

create
collaborate
communicate

NDIA Joint CBRN Conference & Exhibition

March 2012



“Investing in
transformational ideas,
innovative people, and
actionable technology
development for Chemical
Biological Defense
solutions”

DEFENSE THREAT REDUCTION AGENCY

JOINT SCIENCE AND TECHNOLOGY OFFICE

CHEMICAL AND BIOLOGICAL DEFENSE

Dr. Jason Paragas
Senior Scientist, DTRA RD-CB



The Threat is Real

- **Established Bioterrorism Programs**
 - Al-Qaeda: Kandahar, Afghanistan
 - Aum Shinrikyo: Tokyo, Japan
- **Call for BW expertise**
 - Al-Qaeda public call for scientists to develop and test biological weapons

Aum Shinrikyo Hq.



Anthrax Spraying, Tokyo

<http://www.cdc.gov/ncidod/EID/vol10no1/03-0238.htm>



Tarnak Farms,
Al Qaeda training camp,
Kandahar, Afghanistan

<http://www.globalsecurity.org/intell/library/imint/images/011031-D-6570C-003.jpg>

- Emerging infectious diseases create an unpredictable source of pathogens
- Dual Use Research of Concern
- Proliferation of unsafe bio-containment labs
- WMD Commission: Biological attack more likely than nuclear

Evolving Policies Drive Preparedness

HSPD-10, 2004 **Biodefense for the 21st Century**

“The essential pillars of our national biodefense program are: Threat Awareness, Prevention and Protection, Surveillance and Detection, and Response and Recovery”

HSPD-21, 2007 **Public Health and Medical Preparedness**

“The United States must develop a nationwide, robust, and integrated biosurveillance capability”

NSCBT / PPD-2, 2009 **National Strategy for Countering Biological Threats**

“Building Global Capacity for Disease Surveillance, Detection, Diagnosis, and Reporting”

Addressing the Challenge of Preparedness

Our Nation must have the nimble, flexible capacity to produce MCMs rapidly in the face of any attack or threat, known or unknown, including a novel, previously unrecognized, naturally occurring emerging infectious disease
The Public Health Emergency Medical Countermeasures Enterprise Review Aug 2010

The nation does not yet have adequate capability to meet fundamental expectations during a large-scale biological event. Bi-Partisan WMD Terrorism Center: Bio-Response Report Card October 2011

How Ready Are We For Bioterrorism?

NY Times 10/30/2011

Ten years after the anthrax letters—and after billions of dollars of investment in labs and research—debate continues over how much safer the country is
Science September 2011

“ If achieving national goals for developing MCMs is likened to climbing a mountain, then most of the mountain remains to be climbed”

WHERE ARE THE COUNTERMEASURES?
PROTECTING AMERICA'S HEALTH FROM CBRN THREATS March 2010 **A REPORT OF THE NATIONAL BIODEFENSE SCIENCE BOARD**

Pentagon rethinks bio-terror effort
Critics say US\$1.5-billion initiative has not delivered results
Nature News 477, 380-381 2011

This Requires Global Engagement

NATO—HEM, JCDC

Sweden—Oxime Cooperation

Czech Republic (IEA, PA)—MCM (Tularemia)

Poland—TaCBRD, CPWG

UK (IEA, TTCP)—DX, MCM, Detection, M&S, HM

Canada (TTCP)—DX, MCM, Detection, M&S, HM

Israel (IEA, PA)—M&S and MCM, CPWG

France—Biosurveillance

NAMRU-6—Advanced Pathogen
Detection and Discovery and Dx
RDECOM-Americas—Technical
cooperative opportunities within
South America
Chile—Biosurveillance and M&S
Brazil—Technical Cooperation
Developing

Sierra Leone—Geo-temporal
Information Awareness (GIA)

South Africa—Technical
Cooperation Developing

Nigeria—Test point of care Dx,
Biosurveillance, MCM

India (IEA, PA)—CB Defense S&T Workshops, Dx, MCM (Alpha Viruses), M&S, Bilateral
RD Cooperation Forum

Singapore (IEA, PA)—MCM (Burkholderia), M&S, Biosurveillance

Republic of Korea—Able Response Exercise, Comparative Genomics, M&S, Detection

Japan—CDWG, Decon, M&S (Threat Assessment), MCM

Thailand—Test point of care Dx, Biosurveillance, MCM

Australia (TTCP)—DX, MCM, Detection, M&S, HM

New Zealand (TTCP)—DX, MCM, Detection, M&S, HM

AFRIMS—Pathogen Discovery, Genomics

NAMRU-2—Biosurveillance, Dx

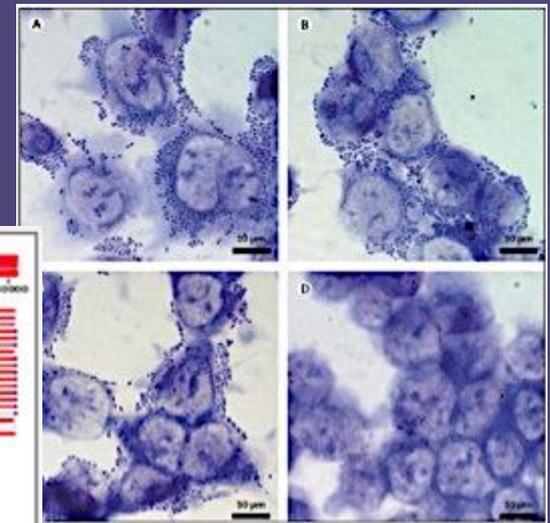
Return on Investment:

