Nano.gov
U.S. National Nanotechnology Initiative

Overview of Resources and Support for *Nanotechnology for Sensors and Sensors for Nanotechnology: Improving and Protecting Health, Safety, and the Environment*

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May 15, 2013
Nanotech2013, Washington, D.C.

www.Nano.gov

Nanotechnology Signature Initiatives

Released February 2010

- Nanotechnology for Solar Energy Collection and Conversion
- Sustainable Nanomanufacturing: Creating the Industries of the Future
- Nanoelectronics for 2020 and Beyond

Released May 2012 with announcement of several other activities related to the Materials Genome Initiative

- Nanotechnology Knowledge Infrastructure: Enabling National Leadership in Sustainable Design (NKI)

Released July 2012

- Nanotechnology for Sensors and Sensors for Nanotechnology: Improving and Protecting Health, Safety, and the Environment

NNI Signature Initiatives

The Nanotechnology Signature Initiatives (NSIs) spotlight areas of national significance that can be more rapidly advanced through focused and closely-coordinated inter-agency collaboration.

The NSIs

- Address R&D gaps within areas of critical national need
  - Identify research *thrust areas*
  - Select *key research targets* associated with near-and long-term expected outcomes
- *Leverage* skills, resources, and capabilities among multiple NNI agencies to maximize scientific and technological progress
- Provide a forum for communication and *ongoing assessment* of direction and progress
- *Catalyze* communities of practice and public private partnerships to accelerate commercialization

Nanotechnology for Sensors and Sensors for Nanotechnology: Improving and Protecting Health, Safety, and the Environment

Agencies involved: CPSC, DOD/DTRA, EPA, FDA, NASA, NIH, NIOSH, NIST, NSF, USDA/NIFA

Goals: Support research on nanomaterial properties and development of supporting technologies that enable next-generation sensing of biological, chemical, and nanoscale materials.

Thrust Areas:

- Using nanotechnology and nanoscale materials to build more sensitive, specific, and adaptable sensors in order to overcome the technical barriers associated with conventional sensors
- Developing new sensors to detect engineered nanomaterials across their life cycles, in order to assess the potential impact on health, safety, and the environment

NSI agencies support nanosensor development and nanomaterials characterization through multiple mechanisms.

Dedicated funding programs and facilities to make and test materials and devices.

- **IMAT, NCL, CNST**
- **Test beds, materials, databases and reference libraries**

Regulatory and technical guidance on standards and requirements for sensors and materials.

