Chemical Biological Defense Program Science & Technology

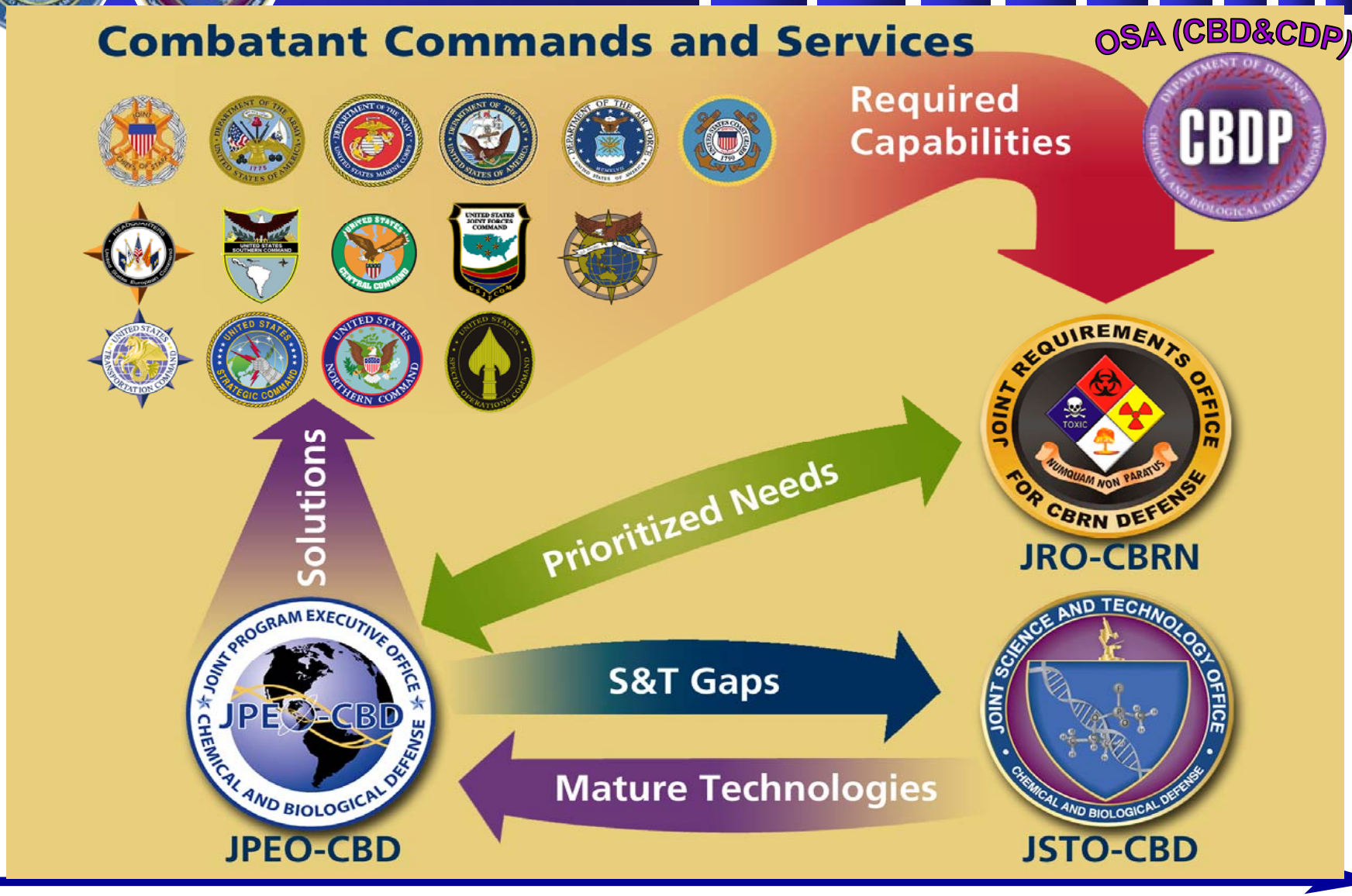
"Science for the Warfighter"

Mr. Fred Crowson

Chemical/Biological Defense Program (CBDP)
Joint Science & Technology Office (JSTO)
Chemical/Biological Technologies Directorate (RD-CB)
Defense Threat Reduction Agency (DTRA)

26 June 2008

The S&T Arm of the CBDP



Warfighter S&T at All Levels

Current

Joint

Future

Service Unique

Prioritized User Requirements

JRO Joint Priority List

1. Chemical Standoff Detection
2. Biological Standoff Detection
3. Chemical Point Detection
4. Biological Point Detection
5. Integrated Early Warning
6. Radiological Standoff Detection*
7. CBRN Reconnaissance
8. Field Analytics
9. Respiratory and Ocular Protection
10. Biological Prophylaxis
11. Radiological Point Detection*
12. Percutaneous Protection
13. Personnel Decontamination
14. Battle or Operating Enviro Management Systems
15. Chemical Prophylaxis
16. Battle or Operating Environmental Analysis
17. Fixed Site Collective Protection
18. Equipment Decontamination
19. Fixed Site Decontamination & Restoration
20. Biological Therapeutics
21. Expeditionary Collective Protection
22. Radiological Prophylaxis*
23. Medical Diagnostics
24. Chemical Therapeutics
25. Methods of Control of Contaminated People
26. Medical Surveillance
27. Radiological Therapeutics
28. Hazardous Waste Control
29. Remains Disposition

* Not addressed in CBDP S&T

JPEO S&T Needs

1. Automated Multi-Platform Sample Preparation
2. Integrated Early Warning
3. Decontamination
4. Medical Therapeutics and Prophylaxis
5. Biological Point Detection/Identification
6. Chemical Point Detection/Identification
7. Improved Respiratory TIC/NTA Filtration
8. Collective Protection
9. Improved Radiological Detection/Identification
10. Open Community of Interest (COI) Medical and CBRN Data Sharing
11. CBRN Tactical Technologies
12. Individual Protection (Improved MOPP)
13. Information Systems (Data Backbone)

