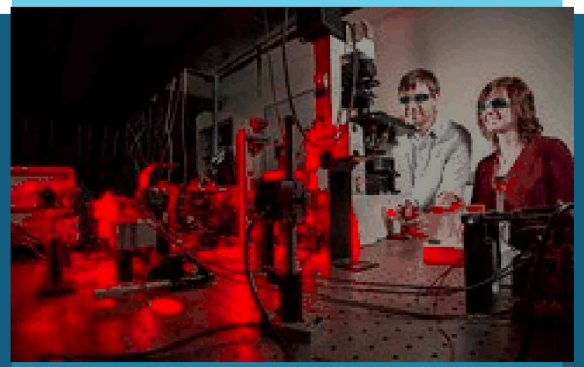
SAND2019-8809PE

Genome Security Academic Alliance Visit



PRESENTED BY

Jim Carney PhD, Manager 8631, Brooke Harmon PhD, 8623

Sandia National Laboratories is a multimission laboratory managed and operated by National Technology & Engineering Solutions of Sandia, LLC, a wholly owned subsidiary of Honeywell International Inc., for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-NA0003525.

The Department Of Energy Executes Its Missions Through Diverse National Labs

Office of Science Laboratories

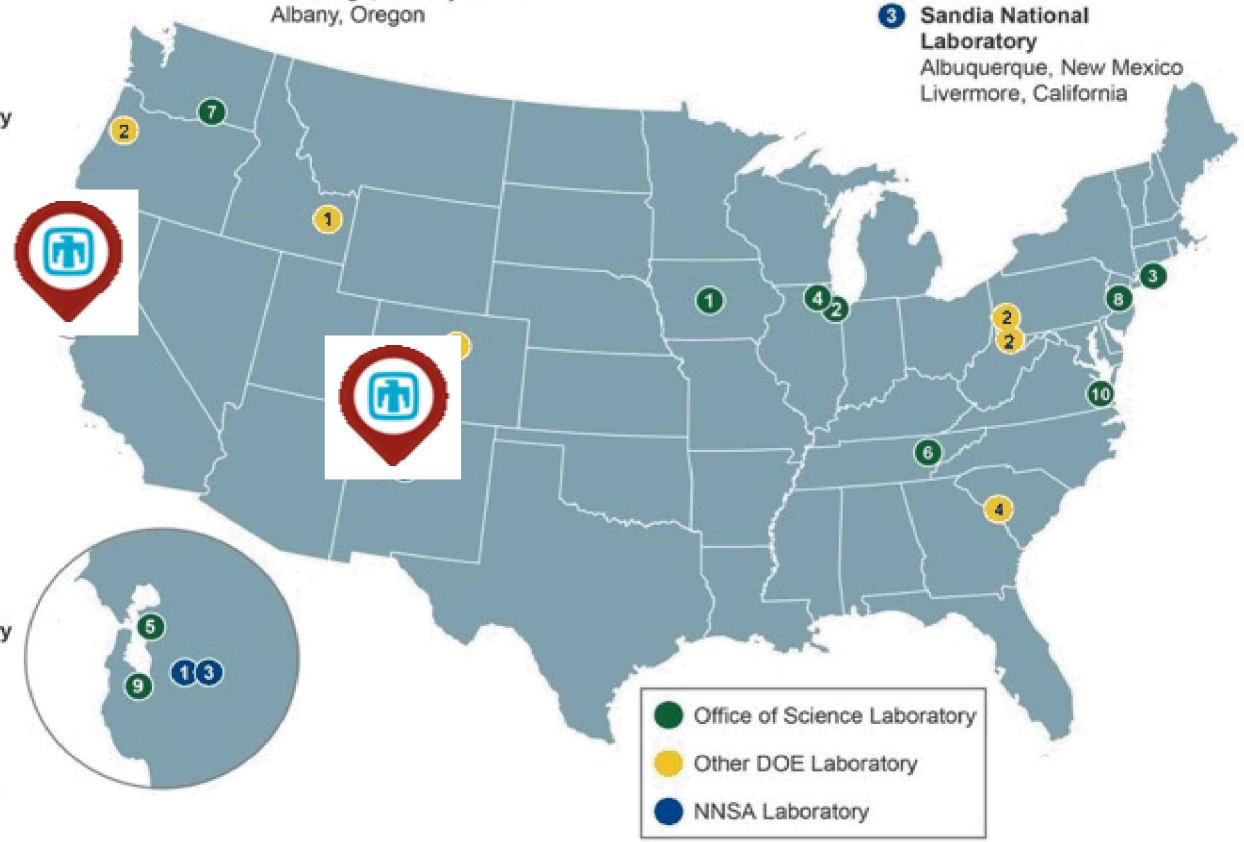
1. **Ames Laboratory**
   Ames, Iowa
2. **Argonne National Laboratory**
   Argonne, Illinois
3. **Brookhaven National Laboratory**
   Upton, New York
4. **Fermi National Accelerator Laboratory**
   Batavia, Illinois
5. **Lawrence Berkeley National Laboratory**
   Berkeley, California
6. **Oak Ridge National Laboratory**
   Oak Ridge, Tennessee
7. **Pacific Northwest National Laboratory**
   Richland, Washington
8. **Princeton Plasma Physics Laboratory**
   Princeton, New Jersey
9. **SLAC National Accelerator Laboratory**
   Menlo Park, California
10. **Thomas Jefferson National Accelerator Facility**
    Newport News, Virginia