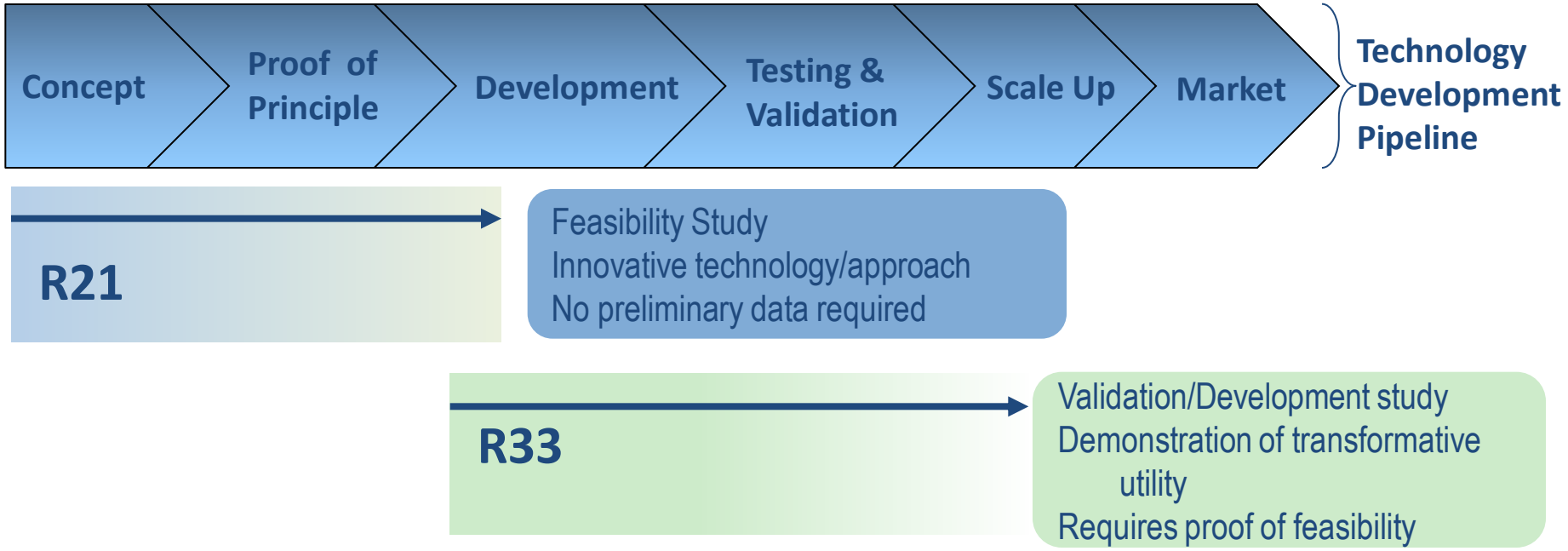
- **CPSC, EPA, NIOSH, FDA**

Identify emerging needs and changing conditions that will drive sensor and material development and partner with the community to meet these needs.

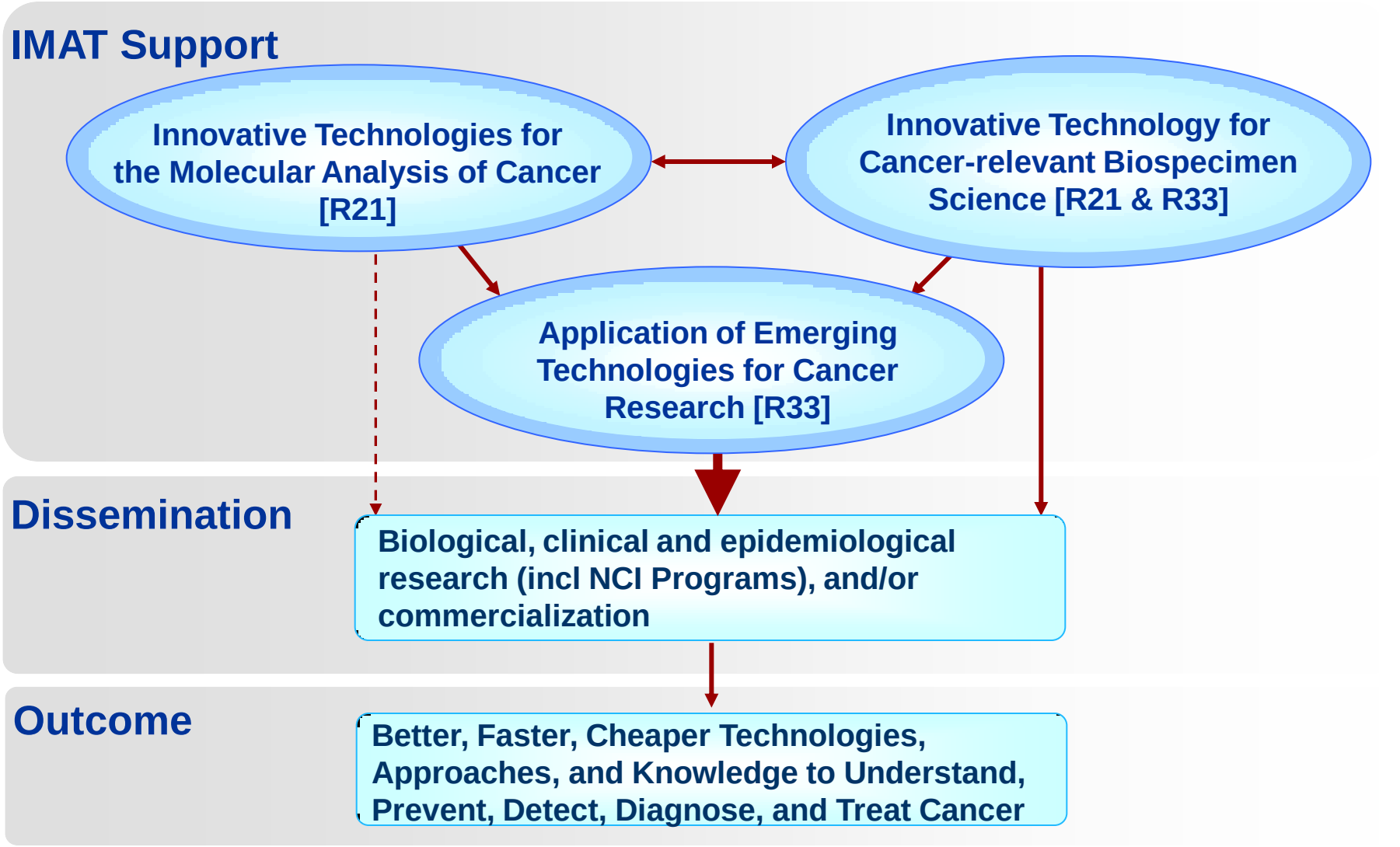
Innovative Molecular Analysis Technologies Program (NIH/NCI)

