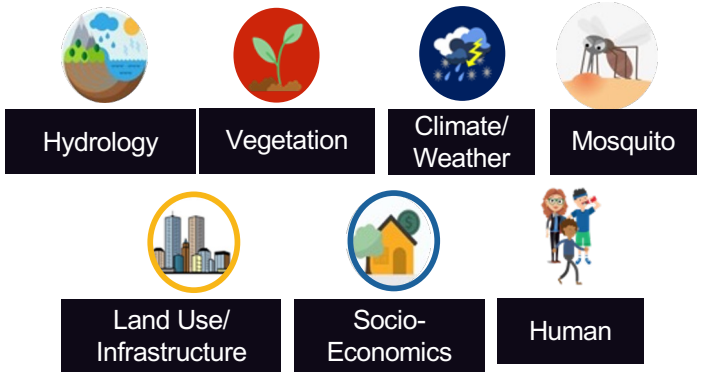


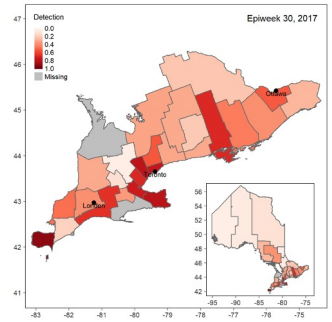
Spherical carbonaceous particles called tar balls were 10 times more abundant than soot.

This data can better inform current computer climate models.

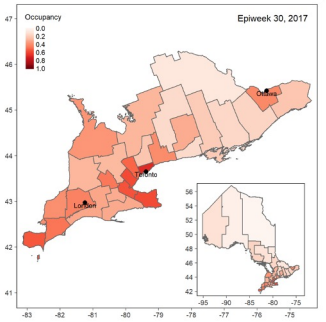
Climate-driven infectious disease modeling

Data-model fusion product across multiple political and grid spatial scales and through time (daily/weekly)





Probability of detection, week 30



Occupancy probability, week 30

West Nile virus detection probability in the Toronto area

Scientific challenges

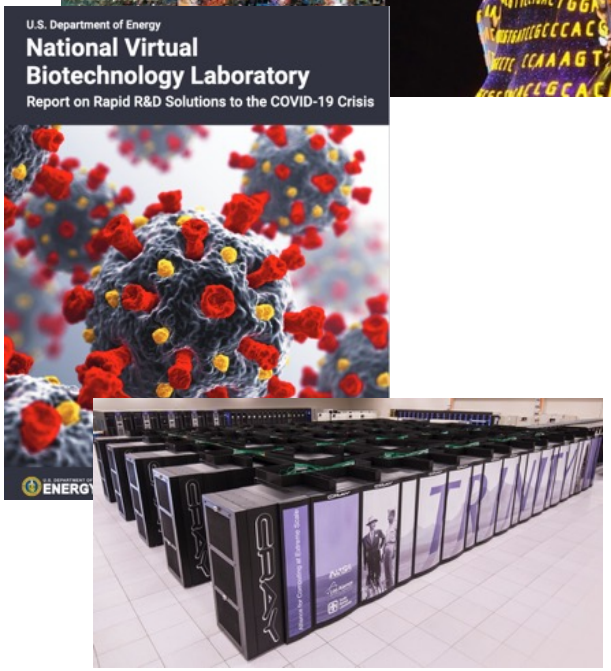
1) Making sense of 'big data' in complex systems –
- Volume – Social media, genomic sequences
- Variety - Multiscale data, heterogeneous data streams
- Velocity - Computational infrastructure, hardware architecture

2) Understanding co-evolution in complex adaptive systems-
Antibiotic resistance, climate change and human health, in vitro organ platforms – understanding the individual parts and co-evolving interdependencies

3) Translating science into decision support and informed policy
Performing the science that leads to signature development or pattern recognition for prediction of complex system behaviors – provide situational awareness to stakeholders

4) Establishing permanent frameworks for key enduring assets
Proposals for Centers for Global Forecasting, Exascale Biology, Pandemic Response, etc. to grow R&D capabilities and maintain a national resource for crisis preparedness and response, particularly between times of emergency

5) Bio is not well structured within the government. Multiple stove-piped "owners": Opportunities exist now to engage in the solution.



More fodder for discussion

- What are the big problems that National Labs should tackle in the biosciences?

- How do you perform effective decadal planning for bioscience research?

Emerging Focus Areas:

- Digital Biosecurity
- Operational & Decision Support
- Remote Sensing
- Microbiology based environmental “remediation”
- Improved Feedstock Conversion
- Flexible frameworks for regionally scaled earth system model predictions