Other DOE Laboratories

1. **Idaho National Laboratory**
   Idaho Falls, Idaho
2. **National Energy Technology Laboratory**
   Morgantown, West Virginia
   Pittsburgh, Pennsylvania
   Albany, Oregon
3. **National Renewable Energy Laboratory**
   Golden, Colorado
4. **Savannah River National Laboratory**
   Aiken, South Carolina

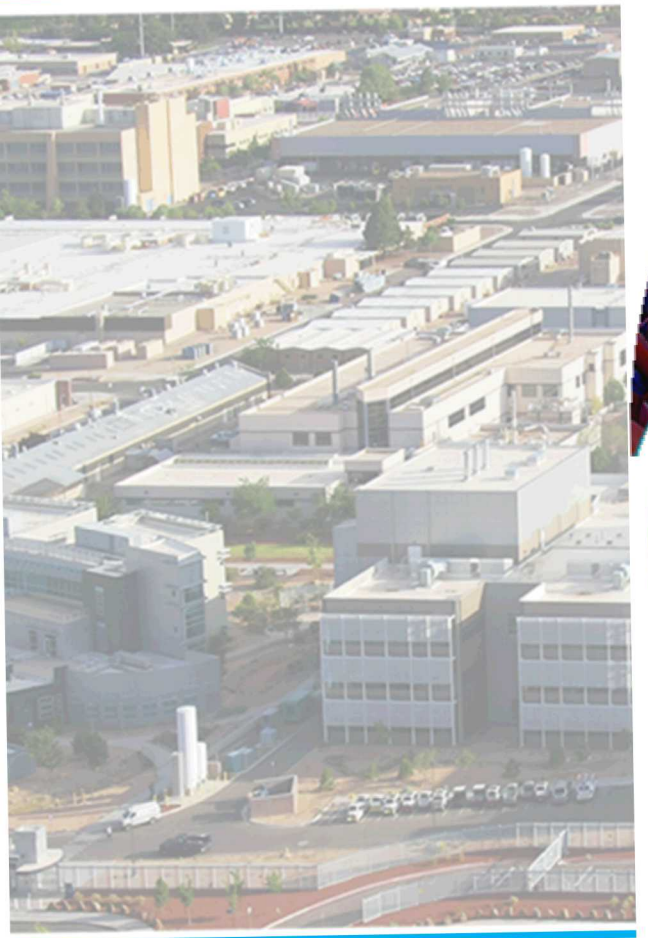
NNSA Laboratories

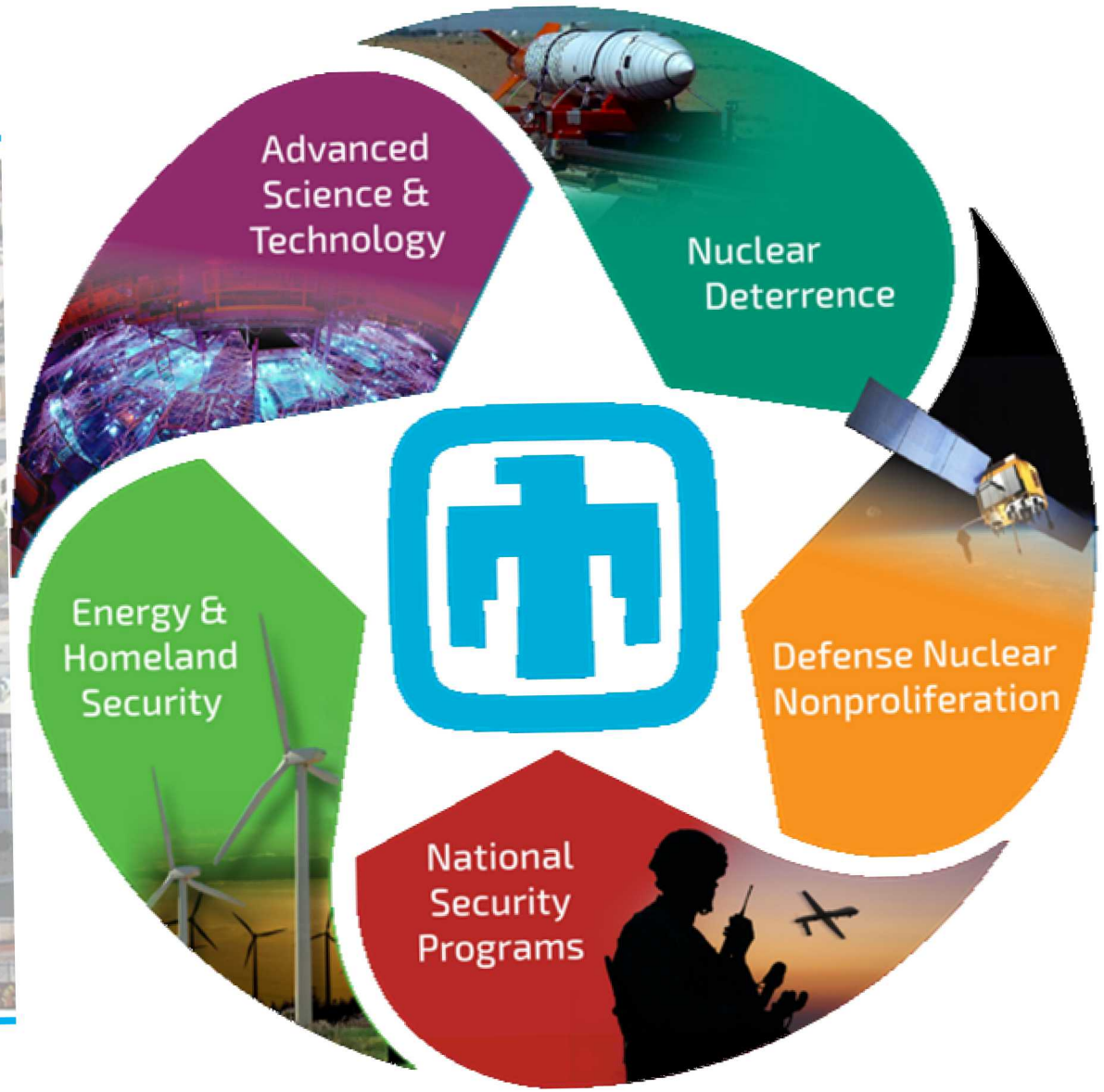
1. **Lawrence Livermore National Laboratory**
   Livermore, California
2. **Los Alamos National Laboratory**
   Los Alamos, New Mexico
3. **Sandia National Laboratory**
   Albuquerque, New Mexico
   Livermore, California