Program Mission:

To support the development, maturation, and dissemination of novel and potentially transformative next-generation technologies through an approach of balanced but targeted innovation in support of clinical, laboratory, or epidemiological research on cancer.



IMAT Development Pathway



Life Cycle of an IMAT Technology Development Platform

Separate Application Process

R21/Phase I

Mechanism:

Exploratory/pilot phase; requires innovative technology/approach; no preliminary data required

Requirements:

- Description of study
- Relevance to cancer
- Quantitative milestones
- Truly novel tool/capability
- Improvement over state-of-the-art

R33/Phase II

Mechanism:

Developmental/validation phase; requires significant feasibility data

Requirements:

- Plan for developing the technology to be useful to a category of cancer researchers or clinicians
- Description of potential impact for the field
- Description of completed milestones or evidence of technical feasibility

Technology Dissemination via:

- NCI Programs and Initiatives
- Collaboration
- Publication
- Licensing
- Commercialization

Technology Tools for Researchers:

- **Entirely new –** Open new areas of research
- **Better –** improved specificity/ selectivity/ sensitivity
- **Faster –** faster processing, massively multiplexed
- **Cheaper –** simpler or more robust design, field-ready

Application Information

Funding Instrument	**R21 & R33 Grants**
Application Types Allowed	• New • Resubmission
Award Budget	• R21: Direct costs are limited to $200,000 per year, with no more than *$500,000 in all direct costs over a 3-year period* • R33: Direct costs are limited to $300,000 per year, and *$900,000 in all direct costs over a 3-year period.*
Award Project Period	The total project period is allowed for up to 3 years for all awards
Letter of Intent Due Date	**August 20, 2013**
Application Due Date(s)	**September 20, 2013, by 5:00 PM local time of applicant organization.**
Earliest Start Date(s)	**July 2014**

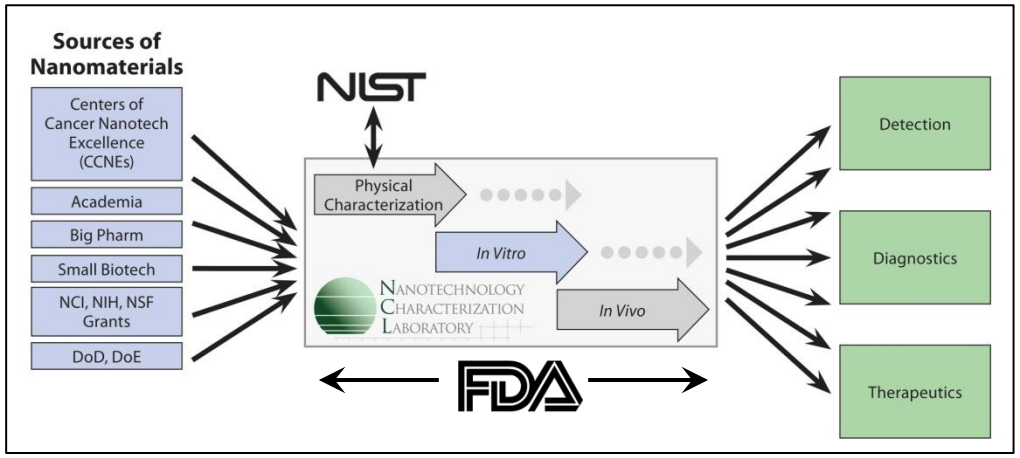
Nanotechnology Characterization Laboratory