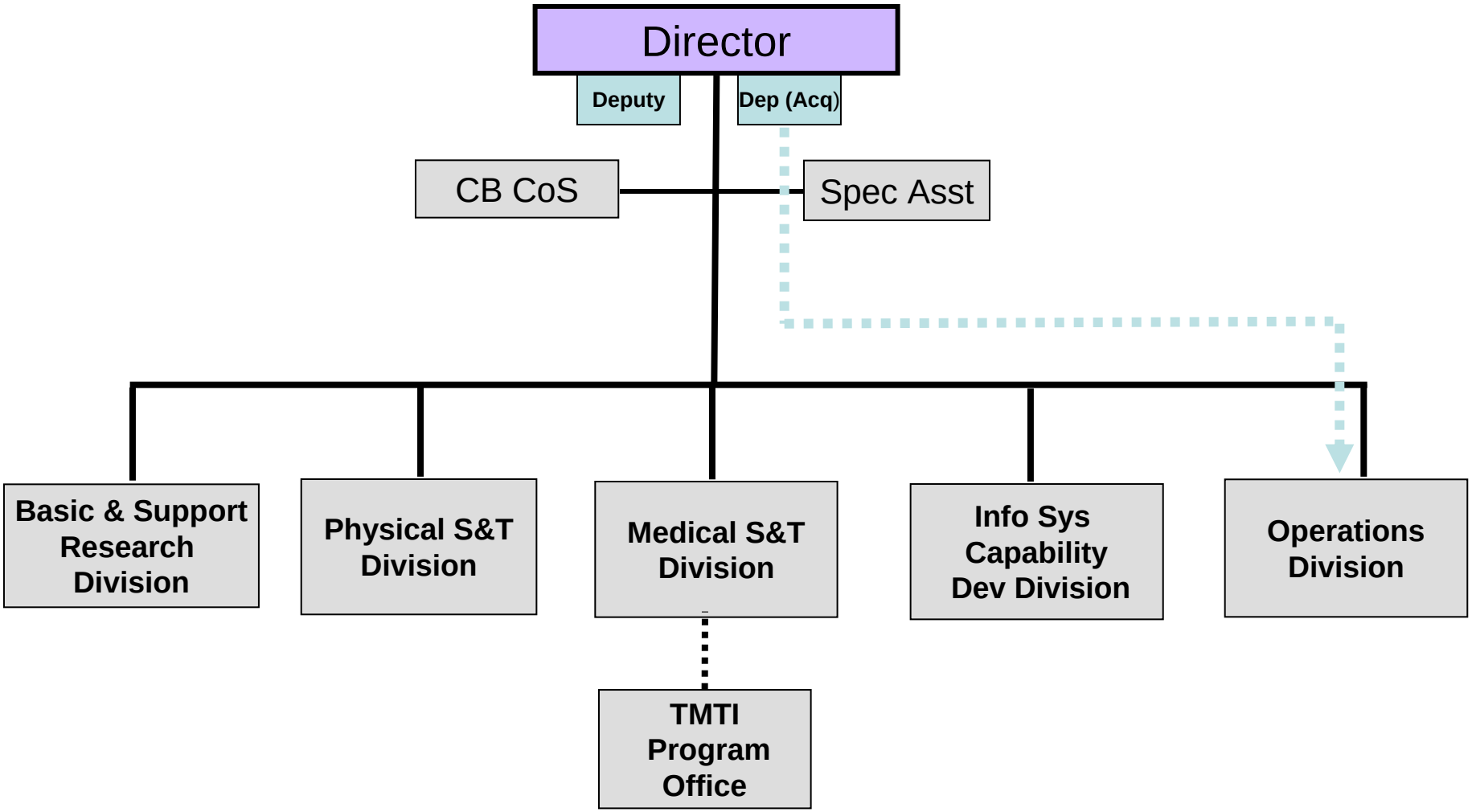
SENSE

SUSTAIN

SHIELD

SHAPE

New Chemical-Biological Technologies Directorate



JSTO Mission and Vision

VISION

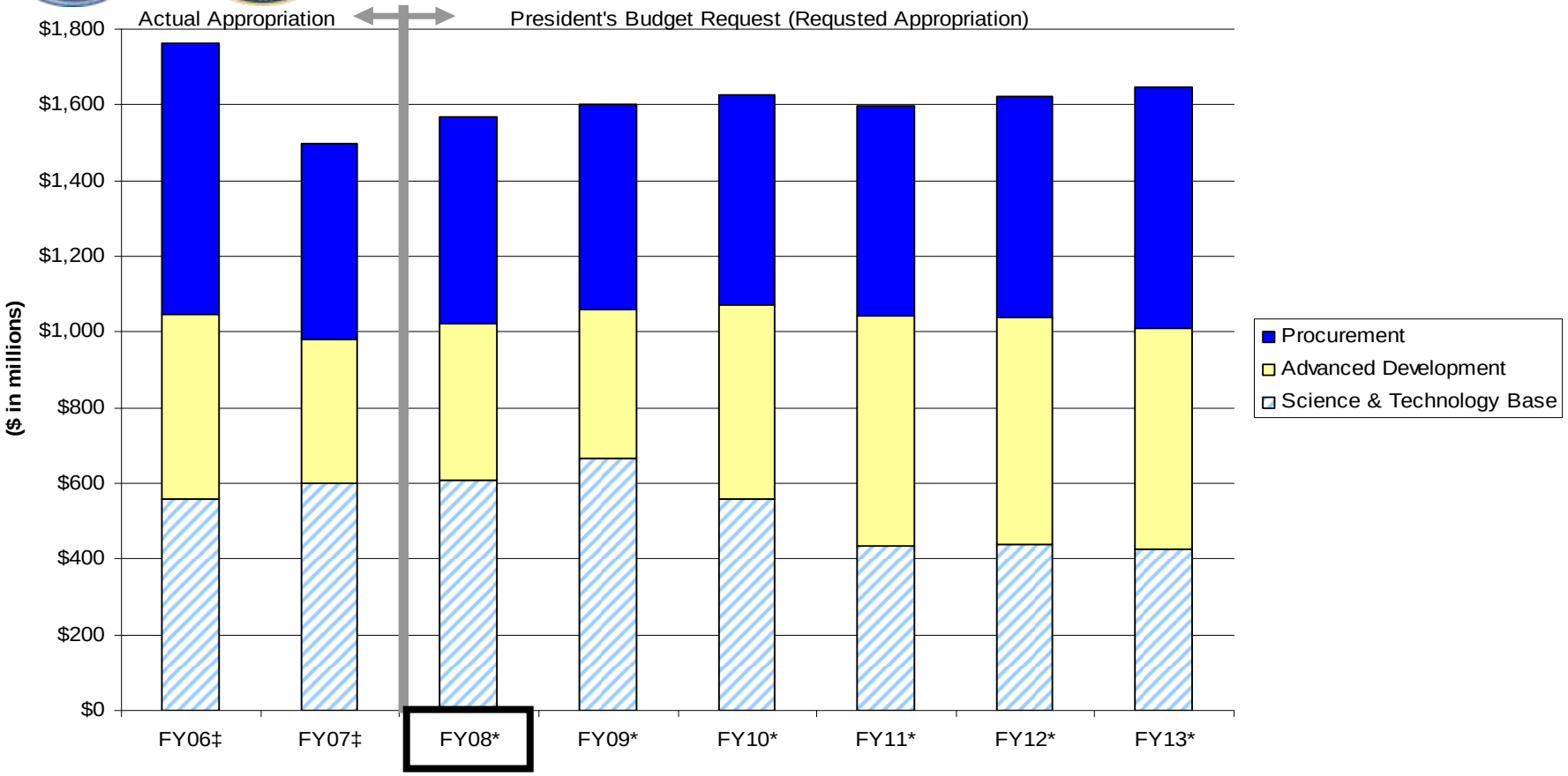
The JSTO will be the leading authority in Chemical and Biological Defense with recognized expertise in the development of future technology solutions that render the impact of chemical and biological hazards ineffective.

MISSION

The JSTO manages and integrates the development, demonstration, and transition of timely and effective chemical and biological defense solutions for the Department of Defense while serving as the focal point for science and technology expertise.

The JSTO will provide the most innovative capabilities by collaborating with mission partners, other government agencies, industry and academia.

CBDP FY2008 President's Budget



Goals

- **Address future challenges (NTAs, emerging threats, transformational medical technologies) and improve the T&E infrastructure**
- **Provide advanced capabilities to the warfighter**

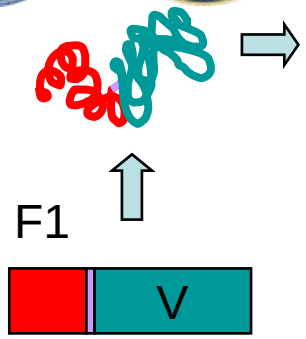
International Agreements

Multilatera

Bilateral

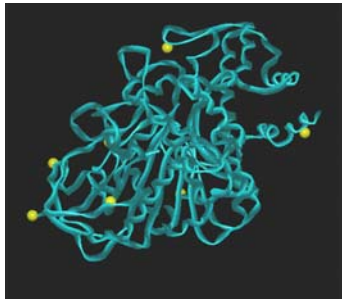
Australia	Netherlands
Belgium	New Zealand
Canada	Poland
Czech Republic	Romania
France	Singapore
Germany	South Korea
Hungary	Sweden
Israel	Switzerland
Japan	United Kingdom

Pretreatments



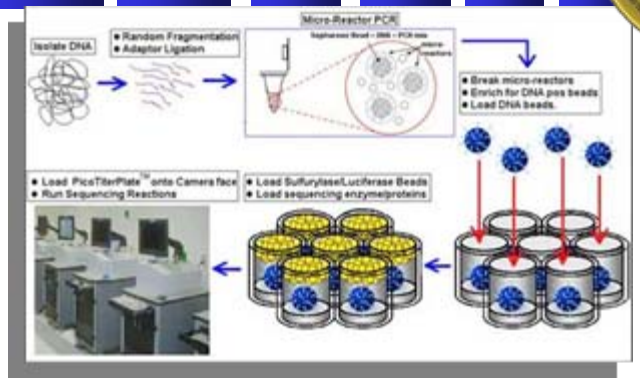
90% (18/20) Macaques Protected from Aerosolized Plague

Efficacy of the Plague Vaccine Candidate



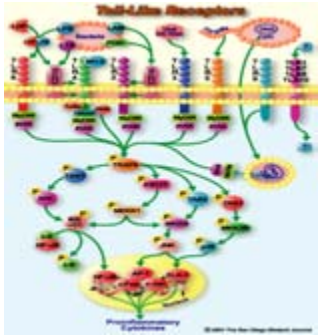
Recombinant Human Acetylcholinseterase

Generation and Evaluation of PEGylated Recombinant Human Acetylcholinesterase as an Optimal OP-Bioscavenger



454 sequencing technology

Novel Conserved Targets for Multi-Agent Biodefense Vaccines using High-Throughput Population Genomics

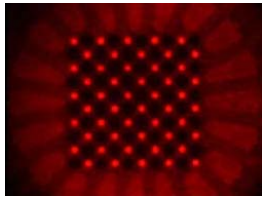


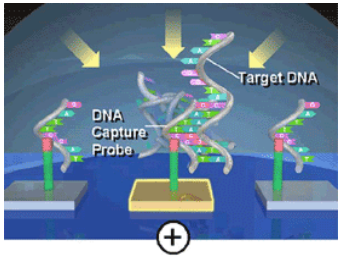
Immune SignallingPathway

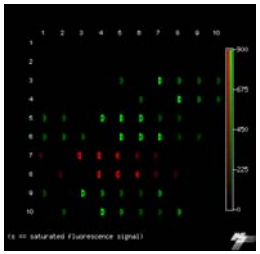
Stimulation of Broad Spectrum Protection via Toll-Like Receptors 7, 8 and 9

Transition mature candidates to advanced development; develop multiagent and molecular vaccines; improve effectiveness of vaccines and boost innate immunity to provide broad-spectrum protection; develop broad-spectrum chemical agent pretreatments

Diagnostics



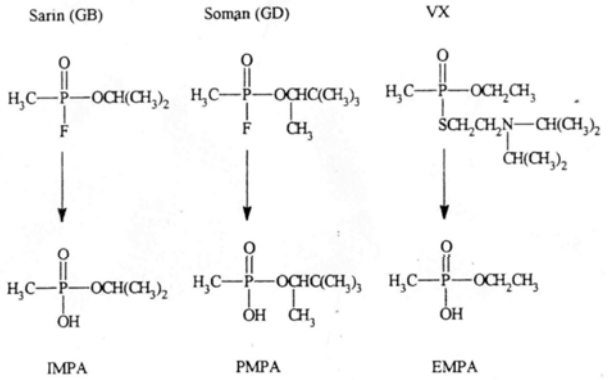




Molecular Methods for Detection and Identification of Biological Warfare Agents

Integrated Simultaneous Detection of Multiple Biological Warfare Agents

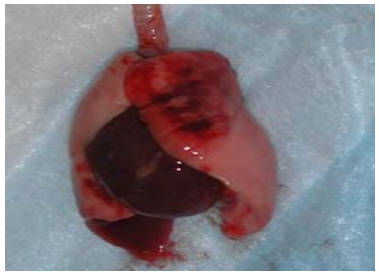
Multi-Center Evaluation of Sample Processing Methods for Nucleic Acid Extraction

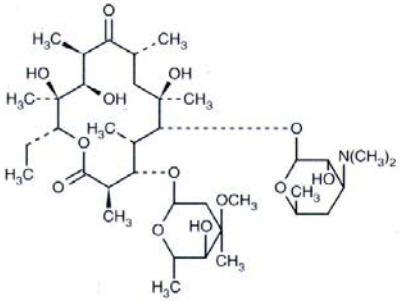


Novel Analytical Screening Methods for Chemical Warfare Agents and their Degradation Products.