- Leverage/Harvest Technologies
- Access to Diseases of Interest
- Biosurveillance
- Building Partner Capacity

Rapid Response to Outbreaks: *E.coli* 0104:H4 Characterization Efforts

- To exercise real world challenge to rapidly explore deep genomic information for a emerging infectious threat agent using a combination of three 2nd-generation sequencing systems coupled with conventional finishing techniques.
- Correlate physical, clinical, and phenotypic observations to the improved genome using the suite of phenotypic assays available to a DoD/CDC lab consortium
- Link Laboratory Response Network (LRN) to Defense Lab Network (DLN)

Also part of an ongoing organic DoD process for enhancing therapeutic and diagnostic countermeasures



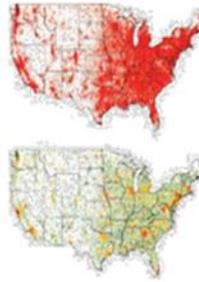
* Bielaszewska, et.al. Lancet. 2011.



Strategic Thrusts and Enablers

Disease Surveillance, Threat Detection and Point of Need Diagnostics

Broad-Spectrum Detection
Fieldable Dx Sequencing
Molecular Recognition
Host Response
Exposure Prediction
Functional Consequences



Threat Activity Sensing and Reporting

Point Detection
Agent Characterization
Mathematical Recognition
Transport & Dispersion
Risk-Based Hazard Plots
Agent Fate



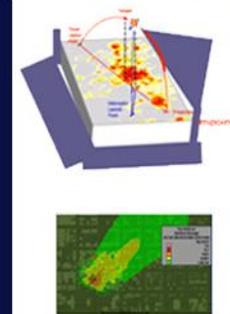
Adaptive Medical Countermeasures and Technologies

Vaccines
Immune Modulators
Bio-Prophylaxes
Bio-Therapeutics
Regulatory Sciences
Mfg Technologies



Rapid Response and Restoration Science and Technology

Individual Protection
Nanostructured Materials
Smart Materials
Simulation and Analysis
Decision Support
Decontamination



Novel Threat Research

Applied Math Tools

Multifunctional Materials

Flexible Design & Manufacturing

Systems Biology

Strategic Thrust: Disease Surveillance, Rapid Threat Detection, and Point of Need Diagnostics