Interagency collaboration among NCI, NIST, and FDA.

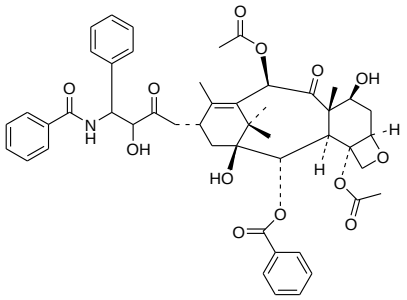
The lab's mission is to accelerate the translation of promising nanotech cancer drugs and diagnostics.

NCL's performs preclinical characterization of nanomaterials and develops standards and protocols for characterization.

- Physico-chemical characterization, *in vitro* assays, *in vivo* testing



Physico-Chemical Characterization

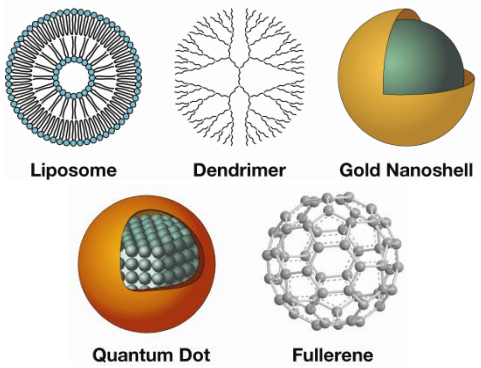


Small molecules

- Elemental analysis
- Mass Spec
- NMR
- UV-Vis
- IR
- HPLC
- GC
- Polarimetry

Physicochemical Parameters

- ***Composition***
- ***Physical properties***
- ***Chemical properties***
- ***Identification***
- ***Quality***
- ***Purity***
- ***Stability***



Nanomaterials

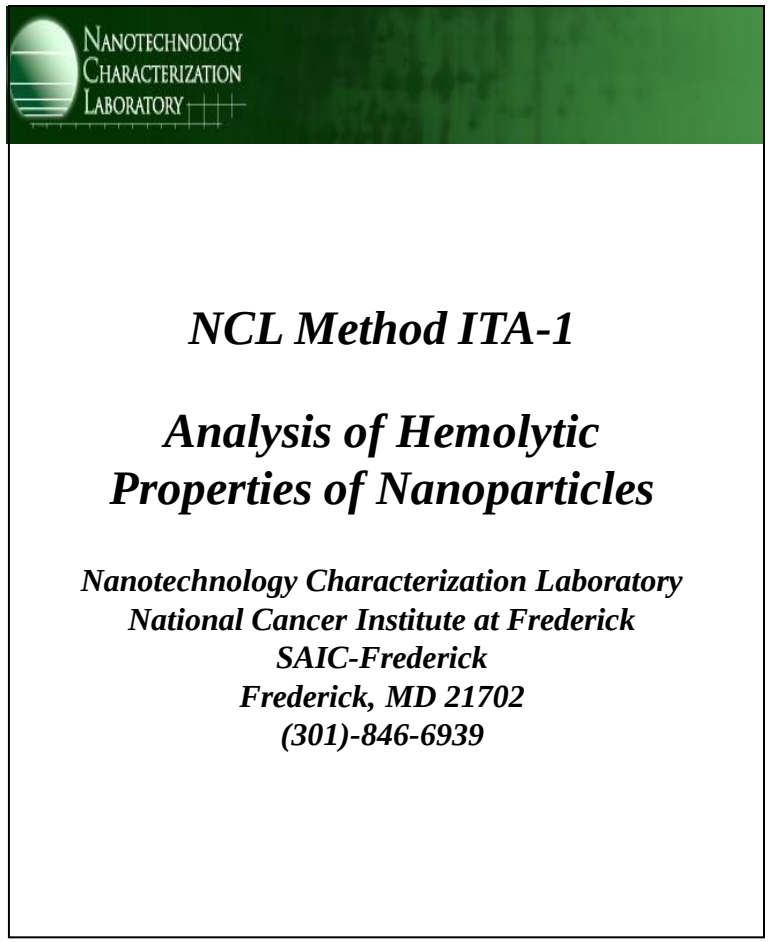
- Microscopy (AFM, TEM, SEM)
- Light scattering (Static, Dynamic)
- SEC, FFF
- Electrophoresis (CE, PAGE)
- Zeta sizer
- Fluorimetry