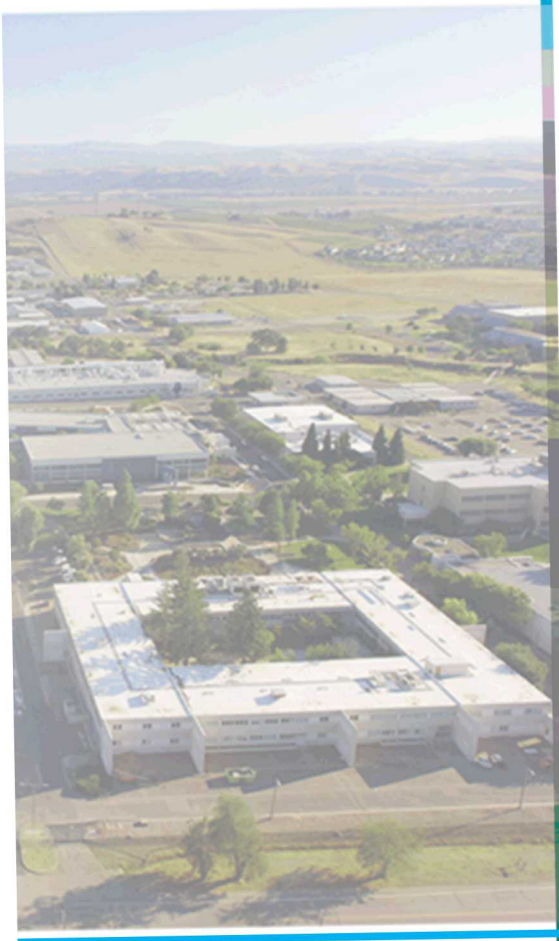


Three NNSA labs are dedicated to the science and technology of keeping the nation safe

Sandia Has Five Major Program Portfolios







Partnering Is A Strategic Imperative

Drivers for a strategic alliance:

- Rapid change in technology
- Complex national security challenges
- Shortage of STEM talent
- Limited R&D funding

Academic Alliance Objectives

Expand our impact on national security through strategic partnerships

Develop
STEM Talent

Accelerate
Technology
Deployment

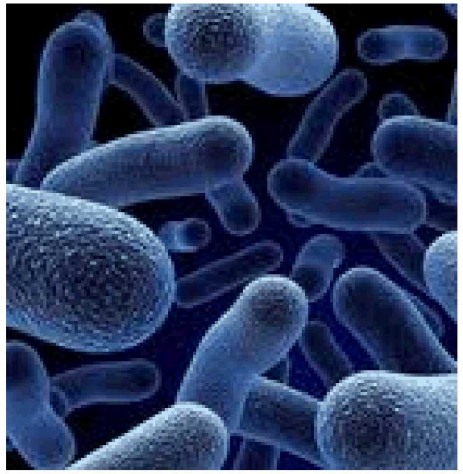
Solve Big
Problems

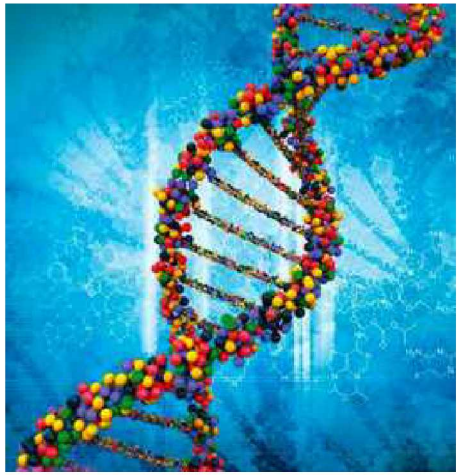
Georgia Tech · ILLINOIS · PURDUE UNIVERSITY · THE UNIVERSITY OF NEW MEXICO · TEXAS

Today's Objectives

- Foster new interactions and partnerships focused on the Genomic Security Strategic Initiative

- Create new relationships
- Stimulate research ideas
- Identify collaboration opportunities
- Clearly define next steps





Genomic Security

Gene editing is a **potential Weapons of Mass Destruction risk**

Technology surprise nature makes it ideal for national labs that work at the intersection of science and national security

Leverage strengths in biology, computing, materials, cybersecurity, non-proliferation and systems analysis

Thrust Areas

Threat Assessment

Detection and Surveillance

Mitigation and Defense

Develop R&D capability for **understanding & countering** the national security risks presented by technology **exploitation to manipulate genomes**.

