Microscale Immune Studies Laboratory (MISL)

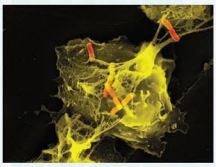
Sandia National Laboratories
PI: Anup Singh, PM: Glenn Kubiak

LDRD
LABORATORY DIRECTED RESEARCH & DEVELOPMENT

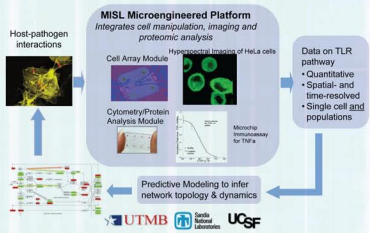
The MISL Grand Challenge

To create an integrated single-cell manipulation and interrogation platform and predictive models to provide molecular- and cellular-level understanding of innate immunity signaling pathways with unprecedented speed, resolution, sensitivity, and multiplexing

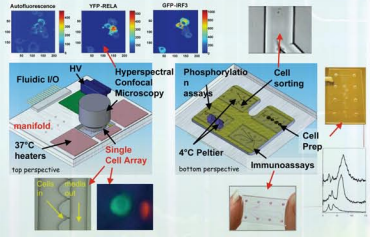
The benefits will be:
- Key discoveries in the understanding and application of innate immunity to anticipate, detect and counter biothreats
- An enabling tool for high-throughput biological pathway studies – also applicable to cancer, asthma, cell differentiation, and microbial communities



MISL uses a Systems Biology approach for the elucidation of cellular signaling in innate immunity

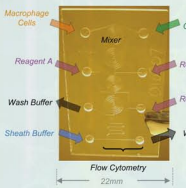


Chips to sort cells, and measure translocation, phosphorylation and cytokines being integrated into a single platform

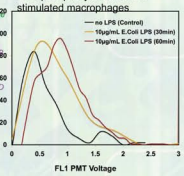


Microfluidic Chips enable assays with single-cell resolution

Microchip for phosphorylation assays



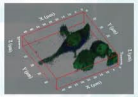
ERK phosphorylation in LPS stimulated macrophages



- Chip allows entire experiment to be performed in one chip (LPS challenge, fixing, permeabilization, addition of antibody and measurement)
- Chips allow single cell resolution

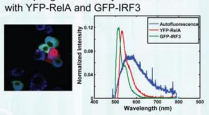
Hyperspectral Imaging & MCR analysis allows 3-D time-resolved imaging

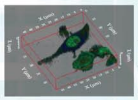
Macrophages infected with *E. coli*



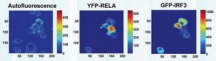
Full image

Macrophages transiently co-transfected with YFP-RelA and GFP-IRF3



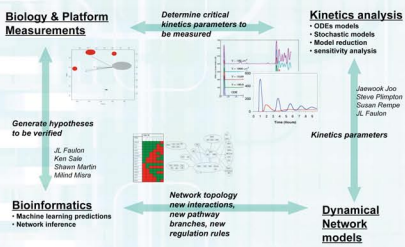


Top of image removed to expose internalized *E. Coli*



Ability to detect autofluorescence greatly improves accuracy of imaging

Computational modeling integrates biology and microfluidic platform results



The Impact of MISL Project

MISL will revolutionize the way host-pathogen interactions are studied, enabling applications that require high sensitivity detection, rapid and high throughput analysis, and understanding at the systems level.

- In work relevant to homeland security, MISL will
  - Address biothreat awareness and characterization
  - Provide next-generation capabilities for new fingerprint technologies
- For biosecurity, biosurveillance and public health, MISL will develop tools for programs such as
  - Risk assessment
  - Terrorist biothreat use
  - Pre-syndromic infectious disease analysis
- In national defense, MISL will
  - Identify biomolecular markers to assure troop readiness
  - Provide next-generation device capabilities for battlefield diagnosis

A Multi-Disciplinary Team

Biology Core Team:
Tony Martino – Coordinator
Steve Branda
Cathy Branda
Bryan Carson
Todd Lane
Jens Poschet
Roberto Rebeil
Bryce Ricken
Meiye Wu
Zhaoduo Zhang

UTMB
Allan Brasier

UCSF
William Seaman

Computational Biology Core Team:
Jean-Loup Faulon – Coordinator
Jaewook Joo
Shawn Martin
Steve Plimpton
Susan Rempe
Ken Sale

Platform and Detection Systems Core Team:
Anup Singh – Coordinator
Mark van Benthem
Jim Brennan
Susan Brozik
David Haaland
Anson Hatch
Conrad James
Howland Jones
Ron Manginell
Matt Moorman
Kamlesh Patel
Thomas Perroud
Ron Renzi
Mike Sinclair
Nimisha Srivastava
Dan Throckmorton

East Carolina University
Paul Gemperline

UNM
Diane Lidke

Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the United States Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000. SAND2007-5963P CreativeArts 80429.LW.8.07

Sandia National Laboratories