Same parameters – different/additional characterization methods

http://ncl.cancer.gov/working_assay-cascade.asp

In vitro Assays

- **Sterility**
  - Bacterial/Viral/Mycoplasma
  - Endotoxin
- **Cell Uptake/Distribution**
  - Cell Binding/Internalization
  - Targeting
- **Blood Contact Properties**
  - Plasma Protein Binding
  - Hemolysis
  - Platelet Aggregation
  - Coagulation
  - Complement Activation
  - CFU-GM
  - Leukocyte Proliferation
  - Macrophage/Neutrophil Function
  - Cytotoxic Activity of NK Cells
- **Toxicity**
  - Phase I/II Enzyme Induction/Suppression
  - Oxidative Stress
  - Cytotoxicity (necrosis)
  - Cytotoxicity (apoptosis)



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Standards, protocols and best practices

ASTM standards based on NCL developed tests

- E2524 (hemolysis), E2525 (macrophage colony growth), E2526 (cytotoxicity)

Characterization protocols and publications available at
http://ncl.cancer.gov/

Lessons Learned Workshop:

- NIH Campus, September 20, 2013
- Presents negative results not available elsewhere.
- One-on-one discussions on specific materials and experiments

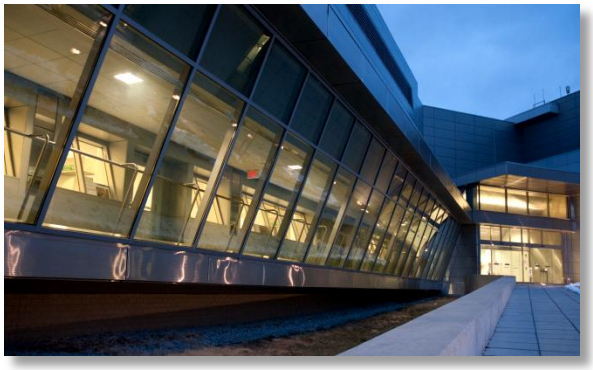
Contact information:

301-846-6939
ncl@mail.nih.gov

NCL Nanotechnology Characterization Laboratory

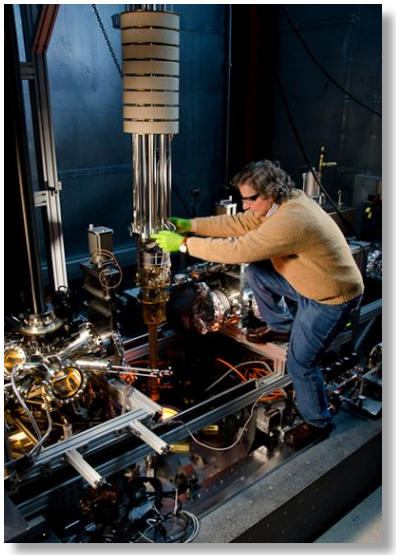
NCI Alliance for Nanotechnology in Cancer

NIST Center for Nanoscale Science and Technology (CNST)



- NIST's nanotechnology user facility.

