DARPA Update

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Protecting a Worldwide Deployed Military

[Map showing regions with heading labels NORTHCOM, SOUTHCOM, AFRICOM, CENTCOM, PACOM, and EUCOM.]
Scalable, high capability, fully automated CBRNE early detection systems remain a grand challenge for national security

SIGMA+ aims to develop and demonstrate a transformative CBRNE early detection system by leveraging advances in sensing, data fusion, analytics, and social sciences

Distribution Statement “A” (Approved for Public Release, Distribution Unlimited)
Extensive testing and integrated system models will validate capabilities and optimize deployments

- Sensors, algorithms, and network: Unit testing and procedures
- Integrated system models: Simulate and optimize deployments
- Analyst and operator teams: Form baselines, actively tests system, vet adversary behavior models
- Real deployment data, simulations, and experiments: Validate system performance

Distribution Statement “A” (Approved for Public Release, Distribution Unlimited)
**Problem:** The spread of disease is caused by people who are contagious prior to developing symptoms.

If contagion can be predicted and prevented prior to symptoms, then outbreak of infectious disease can be forecast and mitigated.

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**Goal:** Discover Prognostic Biomarkers that Predict if a Person Will Become Contagious

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Ascertain Disease Severity: Advanced Ultrasound Diagnostics

Goal: Automated ultrasound diagnostics platform to identify & treat acute respiratory distress syndrome (ARDS)

Hand-held portable Ultrasound

Wave patterns descriptive of ARDS stage & prognostic of treatment strategies

Automated diagnosis of Acute Respiratory Infection (ARI):
- Use by minimally trained individuals
- Simple front end user interface
- Platform completes ARI diagnosis and defines severity

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Program Goal: Field-portable, molecular detection platform to enable rapid pathogen detection and diagnostics in operational environments

Approach: Integrate sample processing, genomic amplification, array hybridization and analysis into a portable microfluidics system

- Disposable microfluidics card with on-card lyophilized reagents and integrated sample prep
- Sample-to-answer in 45-60 minutes

Key Attributes

- High resolution of genetic signatures
- Robust operation
- Compact size (handheld)
- Very fast PCR (15 minutes)
- Low power consumption
- Modular reagent/consumables kits with long shelf life (1 year)
- Ease of operation (seeking CLIA waiver)
- Cloud connectivity – results by Bluetooth and WiFi

Rapid Analysis Molecular Platform (RAMP)

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Rapid Analysis Molecular Platform (RAMP)

1. Collect Sample & Load

2. Analyze

Lysis → RT → PCR → Remove primer → Hyb → Wash → Image

45 - 60 minutes

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How do We Continuously Sense Disease Status to Enable Early Treatment?

Problem: we need highly precise, specific sensing within the body

Nanosensors are cleared from the tissue or taken up by cells if injected as nanoparticles

Solid, hard, sensor platforms are encapsulated by collagen and “walled-off” from surrounding tissue and function poorly

Flexible, tissue integrating sensors become part of the tissue they are sensing for long-term monitoring.

Solution: Profusa tissue-integrating sensors provide long term, continuous physiological monitoring.
Continuous Physiological Monitoring: Profusa

Performers will develop implantable multi-analyte biosensors to continuously monitor:
- Metabolites (oxygen, lactate, glucose)
- Ions (potassium, sodium, chloride, calcium)
- Blood gases (oxygen, pH, bicarbonate)
- Dehydration markers (urea, creatinine, sodium)

1. To make a measurement, near infrared light from the reader is shined through the skin to excite the sensor.

2. The sensor contains fluorescent molecules that are sensitive to analyte concentrations \textit{in vivo} (e.g., glucose). Fluorescent light emitted by the sensor is correlated with analyte levels.

3. The fluorescent signal from the sensor travels to the surface of the skin, captured by the reader. The data acquisition process takes seconds.

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H1N1 Pandemic: 2009-2010

Vaccine shipping began

2009 pandemic H1N1
New US cases
reported weekly

60M (1 in 5) affected
Vaccine averted 1.6% potential flu cases

Borse et al, CDC, 2013
Humoral and cellular immunity without viral vectors
No vector-based immune response on re-administration
Sequence-matched to circulating strains
Multi-antigen expression
Rapid, low-cost, and scalable production
Gene Transfer Platform for Anti-Infective Antibodies

- Immediate, transient expression of multiple monoclonal antibodies (mAbs)
  - Rapid discovery of potent human mAbs
- No vector-based immune response on re-administration
- Transfer of optimal humoral protection
  - Broadly neutralizing or optimized cocktail
- Rapid, low-cost, & scalable production

Protective mAbs \[\rightarrow\] mAb-encoding nucleic acids
Overview of Pandemic Prevention Platform (P3) Program

Develop a functionally integrated platform to deliver pandemic prevention treatments in <60 days

Pandemic Outbreak
Any Virus

Grow Virus
Find Antibody
Evolve Antibody
Manufacture
Deliver

P3
Existing Technology
P3
Existing Technology
P3

60 days to 20,000 doses

Target Product Profile:
- Rapid Response – provide protection in <3 days
- Transient – lasting for months, not years
  - Not a replacement for vaccines
  - Prophylactic for temporary protection before a vaccine is available or elicited an immune response

Prophylactic to Prevent Pandemic

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• 4 years of program funding
• Teams will demonstrate the ability to achieve the program goals by:
  • Capability demonstrations – end-to-end pressure test to achieve the 60 day timeline – tested up to 5 times
  • Phase I clinical trial – to demonstrate manufacturing & safety and efficacy of the final product in human clinical trial

Program based on antibody gene-transfer using DNA, RNA or AAV vectored antibodies