High Throughput Discovery and Verification of Biomarkers for Biodefense

LDRD
LABORATORY DIRECTED RESEARCH & DEVELOPMENT

Sandia National Laboratories

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Project goals

- Develop a high-throughput platform that automates multidimensional processing, mass spectrometry for µl-volumes blood analysis to enable multiple time point analysis of blood for identification of biomarkers.
- Meet gold standard verification criteria on chip for new multiplex immunoassays with improved on-chip preconcentration and detection.

Problem

Early detection of exposure and infection to bio-warfare agents is a most urgent, unresolved issue

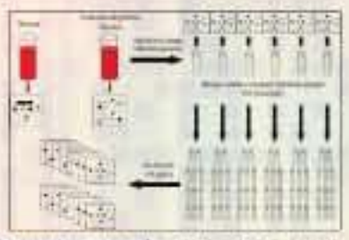
Need: Early-stage biomarkers of infection/exposure to reduce impact of outbreaks/bioterrorism attacks

→ exponentially improved survival rate
→ rapid triage, eliminate "worried-well"
→ monitor efficacy of therapeutics and vaccines
→ cell culture and DNA analysis are not adequate

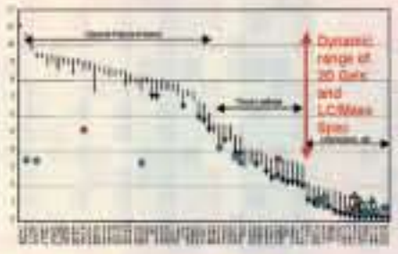
Cutting-edge diagnostics devices have no practical value without biomarkers

No discovered & validated early-stage biomarkers (BM) for infectious diseases

Why? Fundamental limitations are technical:
Complexity of proteome — Low abundance of relevant proteins
High background — Minute post-translational modifications
and biological — Person-to-person variation



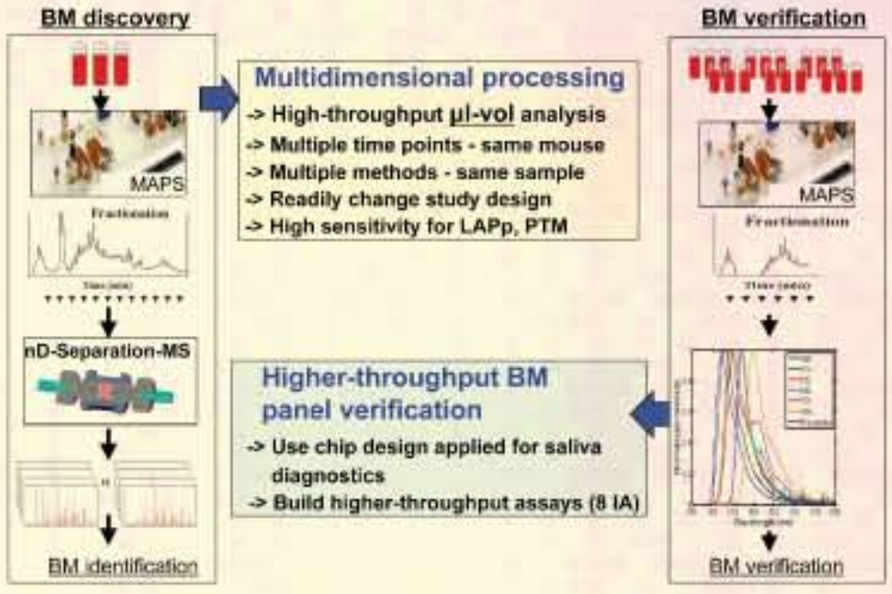
Current approach ~ 66 gels/sample
LABORATORY
↓
CLINICAL TRIAL
~100,000 gels/multi time-point