  Provides rapid access to tools needed to make and measure nanostructures, with emphasis on helping U.S. industry.
- In the ***NanoFab***, researchers can us a commercial state-of-the-art tool set at economical hourly rates, along with help from a dedicated, full-time technical support staff.



- In the ***NanoLab***, researchers get access to the next generation of tools and processes through collaboration with our multidisciplinary research staff, who are developing new measurement and fabrication methods in response to national nanotechnology needs.
- The CNST serves as a hub linking the external community to the nanotechnology-related measurement expertise at NIST (nano@nist.gov)

The CNST NanoFab

A national, state-of-the-art, shared resource for the fabrication and measurement of nanostructures:

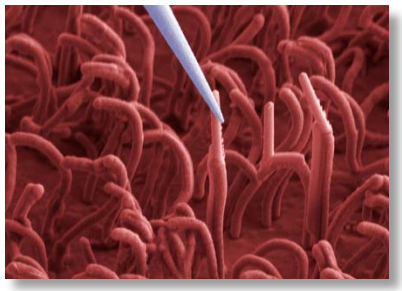
- 60,000 ft^2 (5600 m^2) of labs and cleanroom
  - 19,000 ft^2 (1800 m^2) cleanroom; 8,000 ft^2 (750 m^2) at class 100
  - Open (staffed) weekdays from 7 am to midnight
- Leverages the expensive tools needed for nanotechnology through cost sharing (charged "*a la carte*")
  - About 90 major tools, including advanced lithography (e-beam x2, ASML stepper), microscopy (FE-SEM, FIB, TEM)
- Staffed with talented technical team (15) who train and assist users, operate and maintain the tools, and develop and control the processes
- Connects external researchers to extensive measurement resources in the NIST Laboratories and Centers

Using the CNST NanoFab

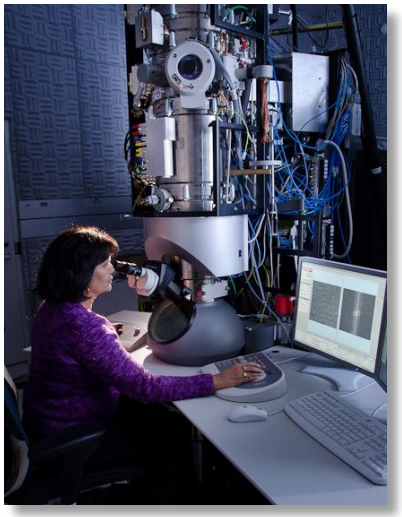
- Shared-use operation based on cost-reimbursement
  - Modeled after US National Nanofabrication Infrastructure Network (NNIN) supported by National Science Foundation (NSF)
- Open to all, including **industry**, government, and academia
- Rapid access: application to orientation in a few weeks
- Charges based on operating costs, similar to charges at NNIN
- Researchers may apply for reduced rates
  - If project advances CNST mission, rates similar to NNIN-NSF “academic” rates
- The NanoFab will train researchers in tool use (at cost)
  - Alternatively, work can performed by staff at additional cost
- Users maintain IP rights for sole and joint inventions
- For more info, contact the NanoFab Manager, Vincent Luciani (Vincent.Luciani@nist.gov)

The CNST NanoLab

- Project Leaders developing measurement and fabrication capabilities, with current priorities in:



  - **Future Electronics:** Nanoscale devices, architectures, interconnects
  - **Nanomanufacturing and Nanofabrication**: Top-down and bottom-up fabrication and assembly
  - **Energy:** Conversion, storage, and transport at the nanoscale
- Provides access to next-generation measurement tools and fabrication methods through ***collaboration*** with the Project Leaders
- Designed to be agile: priority areas will change with NIST and national nanotechnology needs
- Integrated tightly with the NanoFab, providing expert consultation and beyond-state-of-the-art measurements
- Complements and supports the NIST metrology and engineering laboratory programs