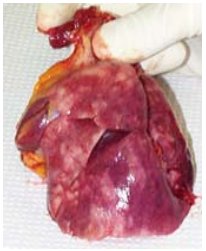
Support JBAIDS block development strategy; exploit new technologies to provide rapid presymptomatic diagnosis; develop assays for rapid diagnosis of chemical agent exposure

Therapeutics



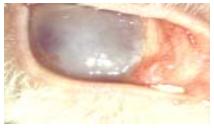


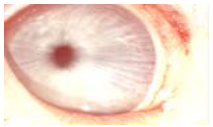
Sulfur Mustard Inhalation Toxicity in Lung Epithelium and Macrophages - Protection by Macrolide Antibiotics



Smallpox Drug Evaluation Models to Meet US FDA Animal Efficacy Rule

Therapy for Smallpox and Other Orthopox Viruses

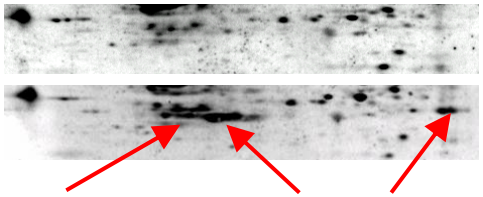




control

treated

Evaluation of the Efficacy of Candidate Anti-vesicant Ophthalmic Treatments against Ocular Sulfur Mustard (HD) Injury



Saline exposed

Soman exposed

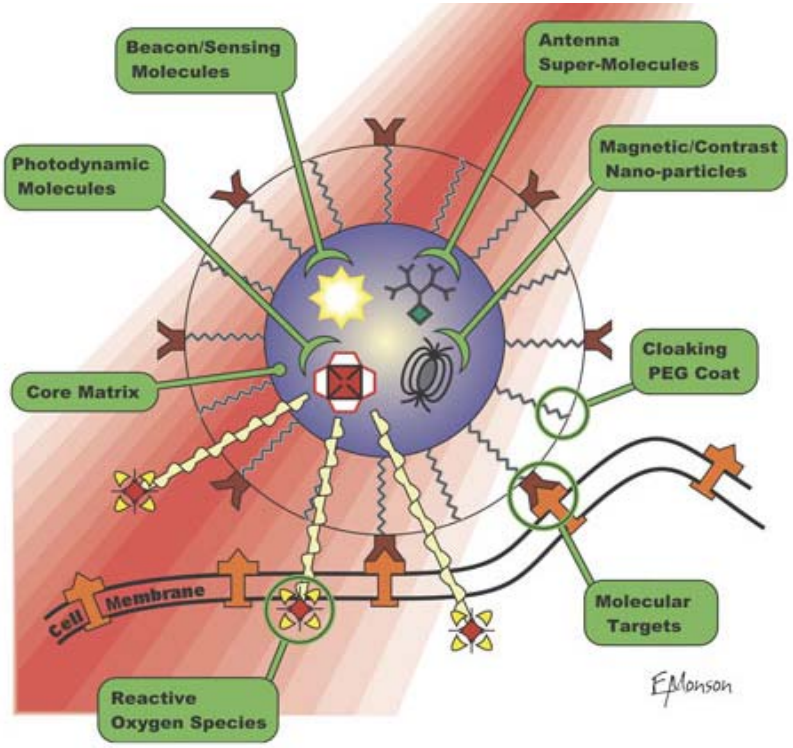
Nerve agent exposure induces significant changes in the phosphoprotein profile of the brain

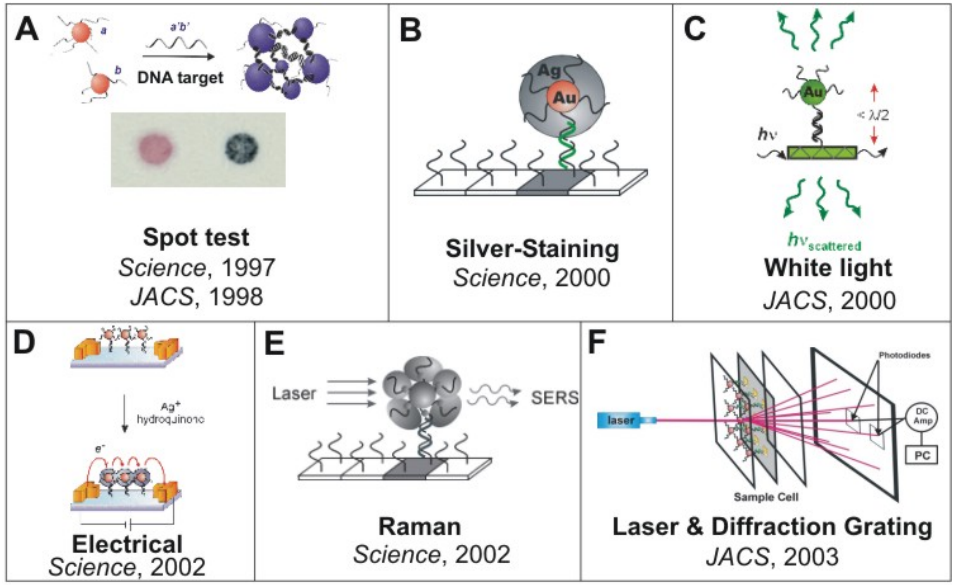
Proteomic Analysis of Neural Signaling Pathways Involved in Nerve Agent-Induced Seizures and Subsequent Neuropathology – Identify Targets for New Neuroprotectant Development

Nano-enabled Diagnostics and Therapeutics

Advectus's Nanocure™

- Nanoparticle-based formulation for the delivery of approved chemotherapeutic (doxorubicin) that does not cross the blood-brain barrier
- Outer layer attracts lipoproteins that camouflage them from the body
- Blood-brain barrier treats the particles as if they were low-density lipoproteins (LDL) - cholesterol





DNA-based diagnostics without PCR

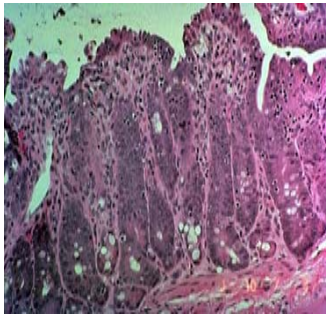
- faster temporally
- diagnostically earlier
- more sensitive
- fewer false positives

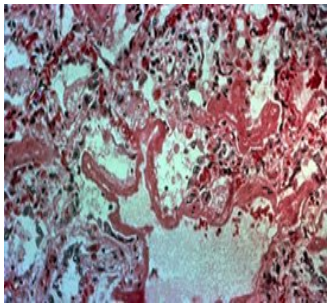
Courtesy Chad A. Mirkin, Northwestern University

Radiological Therapeutics

Objectives:

- Develop safe and efficacious radioprotectants (prophylaxes) and post-irradiation therapeutics for Acute Radiation Syndrome (ARS) for gastrointestinal and pulmonary tracts
- Develop a diagnostic chromosomal biodosimetry



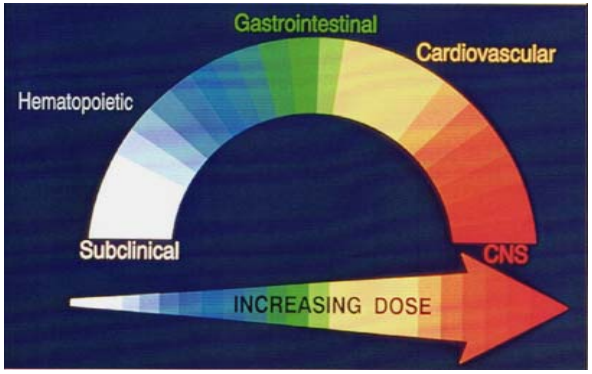


Strategy:

- Accelerate transition of mature candidates to product development
- Leverage on promising candidates that are currently in preclinical development for radiation-oncology

Accomplishments:

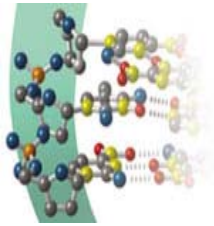
- **2008**: Selected Prochymal™ for FDA-approval
- **2008:** Selected CBLB502 (Flagellin) for FDA-approval



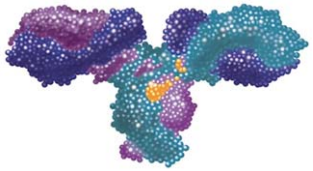
Transformational Medical Technologies Initiative (TMTI)

Scientific Thrust Areas

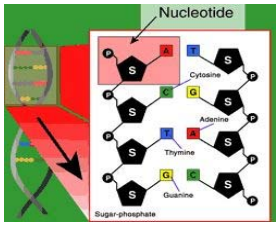
Genomic Identification



Small Molecule Discovery



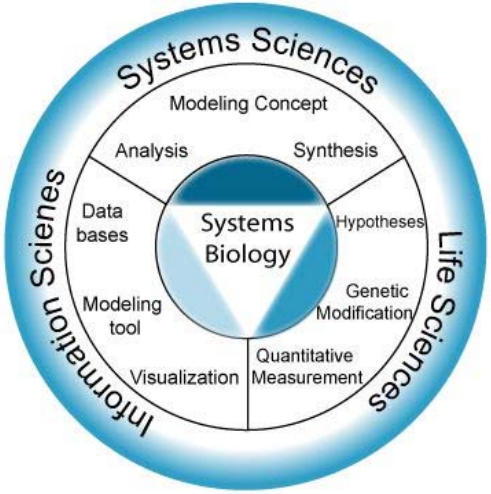
Protein Based Therapeutics



Nucleotide Therapeutics

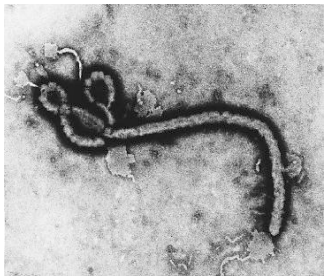
Human Immune Enhancement

Integrated Cross-Cutting Technologies



Microarray Technology
Bioinformatics
Proteomics
Genomics
siRNA

Deliverables



Broad Spectrum Treatments
- ***Hemorrhagic fever viruses***
- ***Intracellular bacterial pathogens***

Genetic ID & Analysis

An innovative approach using revolutionary technologies to expedite the development of products to counter emerging biological threats

Transformational Medical Technologies Initiative (TMTI)

Goals

(QDR driven)

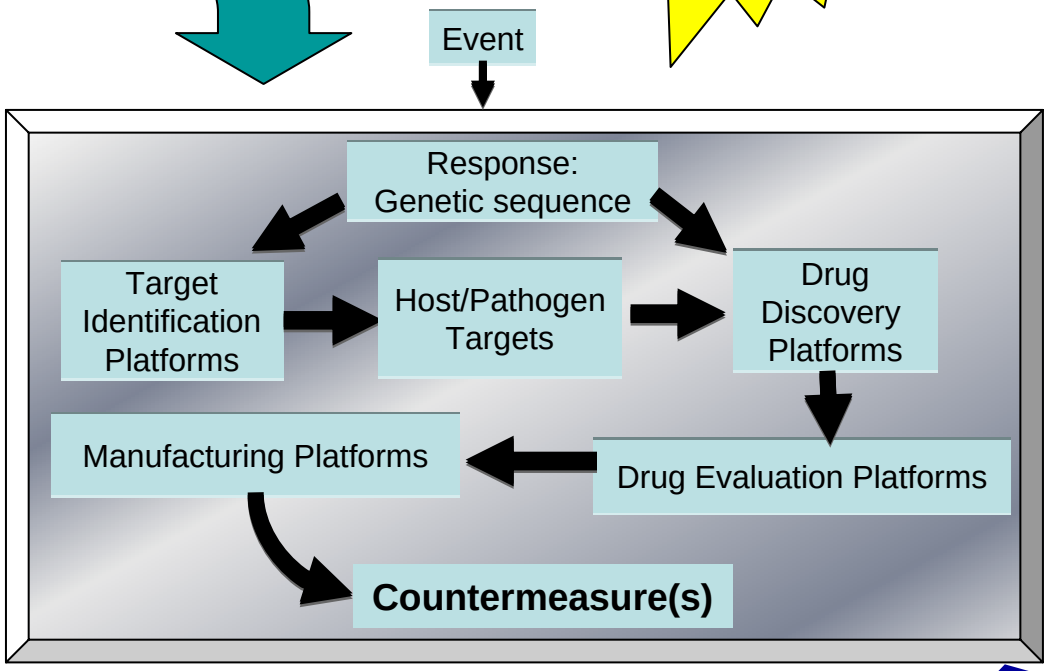
Develop at least two platform technologies
Enabling technologies: Capability to rapidly develop new countermeasures