AGENT/HOST TARGET IDENTIFICATION

Antibiotic Resistance Markers

Pre-symptomatic Biomarkers

Host Biomarkers

Rapid Pathogen ID

Bioinformatics

High Content Data Backbone

- Pathogen Sequences
- Host-Agent Dynamics Signatures
- Characterized Reagents

Diagnostic and Disease Targets

ENABLING CAPABILITIES

Sample Prep & Preserve

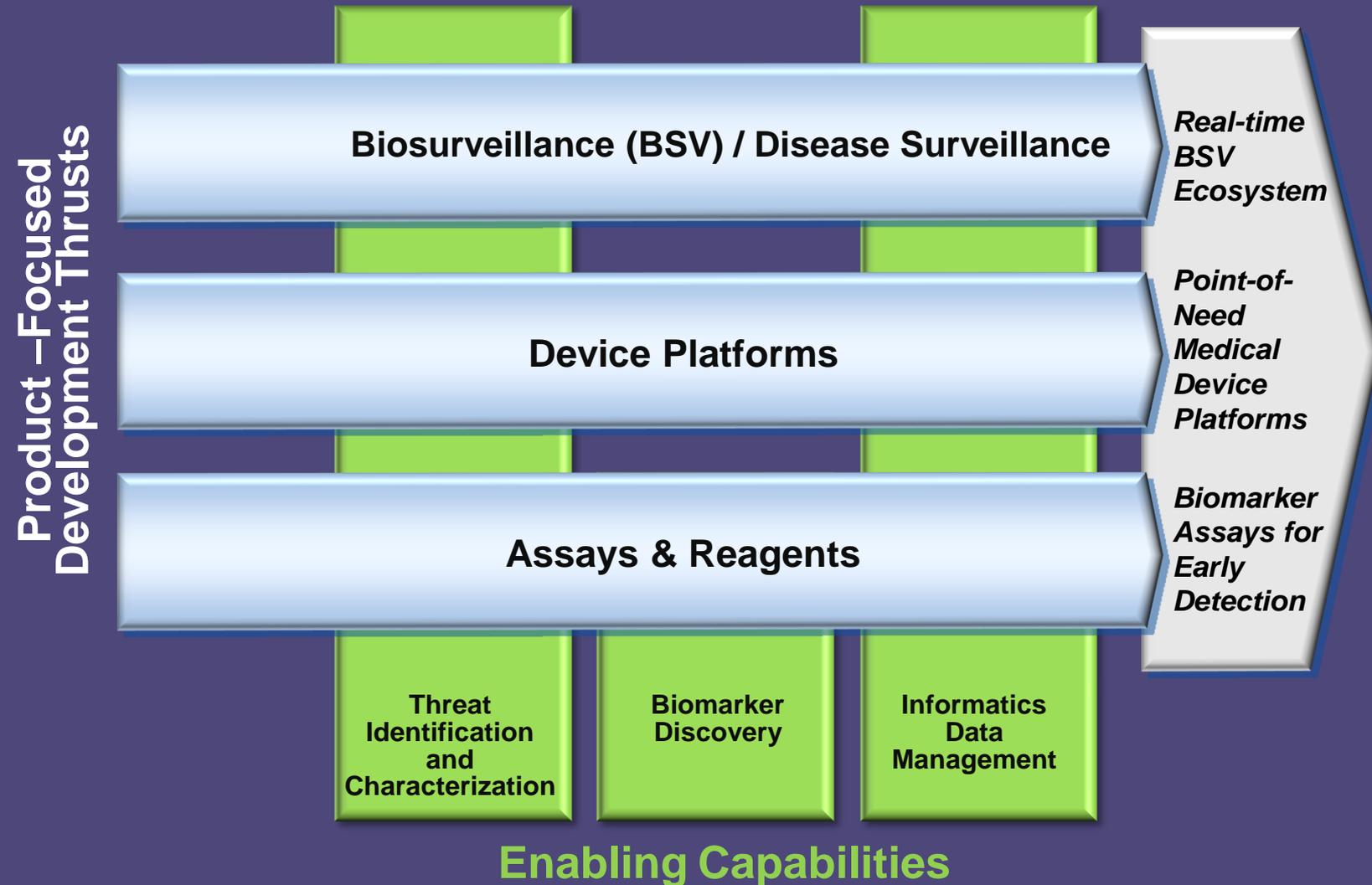
Platform Technologies

Engineering/Performance Drivers

Future Systems Development

- Enabled by informatics and device innovations
- Configurable for emerging threats

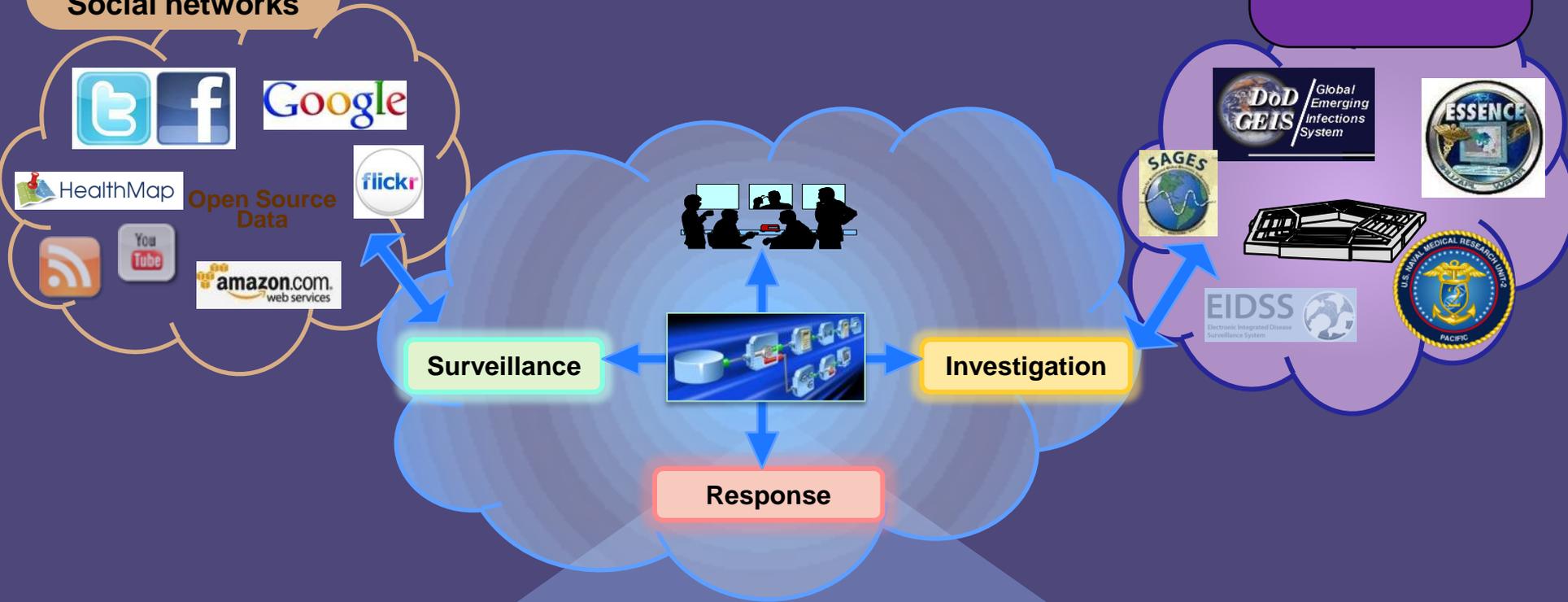
Delivering Diagnostic and Biosurveillance Solutions Across Three Key Areas



New Modalities for Surveillance, Investigation and Response

Public Cloud
citizen sensors,
presumptive
indicators,
Social networks

DoD Cloud
Sensors,
Confirmatory
diagnostics



Level 0 Diagnostics

Level 1 Diagnostics



Link Highly Distributed Affordable Point of Care Diagnostic Devices to Cloud Network