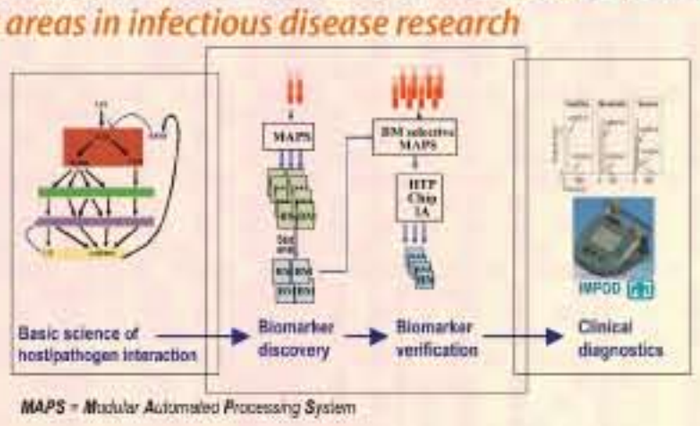
Key proteins are:
→Currently lost / under-sampled
→Difficult to validate due to costly, inadequate sensitivity assays

Approach

Differentiating features of our technology

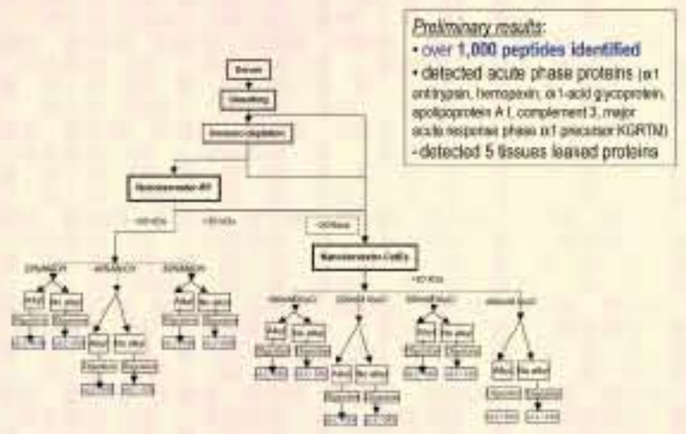


Biomarker discovery and verification will employ expertise in two strategic areas in infectious disease research



MAPS = Modular Automated Processing System

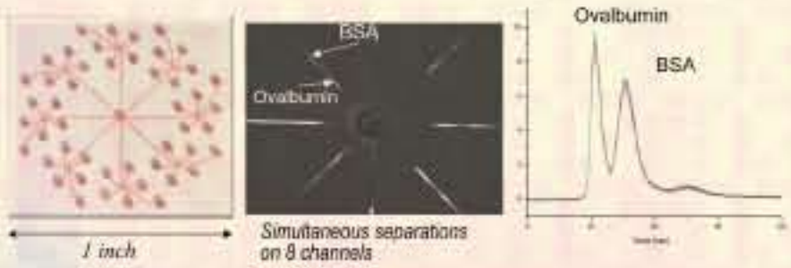
Toward more-comprehensive serum analysis



Results

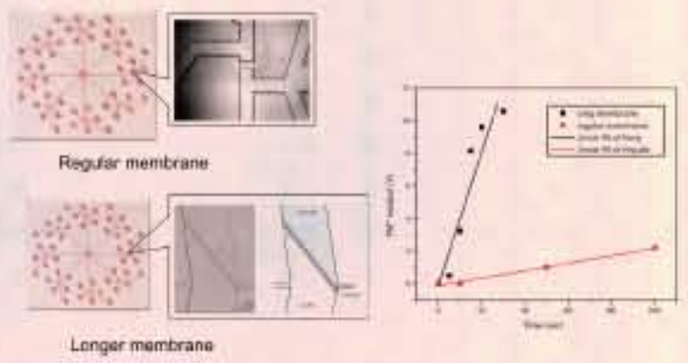
Towards higher throughput biomarker verification

Multiplexed + Faster + Higher sensitivity



- **8 module device** = 8 x (preconcentration + gel separation)
- Prototype electrode plate drives fluids in **49-well** manifold

New design with longer membranes enables 10x faster, 10x higher ratio concentration



Significance

- Early-stage biomarkers will enable rapid/large-scale screening and diagnosis during bioterror attacks
- High-sensitivity analysis of microliter-volumes of serum samples facilitates proteomics studies of infectious diseases in animal models.
- Multi-time points analysis enables reduction of false positives/negatives and control of large phenotype variations.

Potential Users: Pharmaceutical companies and universities invested in clinical studies of infectious disease mechanisms, therapeutics, biomarker discovery and validation

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