Build integrated library: Genetic sequences of BW agents
Capability to rapidly sequence and characterize novel threats

Develop two *broad-spectrum countermeasures to Investigational New Drug filing*

Approach

Capability to respond to unknown threat is real priority



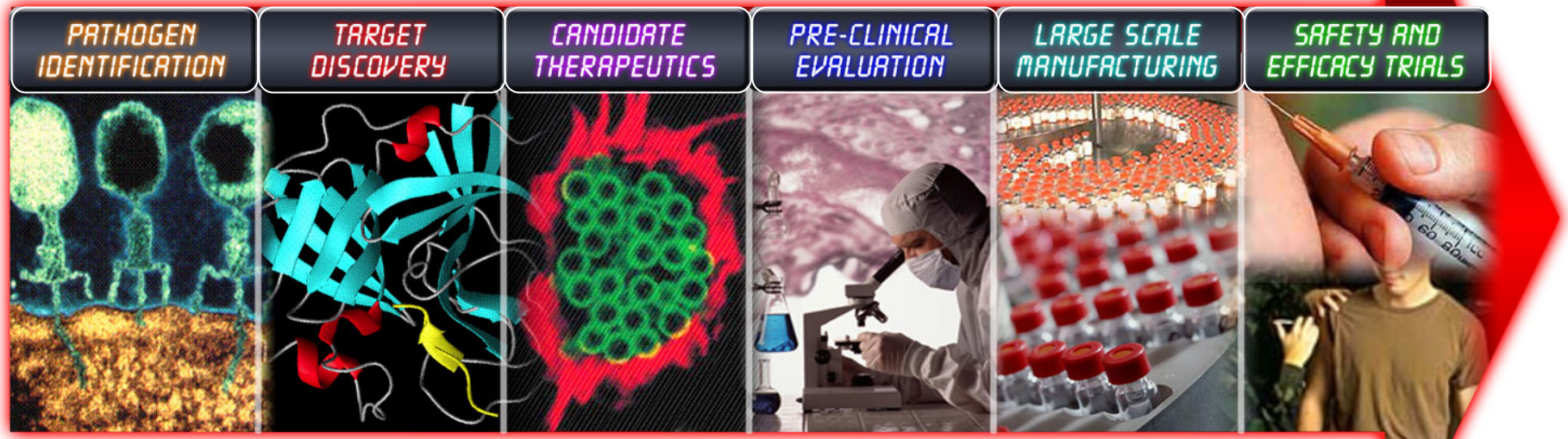
DARPA Thrust: Accelerating Critical Therapeutics

Current Timeline (2004 NIH Roadmap)

Day → Weeks	3 Years → Indefinite	3 Years	1-3 Years	7-8 Years

DARPA Timeline

Hours	2 Weeks	2 Weeks	8-12 Weeks	Situational



SPO

MTO

DSO

Pathogen Countermeasures

In Silico Target and Therapy Discovery

Rapid Vaccine Assessment

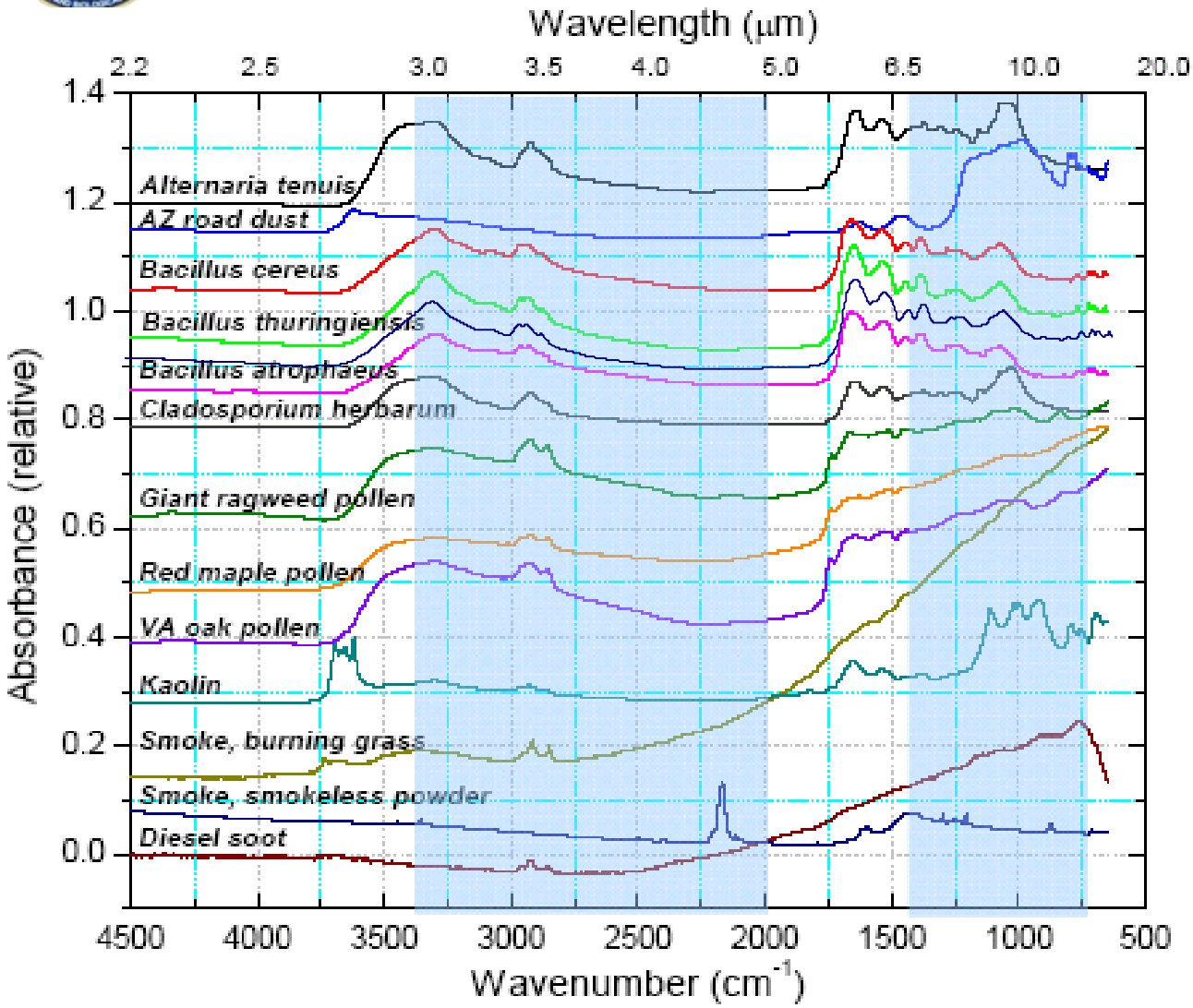
Rapid Manufacture Of Vaccines And Biologics

FDA

DARPA

Accelerated Insertion Methodology

Biological Detection: "Traditional" Approaches are Insufficient



Biological Detection Systems

Current:

JBPDS
- UV-LIF trigger
- Virtual impactor sample collection
- Immunoassays - 10 agents
- 15 – 20 min response time

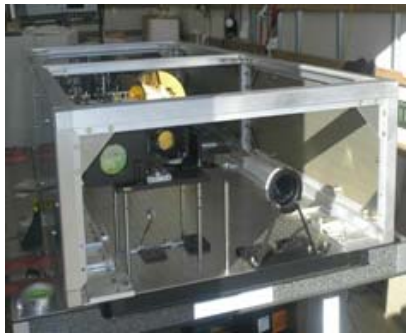
JBSDS Incr I
- IR/UV-LIF
- 5 km IR scatter particle detection
- 1 km UV-LIF bio discrimination

Advanced:

Invitrogen
•MAPP-DS

ECBC

•Tactical Biological Detector



WANDER
- IR depolarization ratio
- Potential bio discrimination

DARPA FASTREAD
- Femtosecond Adaptive Spectroscopy Techniques
- Spectral/temporal info in the backscattered signal
- Potential bio identification

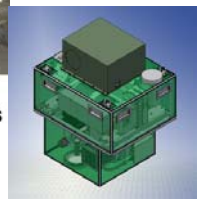
Chemical Detection Systems

Current:

ACADA
- IMS
- Miosis level
- 1 min response

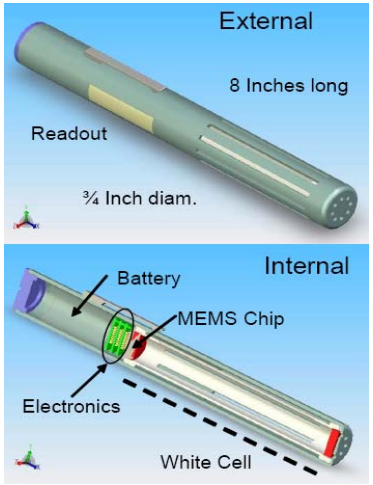
JSLSCAD
- FT-IR
- 1/2 km range
- 360 scanning

JCSD
- IR-Raman
- 40 mph



Advanced:

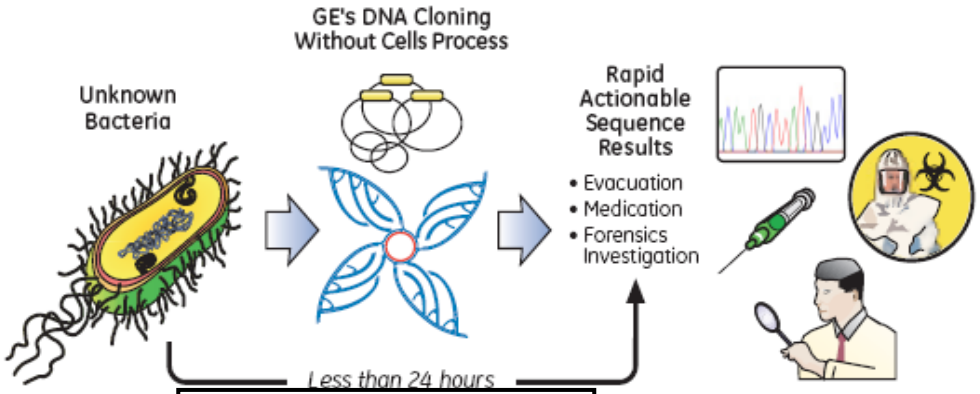
JCAD
- IMS
- Moisis level
- 2 lb



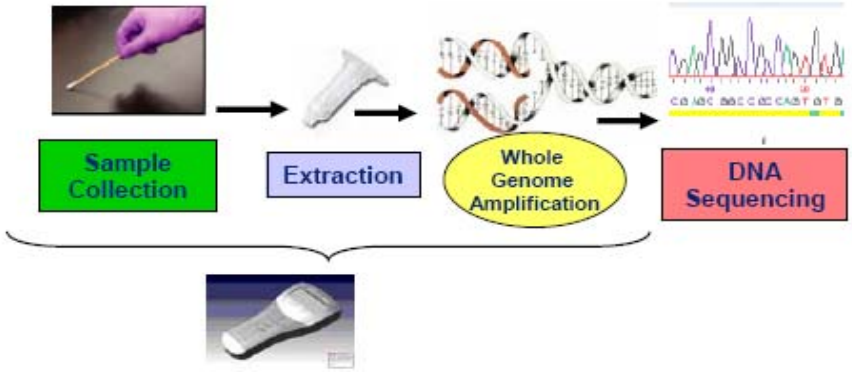
ChemPen
- MEMS
- FT-IR

FirstDefender™
- IR-Raman
- Bulk liquids

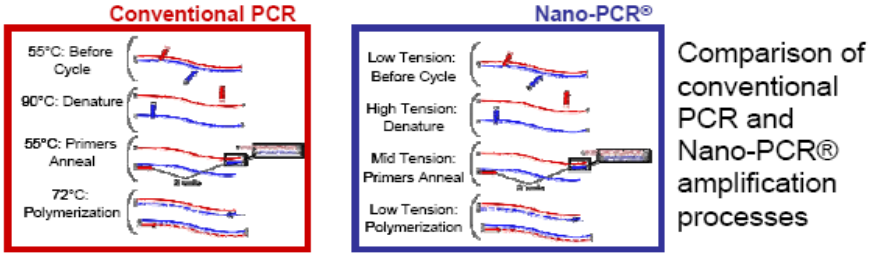
Detection Concepts Using Genomic Sequencing



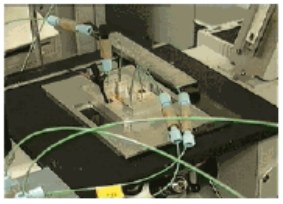
General Electric



Ibis Biosciences



Comparison of conventional PCR and Nano-PCR® amplification processes



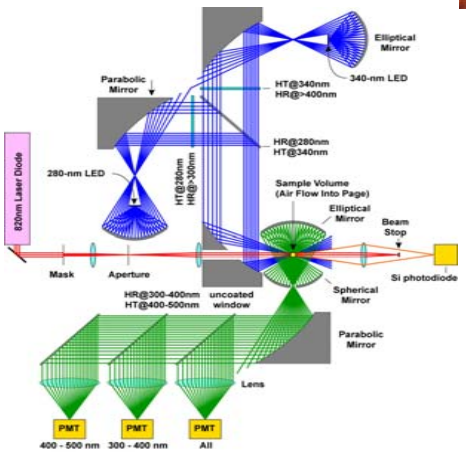
Left: Proposed Effort, benchtop Nano-PCR amplification
Right: Product Vision, handheld amplification and pathogen ID from raw sample

Nanobiosym, Inc
• DARPA MOLDICE

Detection and Identification Recent Accomplishments

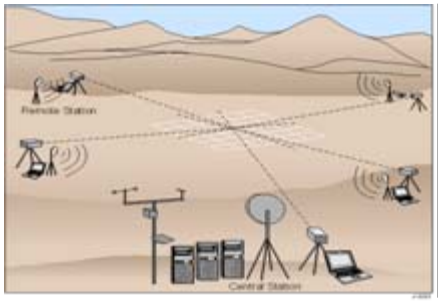
- **Lightweight Integrated CB Detection System**

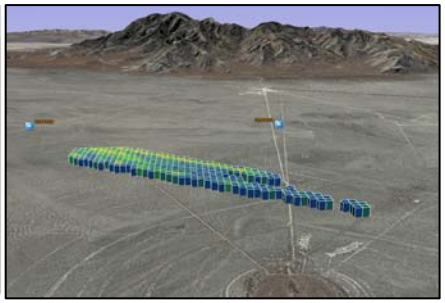
- **Low Cost/Low Power UV Detection**



- **Optical Acceptance Measurements for Test & Evaluation Antigens**

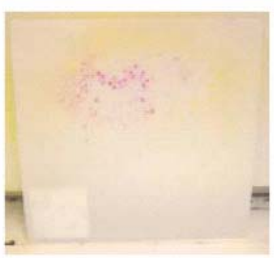
- **Range Test Validation System**

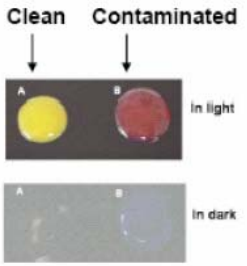




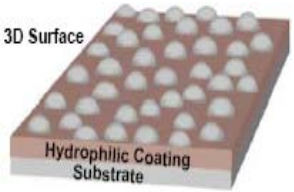
Hazard Mitigation (Decontamination)

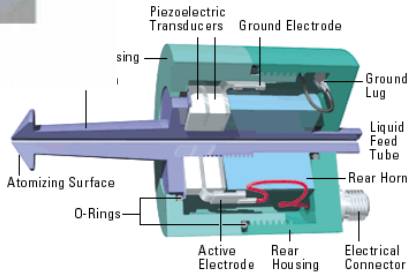
- **Decontamination Assurance Spray**
- **Energetic and kinetic**
- **Self-Detoxifying Surfaces/ Reactive Coatings**
- **Smart Systems**
  - ➢ **Sense**
  - ➢ **Respond**
  - ➢ **Signal**



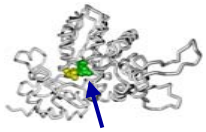


Red area on vertical plate is contaminated and yellow area is clean



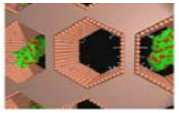


OPH Enzyme



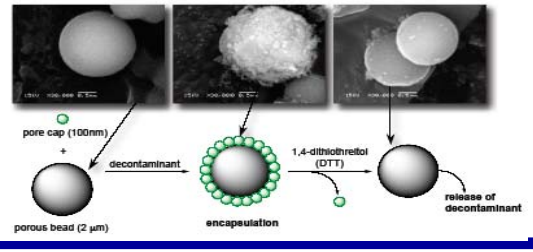
OPH binds and degrades chemical nerve agents

OPH Enzyme Immobilized in Mesoporous Silica



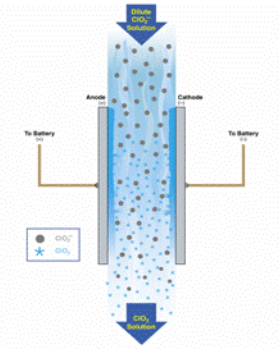
Increases shelf-life from hours to over 6 months

Current Decontamination CONOPS



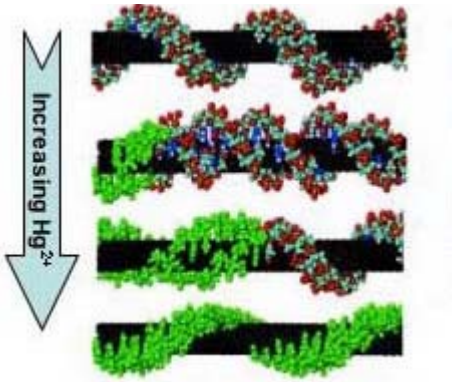
Hazard Mitigation (Decontamination) Recent Accomplishments

- Identified a candidate technology for intra-theater transportation of contaminated human remains
- Transitioned high performance liquid chromotography (HPLC) methodology for determining decon residual
- Developed a new ClO2 formulation with enhanced broad-spectrum chemical and biological hazard reduction efficacy
- Discovered an advanced surfactant system that will lead to development of environmentally-safe product for chemical removal augmentation
- Completed a “decon wipe” development for sensitive surfaces



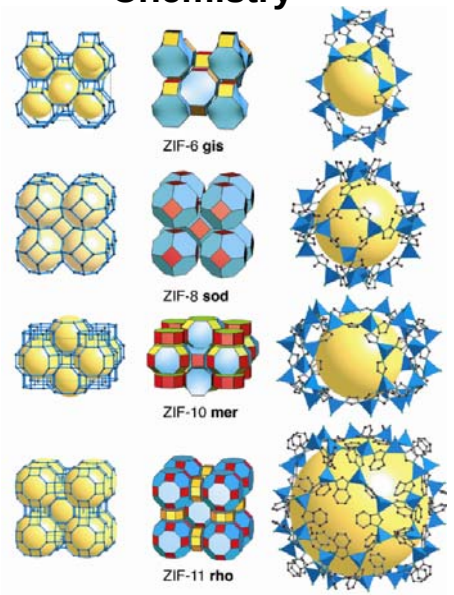
Individual Protection

Carbon Nanotube As Chemical Sensor

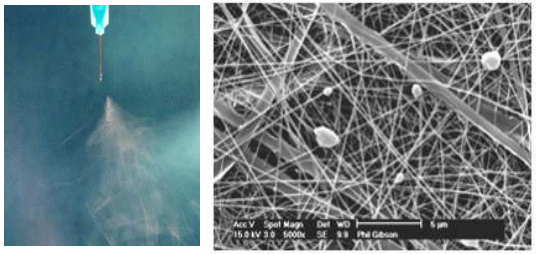


DNA changes structure (electronic properties) to ions and chemicals

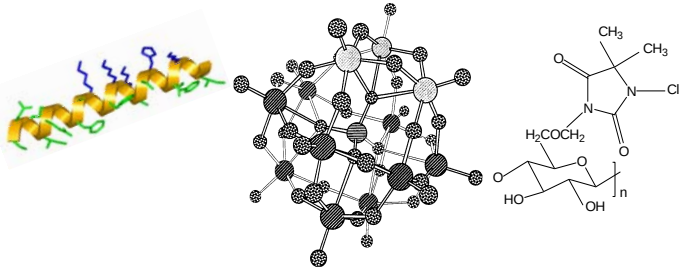
Reticular Chemistry

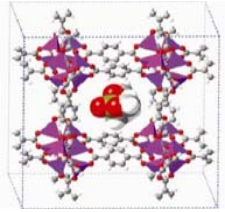


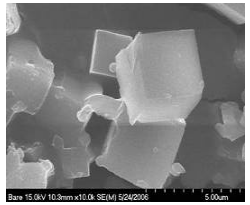
Nano-Fibers



Self-Detoxification







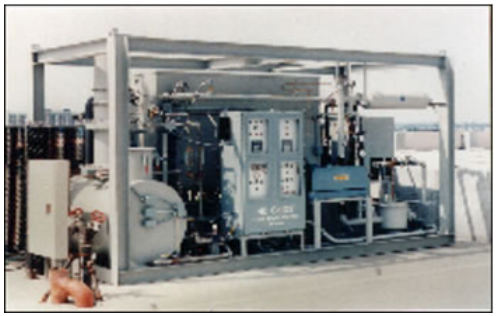
Nanomaterials for sensing, protection and decontamination