Establish an ecosystem to **create a capability to counter the threat.**

Key Research Questions

Push "left" for more options to change the game.

Threat Assessment & Awareness	Surveillance & Detection	Mitigation and Defense
What are the fundamental properties of genomic systems that make them uniquely vulnerable to novel or unexpected threats? What novel or unrecognized threats are created by advances in genomic systems technologies?	What methods are most effective for monitoring and identification of ongoing exploitation or corruption of genomic systems?	What preventative technologies and strategies can we develop to instill integrity and resilience into genomic systems?
What are the indicators that a technology (or actor/institution), or convergence of technologies, can produce a threat, and how can the severity of threat be accurately assessed?	What fundamental science questions need to be answered to develop flexible platform technologies that enable detection, surveillance, and/or attribution of current and emerging threats to genomic systems?	What countermeasures can be developed to mitigate the consequences of unauthorized exploitation or unintended corruption of genomic systems?

- Genomic systems is the ecosystem required to develop a WMD threat comprised of the physical genome, genomic information, biological and computational tools, and the cyber-bio interface.
- Inclusive of threats to human health, food and agriculture, advanced industrial biotechnology applications, law enforcement, the environment, microbiomes and material

Genome Editing Life Cycle Roadmap

Objective

Prioritize, detect and mitigate current and near horizon risk and develop safeguards for the future

	Threat Awareness	Detection and Surveillance	Mitigation and Defense
	Actors and Accessibility: Who is likely to use it and who is enabled by changes in technology	**Monitor changes in supply chain, knowledge, resource availability & searches of threat enabling reagents**	**Discover adaptive methods to inhibit gene editing activity, block gene editing attempts, and reverse or counter effects**
	Discovery of signatures, patterns and markers of alarming technology	**Automatically track the life cycle of genome editing tools**	
	Horizon-scanning to predict future areas and/or actors of concern	**Identify Tech Surprise by Function**	**Develop resistant materials; harden potential targets**
Academia	**Apply vast knowledge gained through community**	**Research and develop new technologies**	**Oversee and Advice on performance, progress and problems**

Safer Genomic Data by Design Roadmap

Objective

Develop methods to acquire, use, and share genomic data safely and Secure DNA as a data storage medium

	Threat Awareness	Detection and Surveillance	Mitigation and Defense
	Identify what and how much genomic data is compromising	**Monitor national security relevant genomic database integrity**	**Control data access to limit release of compromising information**
	Identify indicators of malicious data access/manipulation	**Monitor for indicators identified by TA**	**Validate data integrity before critical use**
	Identify vulnerabilities for storing data in DNA	**Develop methods to monitor the integrity of DNA storage media**	**Implement encryption and transmission protocols**
Academia	**Apply vast knowledge gained through community**	**Research and develop new technologies**	**Oversee and Advice on performance, progress and problems**

Secure Cyber-Bio Interface Roadmap

Objective

Secure the genomic pipeline and the digital/wetware interface

Academia

Threat Awareness	Detection and Surveillance	Mitigation and Defense
Identify critical pipelines vulnerabilities and compromising information with high threat potential	**Develop/improve pipeline surveillance to enable incursion/anomaly detection**	**Design more secure genomic systems Develop methods to recover the integrity of genomic information**
Identify threats enabled by the genomic material/digital information interface	**Develop techniques to detect anomies, information that is out of control**	**Validate that the input to the process correlates with the output**
Apply vast knowledge gained through community	**Research and develop new technologies**	**Oversee and Advice on performance, progress and problems**

Some of Sandia's Current Partners in Genomic Security

UIUC

- Carl R Woese Institute for Genomic Biology
- Long standing collaboration
  - SNL member of CCGBM and Advisory board
- Key partner in IGB proposed theme-GENSEC
- Multiple AA projects

Early Wins w UIUC

- DHS – discovery of vulnerability in sequence infrastructure
- Funded joint projects
- Presentation at BioDefense World Summit
- Joint NIH Proposal Developed