- Levels 0-1 provide rapid, in-field data capture to support biosurveillance and/or medical decision-making
- Common use assay panels, including biodefense-specific agents, can accept different panels congruent with end user needs
- FDA-cleared or on pathway for clearance
 - Used in open architecture format for non-FDA-cleared detection
 - Clinical use with FDA clearance
- Sample-to-Answer systems, CLIA-waived

Level 0*



HOME USE

- Akin to paper-based platform
- Lower plexity

Level 1

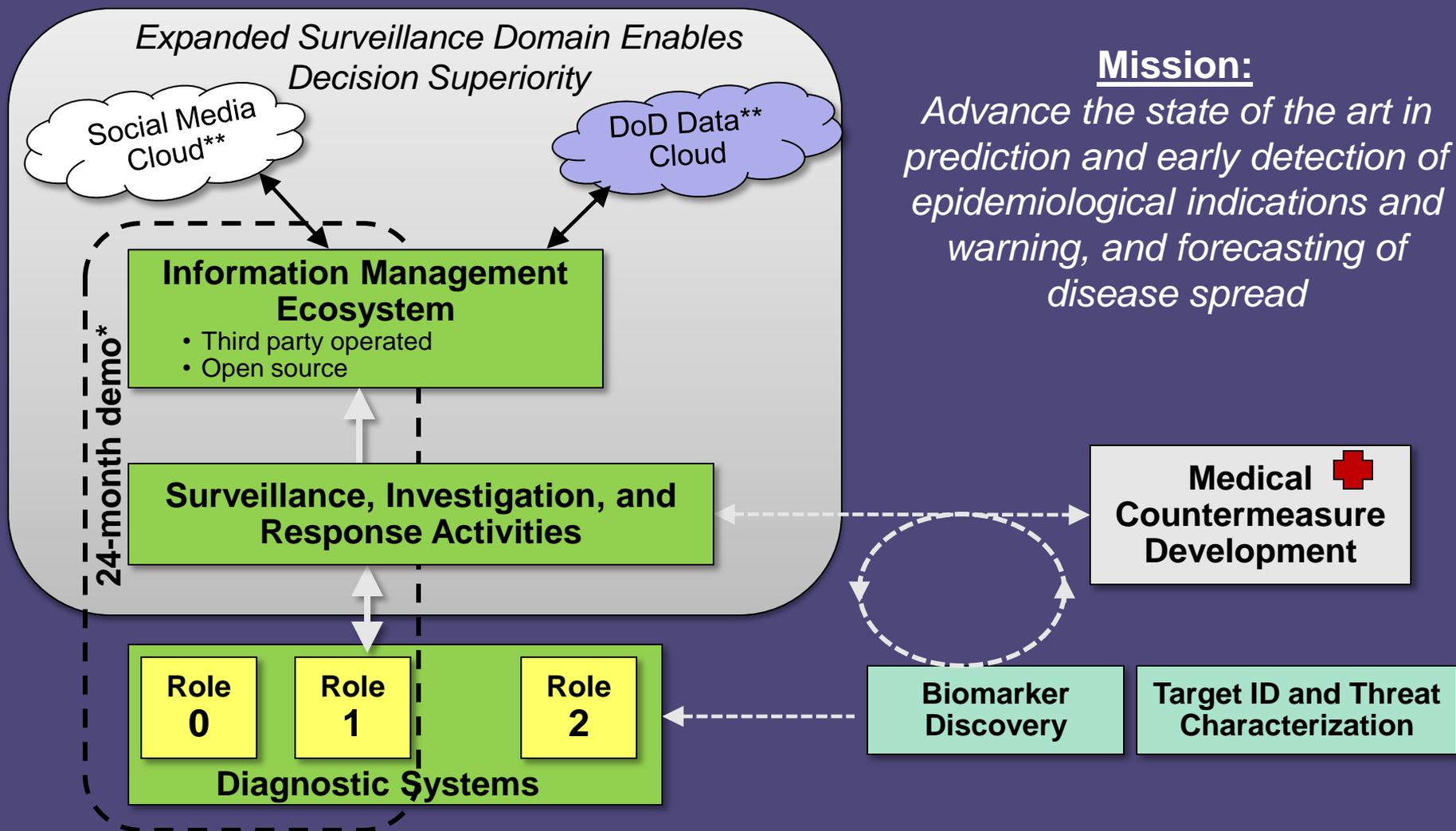


TRAINED MEDICAL PROVIDER

- Increased functionality
- Higher plexity

* Also includes uses with non-human samples (e.g. insect vectors, livestock, food, environment), which will be performed by technical operators

Provide Early Warning and Diagnosis to Ensure Successful Countermeasures



Mission:

Advance the state of the art in prediction and early detection of epidemiological indications and warning, and forecasting of disease spread

•Key prototype elements for Device, Biosurveillance and Information Management will be demonstrated in the next 24 months

•** Data clouds are pervasive information sources that do not need to be developed or maintained by DTRA

Strategic Thrust: Adaptive Medical Countermeasures

Pre-Event

EVENT

Post-Event

Post-Exposure,
Pre-Symptomatic

Symptomatic

Wide Spectrum Rx Threat and Host Strategies:

Anti-virals, Anti-bacterials, Host Immunomodulators, Chem/Rad Therapeutics

Pretreatments

**Dx-Directed Treatments
& Countermeasures**

Therapeutics

Antibiotic
Resistance
Markers

Pre-symptomatic
Biomarkers

Host
Biomarkers

Pathogen ID

High Content Data Backbone
• Pathogen Sequences
• Host-Agent Dynamics Signatures
• Characterized Reagents

Flexible
Adaptive
Manufacturing

Disease
Targets

Regulatory
Sciences



Translational Medicine S&T Responsibility and Risk Reduction

Establish early criteria and translational teams for robust transition

Team 1: S+T ad

Team 2: S+T AD

Team 3: AD + s+t

Minimum Criteria

PK/PD in Relevant Animal Models

Pre-clinical Safety & Efficacy (NHP)

Therapeutic Index for Military Utility

Route of Administration

Standard of Care Comparisons

Biomarker Utility

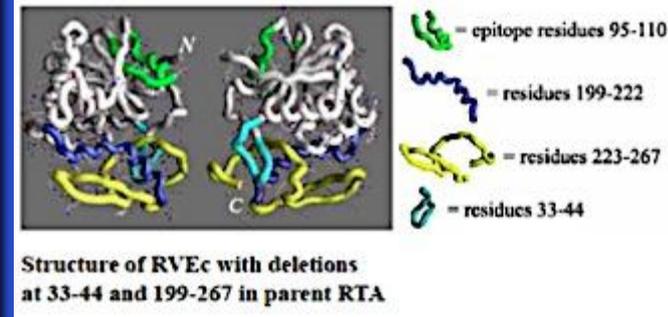
Phase 0 exploratory IND

Robust
Decision to
Human Phase
I studies

“FIRST IN HUMAN” TRIALS



- Recombinant vaccine antibody molecule (RVEc) binding to Ricin toxin
 - Pre-Clinical RVEc experiments
 - Tested parenteral and aerosol challenge
 - 6+ month protection following last vaccination
 - Passive transfer studies against lethal subcutaneous challenges (i.e., 2.5, 5 or 10 LD50s) indicate antibody-mediated immunity
 - Clinical Phase 1 escalating, multiple-dose study (June - Sept 2011)
 - 9 first vaccinations w/ only minor adverse events; those vaccinated producing antibodies directed against the Ricin toxin
 - PI: USAMRIID investigators
- Transformational Medical Technologies Division funded the early stages



CBDP Medical Countermeasures Biological Therapeutics

Bacterial Therapeutics

• Strategies

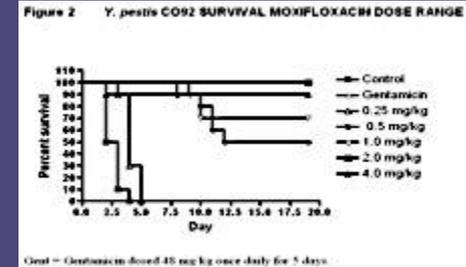
1. Discovery of unprecedented compounds (not necessarily a new target)
 - antimicrobials targeting bacterial biosynthetic pathways, virulence factors, resistance mechanisms, & host factors
 - antibiotic potentiators and immunomodulators
2. Evaluation/re-purposing of FDA-approved antibiotics against select agents of interest

• Technical Highlights

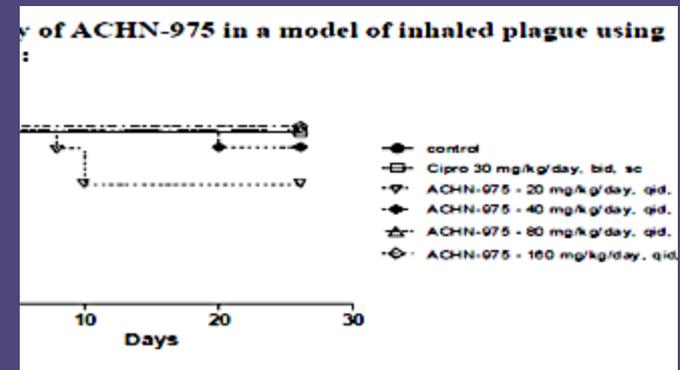
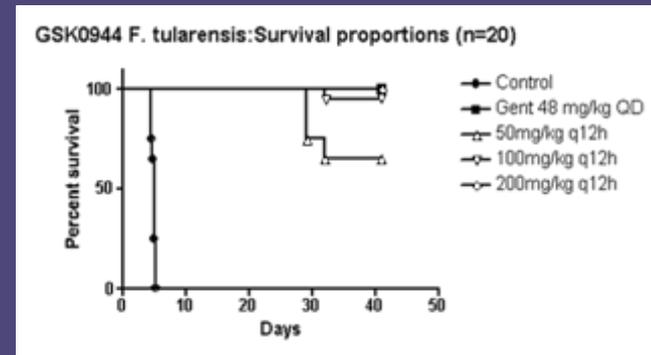
- 90% protection from death in mice after aerosol *Y. pestis* exposure with moxifloxacin
- Greater than 90% survival in mice treated with GSK0944 after *F. tularensis* infection
- ACHN-975 provides 100% protection from aerosolized *Y. pestis*