Protection
Recent Accomplishments

- Completed transition of end-of-service-life indicator for gas mask canister and novel closures for protective garments

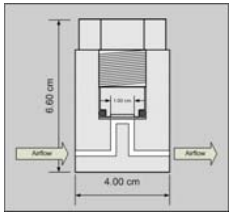
- Focused individual protection mid-term efforts on low-burden and novel concepts to integrate with a developmental warfighting ensemble

- System demonstration of a catalytic oxidation air purification technology to support transition of this technology

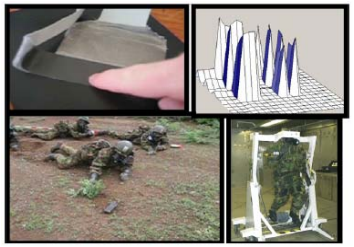


Test & Evaluation Methodologies & Capabilities

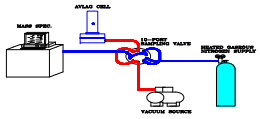
Test Standard Development for Collective Protection Technologies



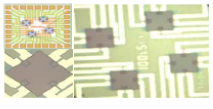
Characterization of Swatch Test CRMs

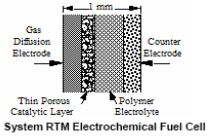


IPE Field Operations Effects Standard

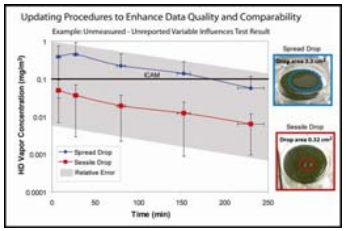


TIC/Battlefield Contaminant Set Standard for IPE & ColPro

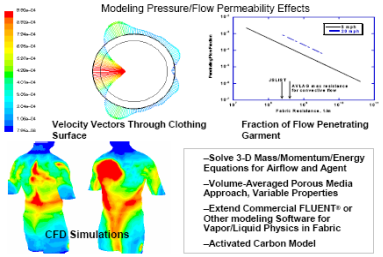




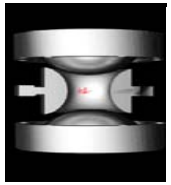
Standardized Procedure for Individual Protection Whole System Assessment



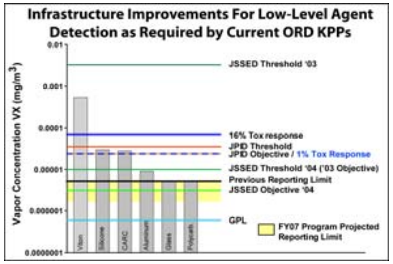
Improved Decontaminant Performance Evaluation Methodology



Body Region Hazard Assessment Model



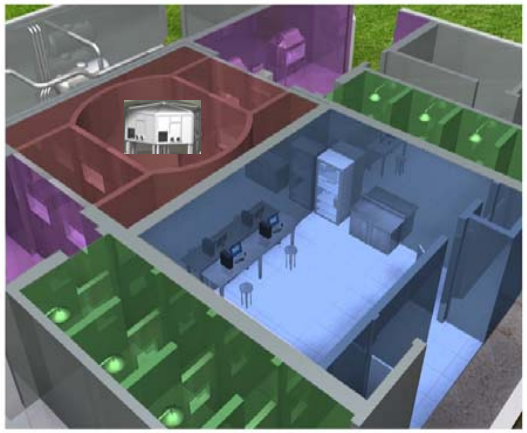
Chem-Bio Agent Resistance Test (CBART)



Achieving Low-Level Detection of Residual Agent and Reaction Products

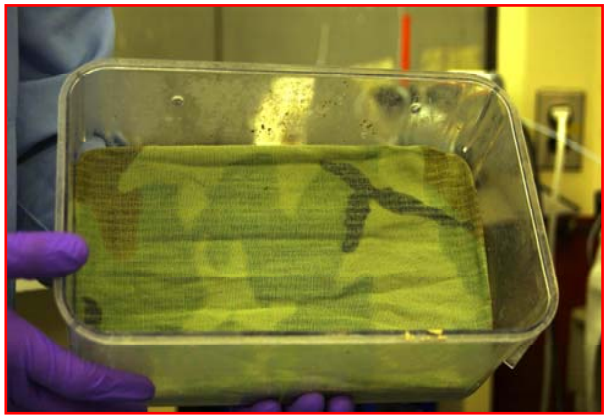
Decon Hazard Byproduct and Residual Agent Test Standards

Non-Traditional Agent (NTA) Facility



Notional Concept for NTA Facility

Personal Protective Equipment



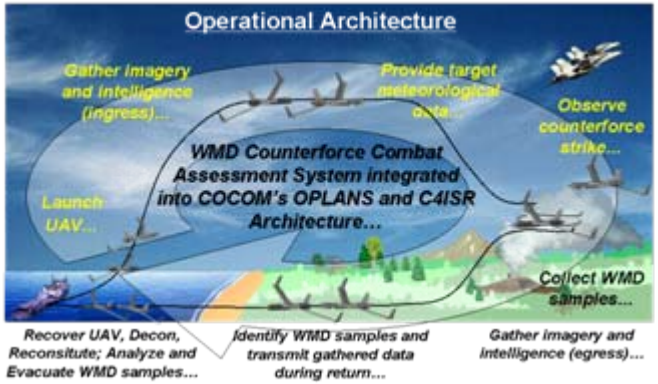
Decon to Safe Levels for Disposal

Materials Compatibility Tests

Decontamination Efficacy Tests

Advanced Technology Demonstrations - FY07-FY10

Hackensack University Medical Center
Mobile Emergency Trauma Unit



Biological Combat Assessment System (BCAS)

CBRN Unmanned Ground Reconnaissance (CUGR)

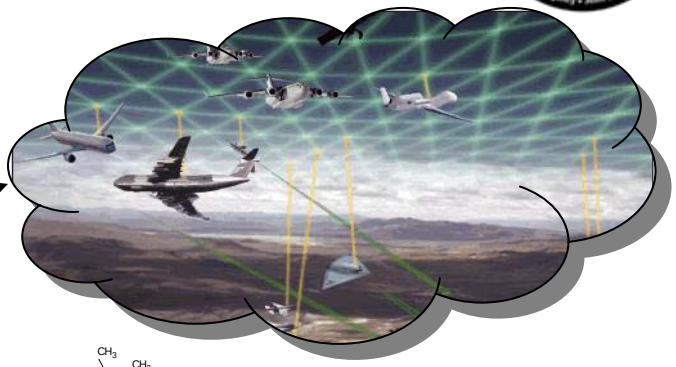
Expeditionary Biological Detection (EBD)

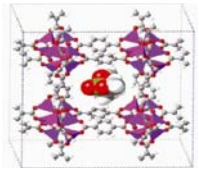
Interagency Biological Restoration Demonstration (IBRD)

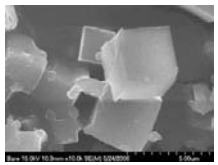
Systems of Systems Decon

Future Force Warrior Advanced Technology Demonstration – FY10

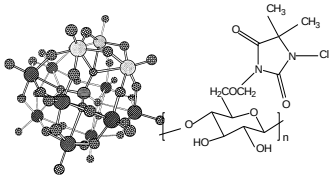
Helmet/ Respirator Integration



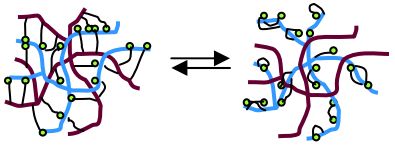




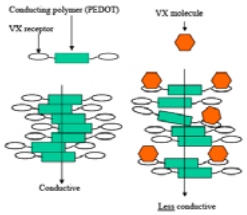
Reticular Chemistry



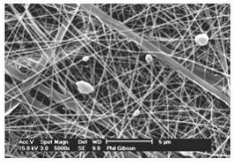
Self-Detoxification



Switchable Fabrics



Agent Detecting Fibers



Nano-Fibers

Soldier-as-a-System-Ground (SaaS-G) Leader Concept

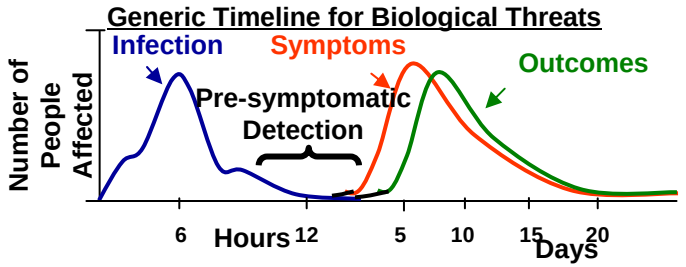
Demonstrate an integrated materials concept in FY2010 using thermal burden as an independent variable to achive low-burden protection

Information Systems Technology

Bioinformatics: Key to Systems Biology and Medical S&T

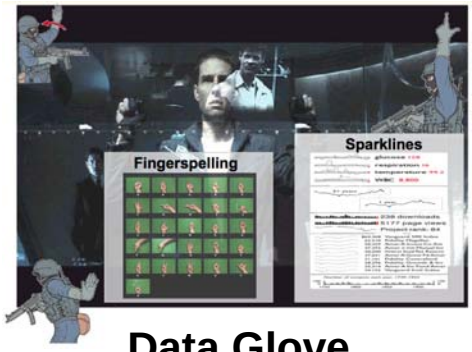
Essential for:

- Expression analysis for molecular function interrogation – technology dependent (genomics proteomics, metabolomics)
- Data mining/Database management
- Machine learning
- Molecular structure & molecular interaction prediction
- Modeling biochemical pathways and biological networks



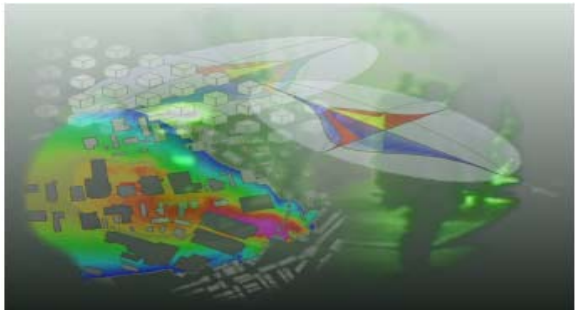
Pre-Symptomatic Detection

Modeling/Data Assimilation: Relevant to Physical S&T

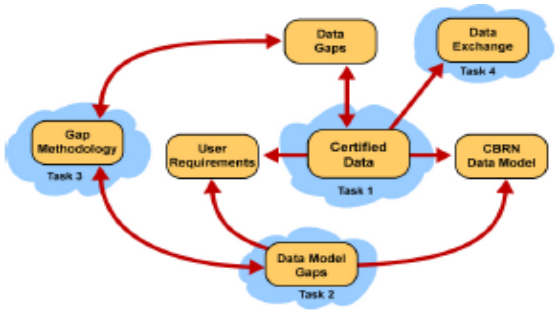


Data Glove

Allows silent communication between soldiers through uniform (glove) based sensors.