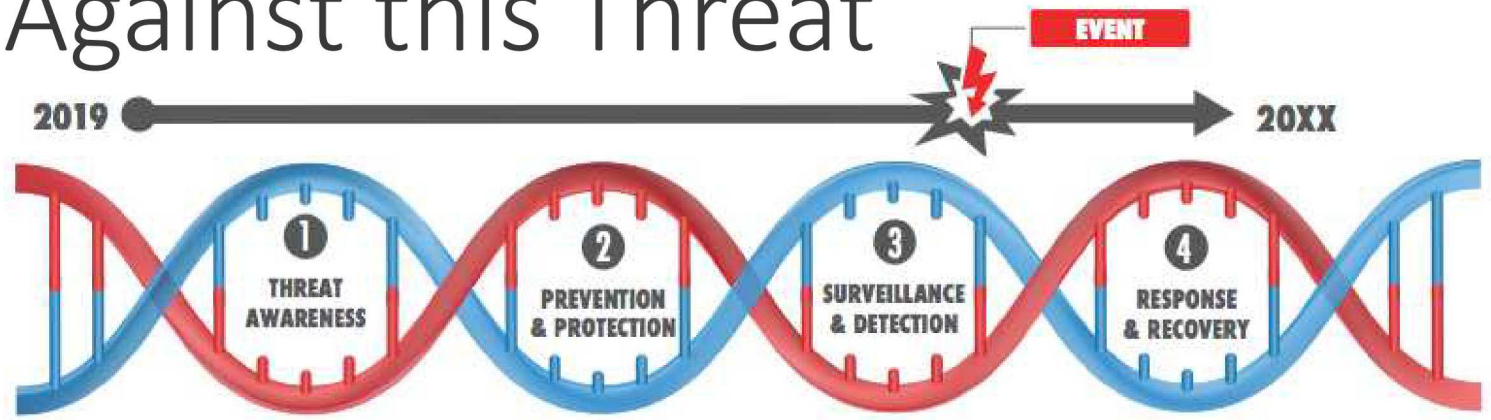
UCB

- Jennifer Doudna – NanoCRISPR Grand Challenge
- Long Standing Collaboration
- Campus Executive Collaborations
- JD and others

Early Wins w UC Berkeley

- Joint patents
- Funded joint project: DARPA SafeGenes with Jennifer Doudna, Luke Gilbert, and Jonathan Weismann
- Joint publications: Discovered RNA-targeting Cas9
- Joint proposals submitted

Our Nation Needs a Comprehensive Plan to Defend Against this Threat



Leading Federal Agencies

THREAT ASSESSMENT & AWARENESS

SURVEILLANCE & DETECTION

MITIGATION & DEFENSE

Sandia+ Academic Alliances

Mechanisms For Collaboration Internally

Funding mechanism used to foster collaborations and technical advances

Mission Campaigns
Provides an agile, strategic process to bridge ST&E and mission and move intentionally from idea to impact. *(5-7 years)*

Grand Challenges
Address major research challenges to develop bold solutions to important national security challenges. *(3 years)*

PI Driven Projects
Conduct applied research in areas directly relevant to current/anticipated missions to develop and demonstrate new capabilities and prototype new solutions. These include LDRD Proposals, Joint Publications, Filing Joint IP/Technical Advances, Commercialization Agreements. *(1-3 years)*

Exploratory Express
An agile mechanism to test and mature novel R&D ideas. *(<6 months)*