Fast Track Initiative to Accelerate Programs to First in Human Trials

USAMRIID/Bayer



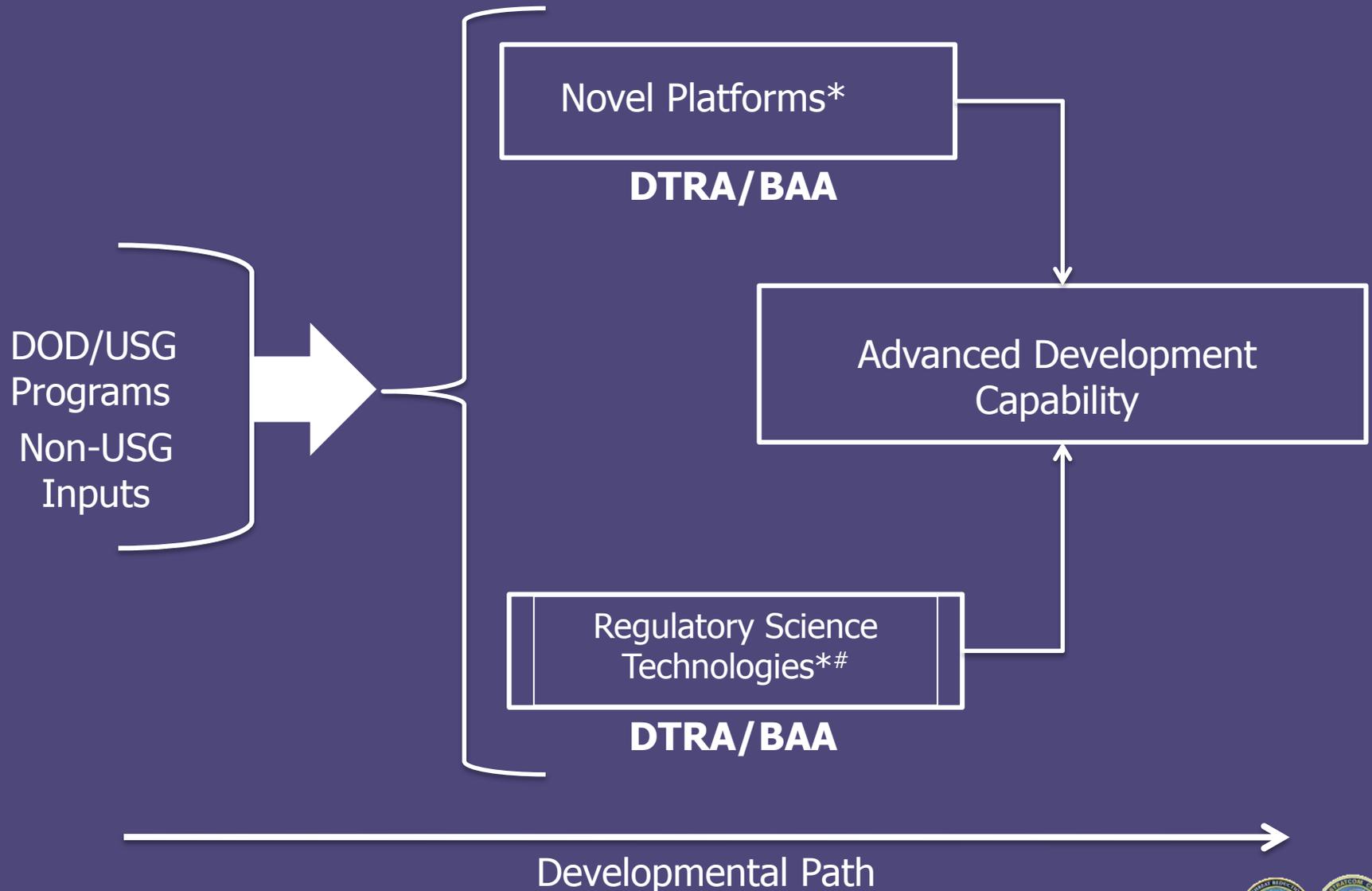
GSK



Achaogen



New Medical Countermeasures Initiative: S&T Into Advanced Development Capability



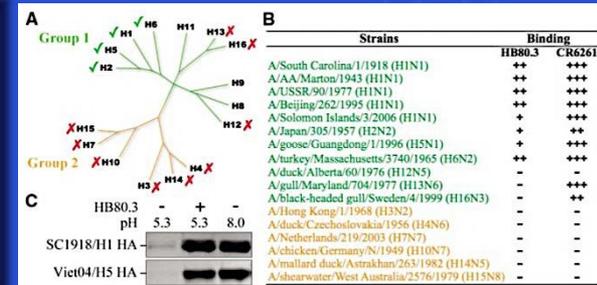
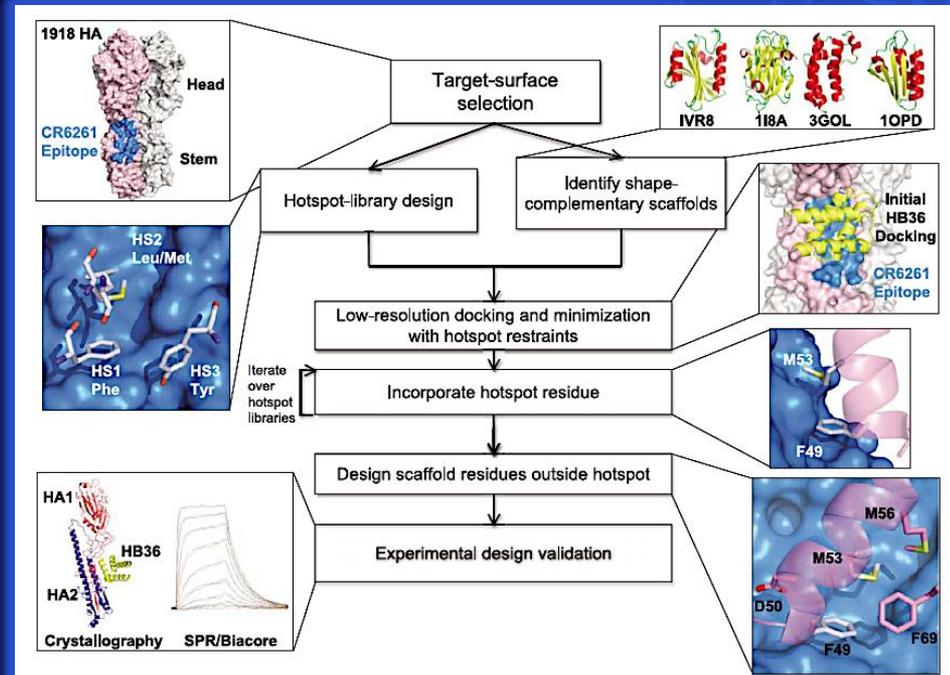
Rapid Design of Medical Countermeasures