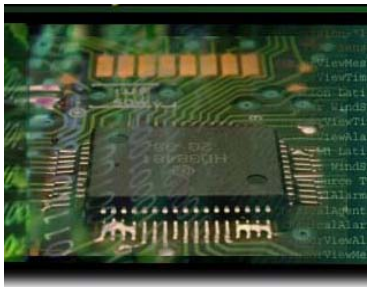
CBRN Modeling



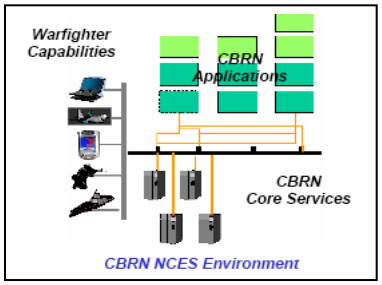
Data Backbone

Utilizing current IT to log, evaluate, synthesize disparate sources of CBRN information and develop predictive models

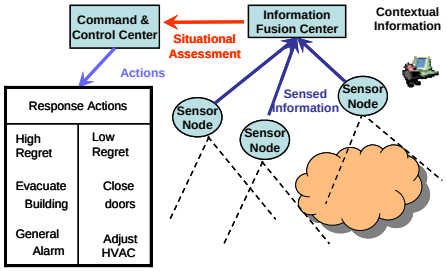
Information Systems Technology Recent Accomplishments



JWARN Component Interface Device (JCID) software-based sensor system

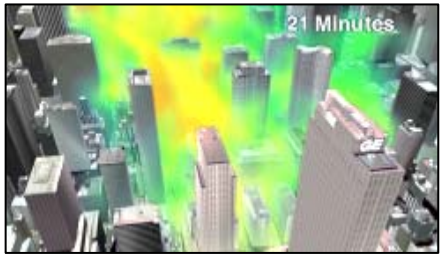


Common CBRN Software Services

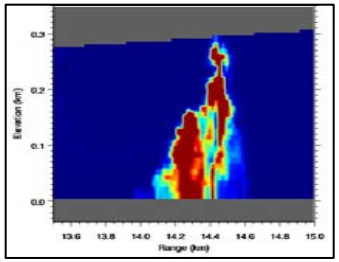


Sensor Alert Verification for Incident Operational Response (SAVIOR)

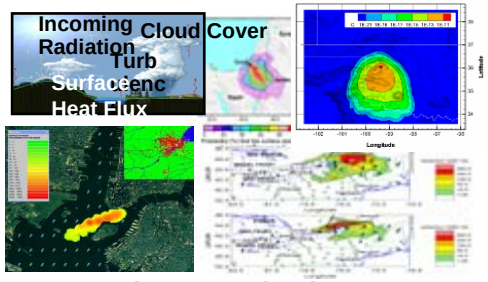
JWARN
Joint Warning and Reporting Network



Urban Capabilities

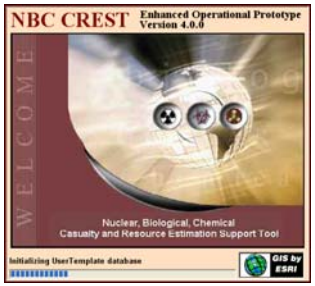


Rapid Assimilation of Sensor Data

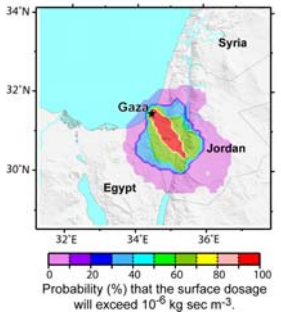


Environmental Sciences

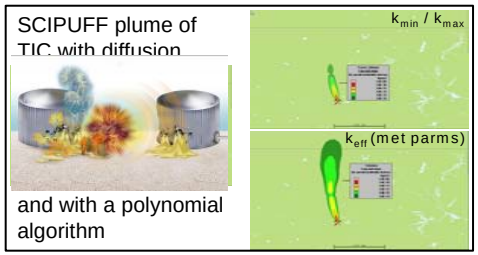
JEM
JOINT EFFECTS MODEL



NBC CREST



Climatology Database



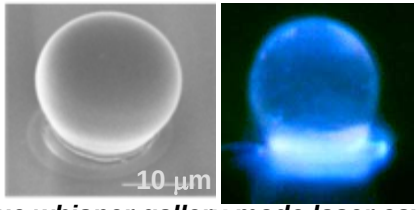
Modeling the Atmospheric Chemistry of TICs

JOEF

Basic Research

Nocera, MIT – Ultrasensitive Chem-/Bio-Optical Sensors on Small Scales

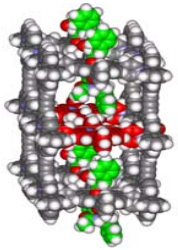
Developed blue semiconductor nanocrystal laser, micro laser cavities for chemosensor, and induced chemical sensitivity of nanocrystal quantum dots (Nocera: 2007 Mack Award, ACS Harrison Howe Award)



Blue whisper gallery mode laser cavity

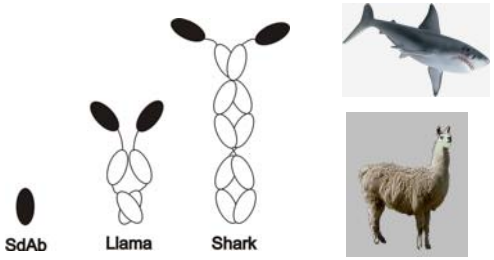
Mirkin, Northwestern U. – Molecular Machines

Developed supramolecular catalysts for acyl transfer reactions; designed flexible type of supramolecular allosteric catalysts and MOFs, pseudo-rotaxane supramolecular structures



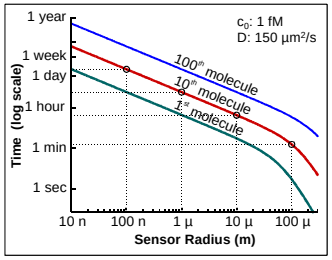
Goldman, NRL – Development and Testing of Recombinant Single Domain Antibodies

Developed hyper diversified shark new antigen receptor display library to be used against toxins. Expressed sdAb and variants characterized in terms of stability and regenerability (Goldman: 2006 Alan Berman Research Publication Award)



Whitman, NRL – Biophysical Fluid Dynamics Near Surfaces

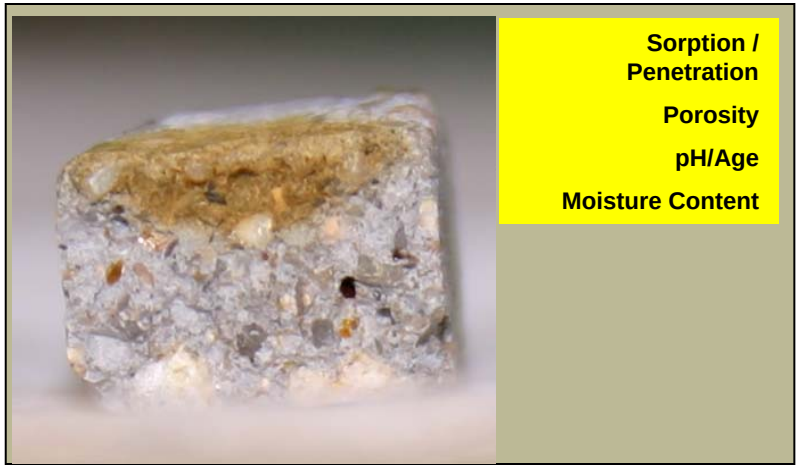
Developed total internal reflection fluorescence microscopy system to image single fluorophores, developed non-equilibrium biomolecular molecular dynamics (BioNEMD) computational capability (Whitman: Nanotech Briefs Magazine's Nano 50 Award)



Calculation of the time required for DNA molecules at 1 fM to diffuse to a sensor surface versus sensor size.