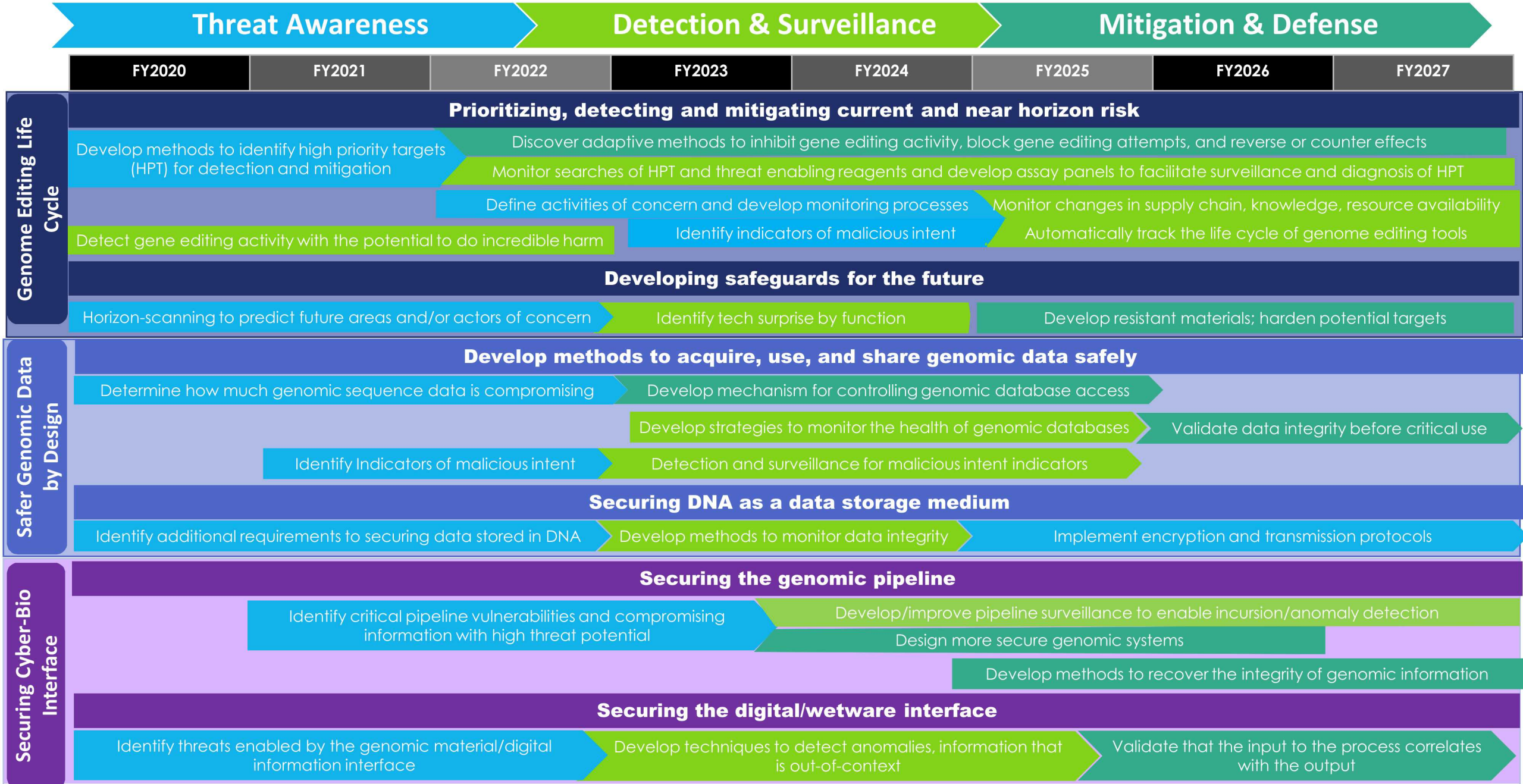
Portfolio of Internal Investments Building Capability for the Labs