- **Novel Computational Design**

- Demo to inhibit influenza hemagglutinin infective potency
- Promoting energetically-favorable clustered interactions between disembodied amino acid residues and target surface area patches to anchor *de novo* designed interfaces
- Incl. proxies to Negative Design: design for binding *and* precluding of binding to off-target molecules
- May 13 issue of *Science*
- PI: Dr. David Baker, University of Washington

- **DTRA Transition of DARPA Protein Design Program**

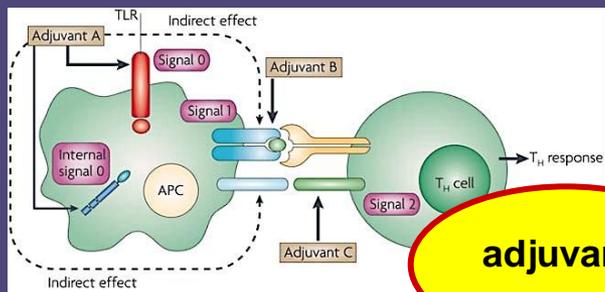


“Computational design of proteins targeting the conserved stem region of influenza hemagglutinin”

Fleishman, Baker, et al
Science. 332(6031), 816-21.

Platforms & Research Tools Thrust Area Strategy

- Invest in enabling technologies required to develop candidate vaccines against known and emerging threats



adjuvants

stabilization methodologies

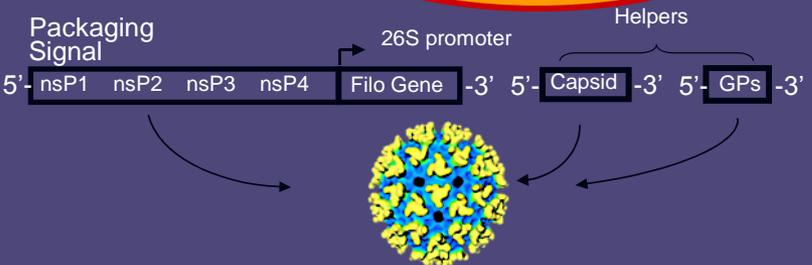
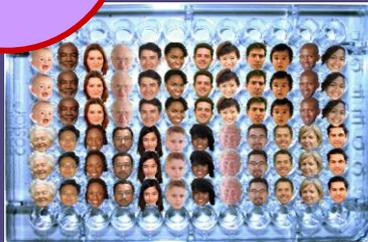