Threat Agent Science

Environmental Fate of Agents

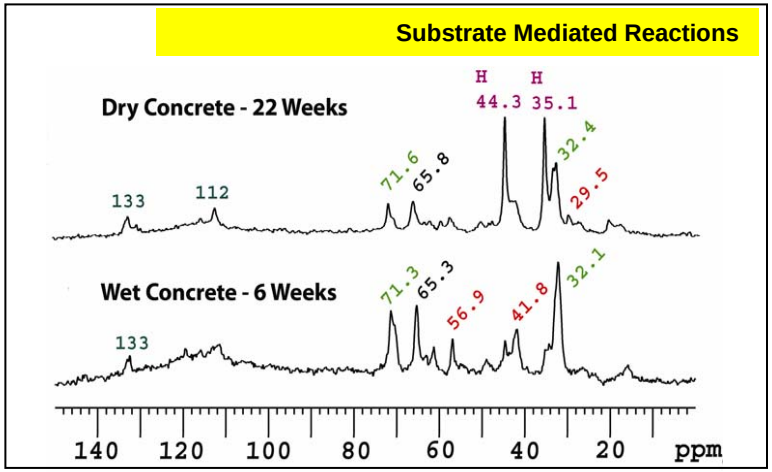


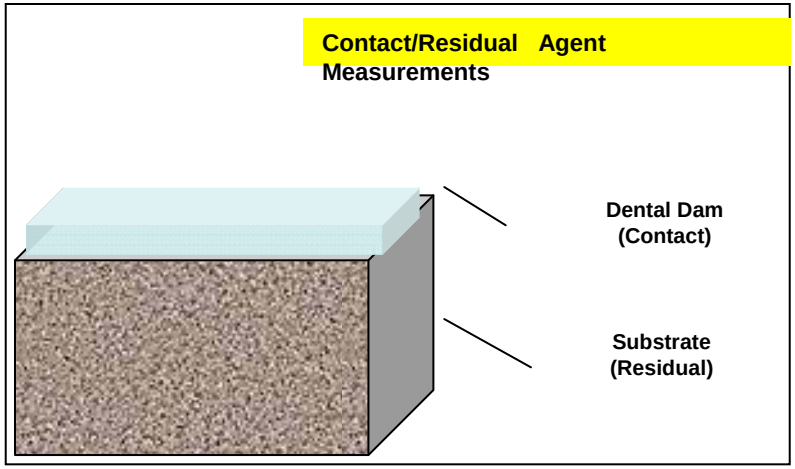
Sorption / Penetration

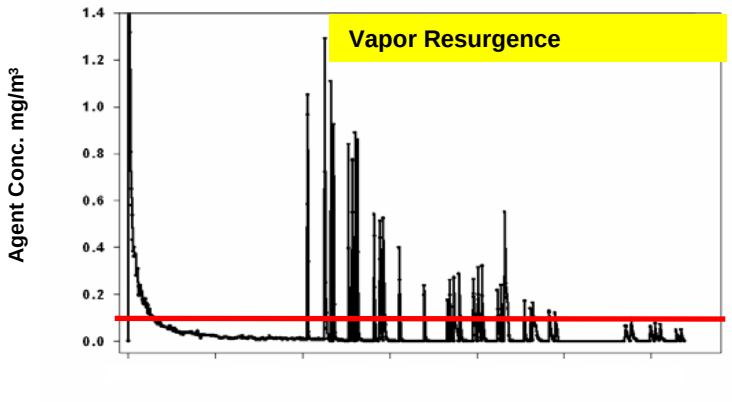
Porosity

pH/Age

Moisture Content

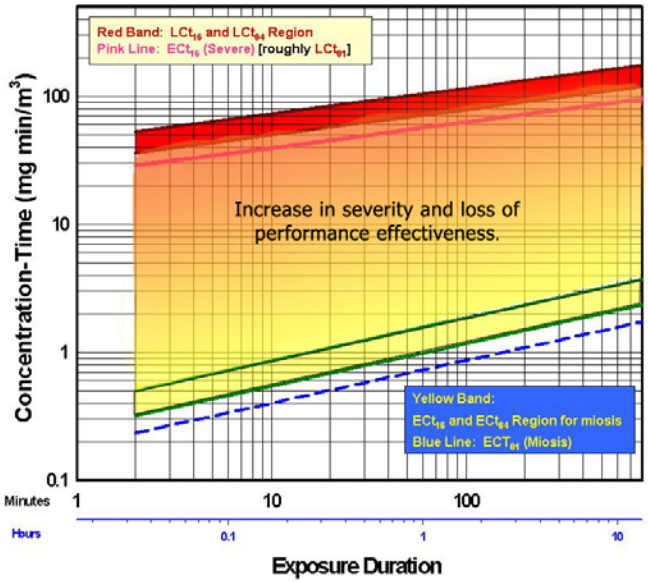






Threat Agent Science

Low-Level Chemical Agent Exposure Effects



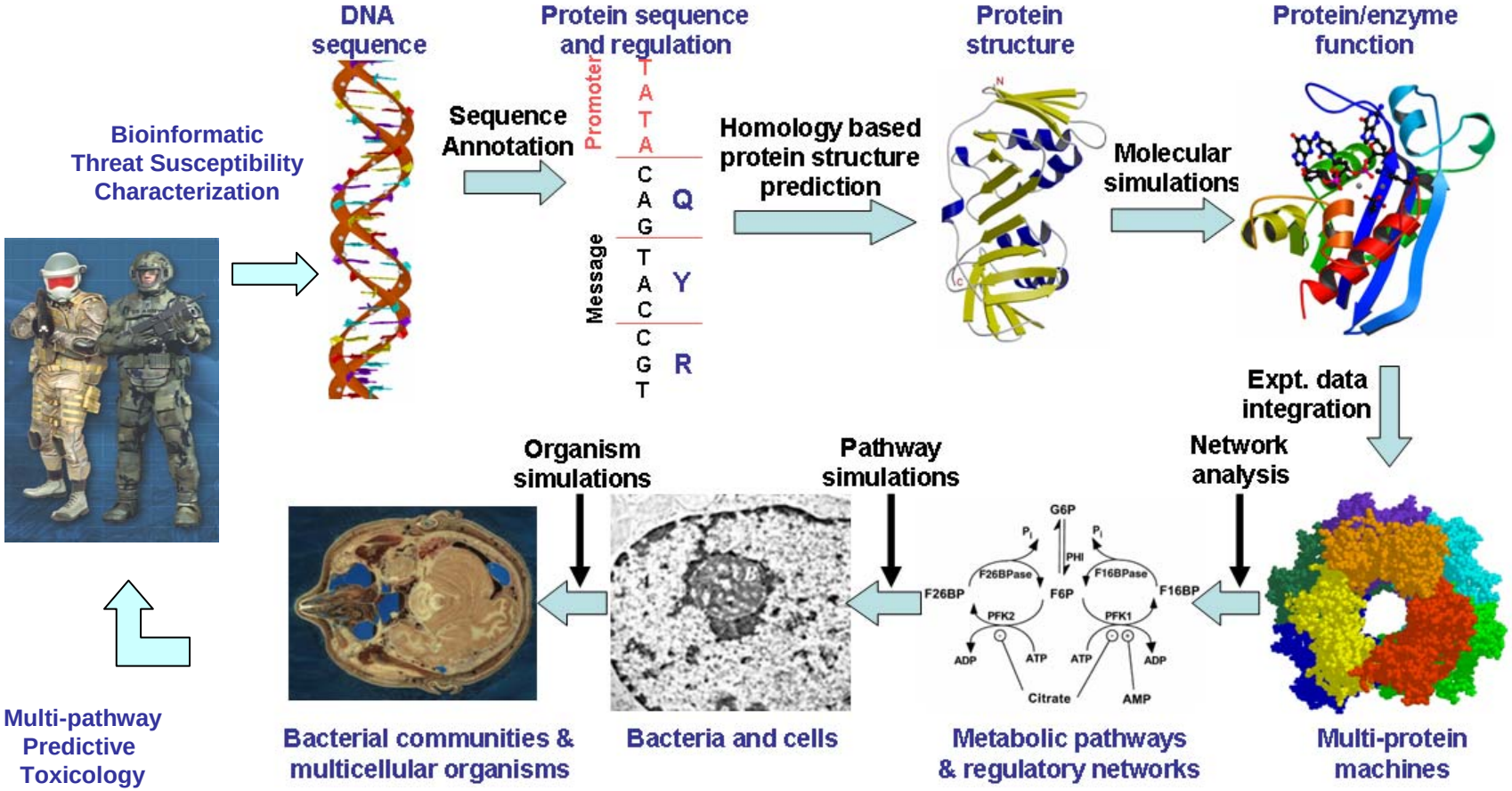
AGENT	CONFIDENCE IN ESTIMATES					
	PCV—Lethal	PCV—Severe	PCV—Mild	PCL—Lethal	PCL—Severe	PCL—Mild
GA						
GB						
GD						
GF						
VX						
HD						

KEY: ■ no estimate; ■ low; ■ high; ■ moderate; ■ moderately low

Science-Based Exposure Standards for Deployed Forces

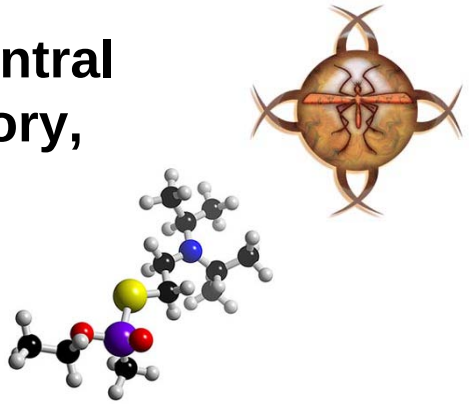
Threat Agent Science

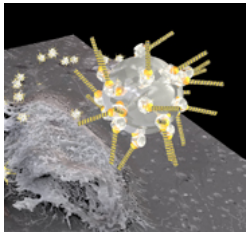
Computational chemistry and biology enables full spectrum real time response



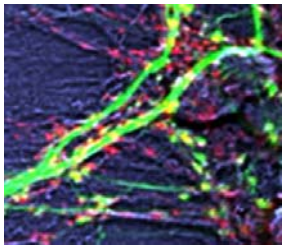
Cognitive Science Impacts on CBD and the Warfighter

- **Chemical / biological threats target central nervous system (CNS) to impair sensory, motor and cognitive function**
  - Biological neurotoxins
  - Chemical nerve agents
  - Nano-enabled?

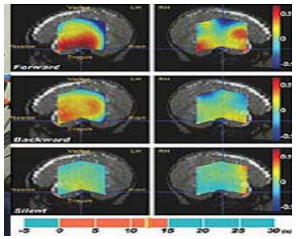




- **Warfighter performance studies – "cognitive readiness"**
  - Understanding cognitive functions under stress during CW/BW event
  - Understanding molecular processes of neuron and brain function after exposure CW/BW agent



Neurons grown in culture and labeled to measure plasticity in a living system. (courtesy Liu Laboratory, MIT)



Hitachi – prototype allows simple control of switches with thoughts by monitoring blood flow associated neuron firing

Non-Invasive Blood Monitoring

Summary

- User's needs and priorities are met by providing timely scientific information and technology transitions
- Processes are in place that find and fund sound science and innovative approaches from concept to advanced development including international collaborations
- Test and evaluation methodology and capability development and procedures for FDA approval are an integral part of the S&T program
- Projects align with spiral upgrades and transition technologies to meet S&T needs of acquisition programs

Words for thought…

"New ideas pass through three periods:

- ✓ *It can't be done.*
- ✓ *It probably can be done, but it's not worth doing.*
- ✓ *I knew it was a good idea all along !"*

— Arthur C. Clarke

"If we knew what we were doing, it wouldn't be called Research."

— Albert Einstein

Questions?