FY	LDRD Project title	PI	IAT/ Partners
FY19-21	Detection of Cas9 Expression in Single, Living Mammalian Cells	Kim Butler 8635	Bioscience
FY19-21	Data Science for Detection of Genome Editing	Steve Verzi 8722	Bioscience
FY19-21	CERES: CRISPR Engineering for Rapid Enhancement of Strains	Anne Ruffing 8631	Bioscience
FY19-21	The Engineered Single Guide RNA Structure as a Biomarker for Gene-editing Reagent Exposure	Josh Podlevsky 8631	Bioscience
FY18-20	209190 Engineering Cells for Personalized Antimicrobial Therapy	Raga Krishnakumar 8623	Bioscience
FY16-18	Engineering 'Green' Algae: Reducing Metabolic Waste for High Biomass Productivity	Anne Ruffing 8631	Bioscience
FY17-19	Examination of Dual Use Concerns of Gene Editing	Jeri Timlin 8631	Bioscience/ UIUC/UC Berkeley
FY19-21	Utilizing a Single Particle Aerosol Mass Spectrometer (SPAMS) as a CBRNE Forensic Tool and Detector	Sean Kinahan 6633	DNN
FY18-19	Information-Theoretic Algorithms to Quantify Genomic Information for Genomic Security	Christina Ting 5854	DNN
FY19-20	Realistic Emulation of Automated Synthetic Biology Facilities to Prevent Risk of Unintended Manufacture	Corey Hudson 8623	DNN / UIUC
FY17-19	Controlling the Activity of Gene Editing Tools	Brooke Harmon 8623	EHS/ UC Berkeley
FY19	Cas9 Protein Post-Translational Modifications (PTMs): A Potential Biomarker of Gene-editing	Josh Podlevsky 8631	Exploratory Express
Grand Challenge FY16-18	NanoCRISPR: A Revolutionary Therapeutic Platform for Rapidly Countering Emerging and Genetically Enhanced Biological Threats	Darryl Sasaki 8621	GC/ Purdue/ UC Berkeley, UTA, Georgia Tech

Investment Area Team would enable tighter coordination to drive mission impact

Back-up Slides

Technical Roadmap and Phasing Plan DRAFT working on demonstrating time and dependencies



Vision Statement

The Genomic Security Strategic Initiative will develop a robust research and development capability for understanding and countering the national security risks presented by exploitation of advanced technology for the manipulation of genomes

External Sponsor Mechanisms

Agency	Areas of Interest
DTRA	Research areas: Counter WMD technologies, data integration & analysis, chemical/biological technologies, nuclear technologies
DARPA	Bio Tech Office - Foster, demonstrate, and transition breakthrough fundamental research, discoveries, and applications that integrate biology, engineering, computer science, mathematics, and the physical sciences Cyber Genome Program, Genome Protection Technologies
SoComm	Protection of the Warfighter – Ready, Mature, & Invest • Ready – optimize capabilities and processes to better position the force for new environments • Mature – advance capabilities to meet mid-term demands • Develop capabilities to track, monitor and counter WMD, incorporate into training programs • Invest – develop capabilities to meet challenges in future environments
ASPR & BARDA	ASPR - Leads the country in preparing for, responding to, and recovering from the adverse health effects of emergencies and disasters by supporting our communities ability to withstand adversity, strengthening our health and response systems, and enhancing national health security BARDA select goals: • Development pipeline replete with medical countermeasures and platforms to address unmet public health needs • Responsive and nimble programs and capabilities to address novel and emerging threats. • Advances in genetic engineering and synthetic biology- means for bioterrorists using virulence factors or drug resistance genes
IC	
DHS	Chem Bio Defense Division Priorities: • Threat awareness- inform effective prevention, preparedness and response/recovery actions to biological and chemical terrorism events • Surveillance, detection, diagnostics- real-time situational awareness to reduce agent spread to minimize consequences, develop tools for rapid identification and confirmation of a threat • Response and Recovery- enhance return to normalcy after a chemical/biological contamination
SC	Biological and environmental sciences focused on exploring genome enabled biology (discovering the drivers of climate change)
CDC	Securing global health and America's preparedness- stopping the spread of contagions, revitalizing public health infrastructure, and addressing bioterrorism threats and vector-borne diseases
NIH	NIH strategic vision - advance opportunities in biomedical research, foster innovation by setting NIH priorities, enhance scientific stewardship, excel as a federal science agency by managing for results

Genomic Security Will Require Interagency Participation And Coordination

IC- Advance national security, economic strength, and technological superiority

Office of Science- biological science focused on exploring genome enabled biology

DTRA- data and integration analysis and chemical/biological technologies

CWMD Office- Threat awareness, surveillance, response and recovery

Multiple congressional briefings

National Security Council & Office of Science & Technology Policy

SOCOM-Protection of the Warfighter: Ready, Mature, & Invest

Biological Weapon Council Engagement