delivery technologies

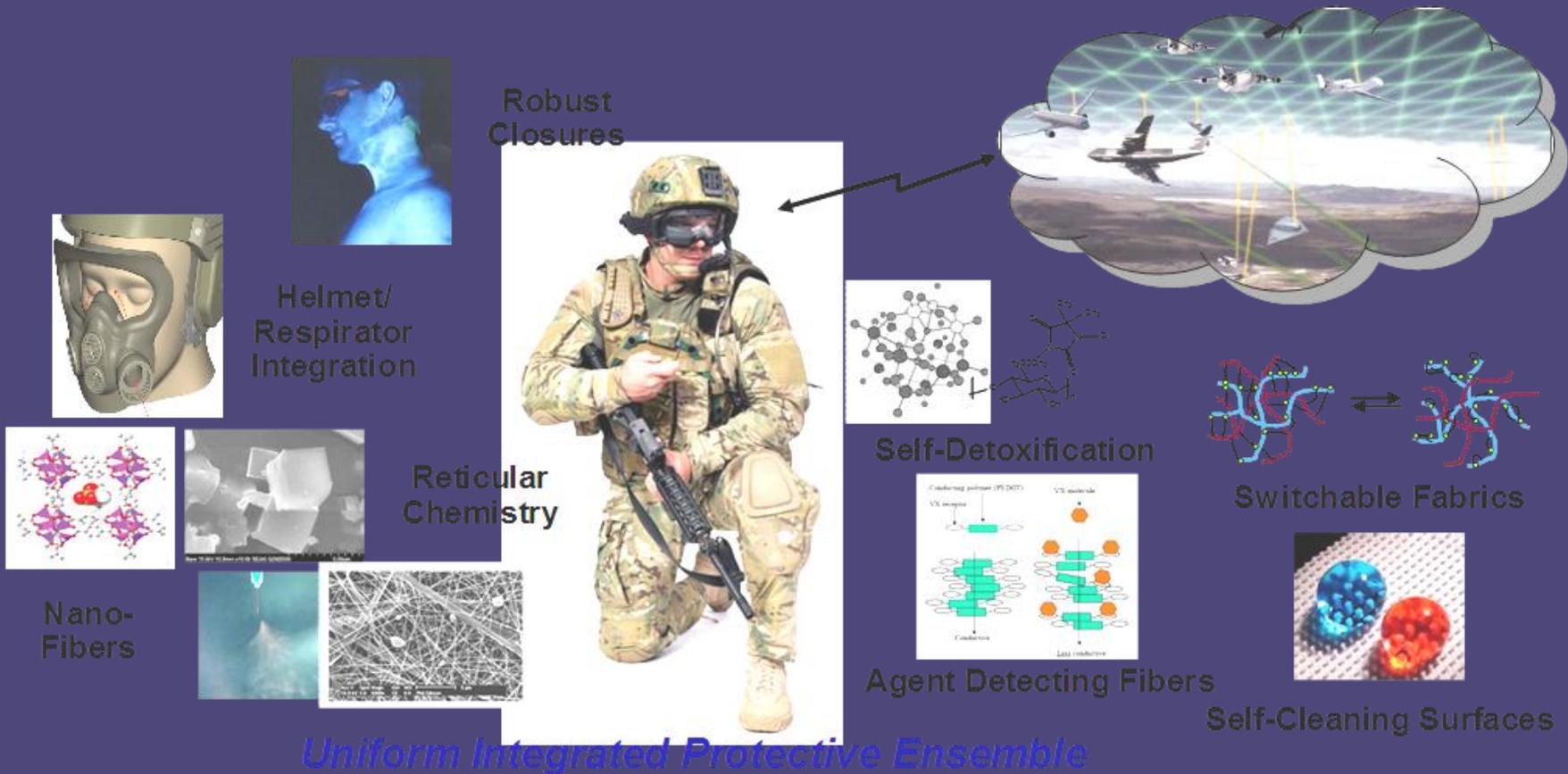


Human System responses

Multi-use expression platforms



Rapid Response & Recovery S&T: INDIVIDUAL PROTECTION PROGRAMS



Goals:

- Reduced thermal burden – target thermal burden to Fire Resistant Army Combat Uniform (FRACU)
- Integrate CB ensemble with warfighter ensemble to reduce cognitive burden
- Demonstrate network integration

Rapid Response and Recovery S&T WIDE AREA DECONTAMINATION



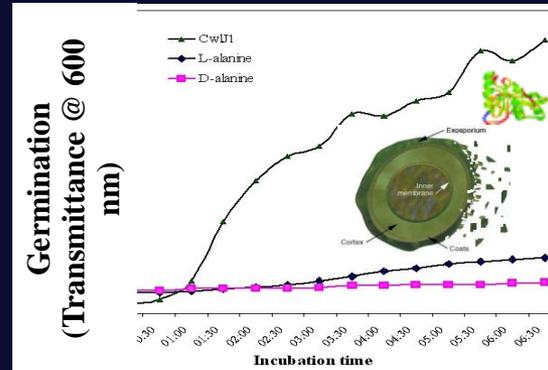
- ***B. anthracis* is virulent, persistent, and resistant to decontamination**

- Spores a threat for decades
- Current decontaminants corrosive or hazardous
- Large volumes of decontaminant needed

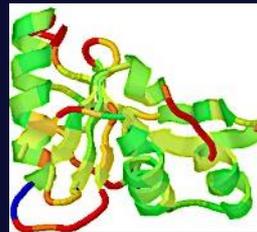
- **Seeking Innovative approaches to mitigate the effects of wide area dissemination of spores**

- Fast-acting and robust
- Low-cost
- Logistically acceptable
- Long shelf & pot life
- Environmentally-friendly

Breakthroughs will be leveraged for new innovative solutions



CwJ1 germination enzyme germination of *B. Cereus* spores faster than L-Alanine



- **Restorational Decon < 2 weeks**
- **4-6 log reduction of spores**
- **Improved Logistics**
- **6+ hour pot life (if applicable)**
- **3+ year shelf life**
- **Tarmac, buildings, soil, veg**
- **Min environmental impact**

How We Are Addressing The Challenge

- **Establish S&T Imperatives** that emphasize urgency and accountability surrounding knowledge creation and translation into robust pipeline of CBRN capabilities and products
- **Create New Opportunities For Sourcing and Managing Innovation**
 - Sourcing new Investments through Poractive Scouting and Competition
 - Managing investments to Milestones and Ceasing unproductive investments
 - Addressing the pipeline of products and capabilities needed for enhanced preparedness
 - Focusing investments into critical mass programs – Focused Innovative Technology Programs (FITs)
 - Measuring performance of knowledge products and holding ourselves accountable

“Those who have knowledge, don't predict.
Those who predict, don't have knowledge.”

Lao Tzu