Sensors and the Environment – EPA Interest in Nanotechnology

Test materials: Chemical emissions from air pollution sources

- *e.g.*, motor vehicle exhaust, diesel exhaust, new fuels (e.g., biofuels), forest fires, prescribed agricultural burns
- Field studies at specific industrial sites
- Large network of existing monitoring locations coordinated by regional offices
- Example target analytes are benzene, formaldehyde/acrolein, and methane

Funding opportunities:

- National Center for Environmental Research (NCER): http://epa.gov/ncer/
- Small businesses: http://epa.gov/ncer/sbir/

David Olson, Ph.D.
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National Exposure Research Laboratory
U.S. Environmental Protection Agency

Sensors and Consumers – Consumer Product Safety Commission

Sensors are used in a wide range of consumer products

- Reduce injuries (smoke and CO alarms, gas monitors)
- Monitor health (blood pressure, glucose)
- Monitor home integrity, boundaries and environment (burglar alarms)

Nanosensors in consumer products – improved performance

Acceptance for manufacturers:

- Reliable – The sensor must be reliable to avoid false tripping and drifting over time.
- Low cost – To be competitive in the industry, the sensor must not significant increase the base price of the product.
- Implementation – The sensor must be easy to implement, such as standard power, pin configuration, and hardware.
- Maintenance – The sensor must be low or no maintenance for the manufacturer and the end customer.

Smoke Alarms – The New Era on the Horizon

The standard for smoke alarms will require better detection and less nuisance alarms.

Manufacturers will be forced to shift from standard sensor technology (ionization and photoelectric sensors) to multi-criteria technology.

- Incorporate more sensors for better discrimination
- Explore and use different sensors such as CO, O_2, and CO_2.

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FDA and Nanotechnology

The U.S. Food and Drug Administration (FDA) regulates a wide range of products, including foods, cosmetics, drugs, devices, veterinary products, and tobacco products some of which may utilize nanotechnology or contain nanomaterials.

FDA main website on Nanotechnology:

http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/default.htm

Draft Guidance: Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology:

http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/ucm257926.htm

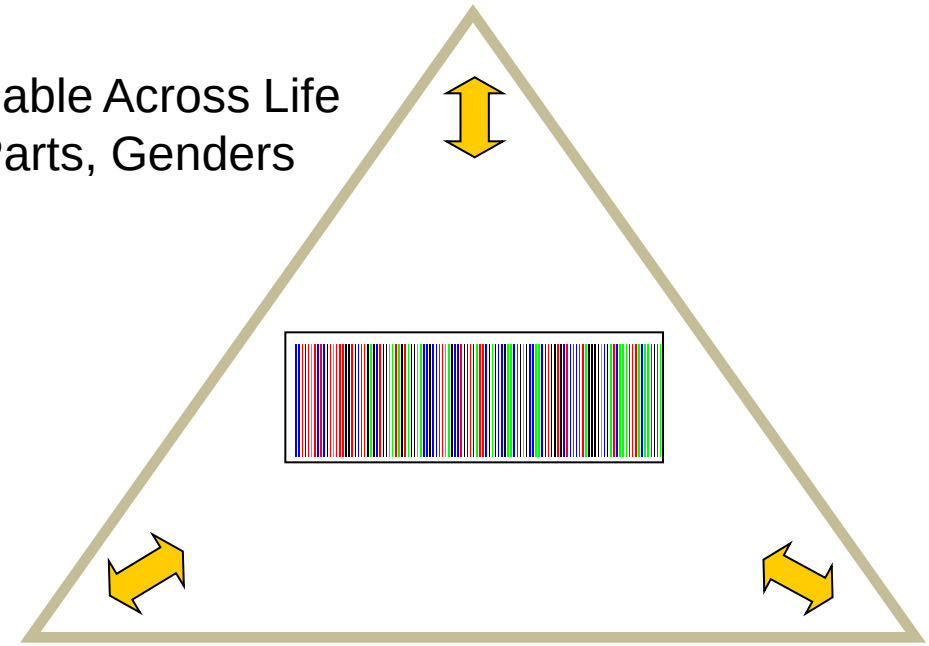
Nanosensors for Healthcare applications are likely to be regulated by the Center for Devices and Radiological Health (CDRH)

CDRH main page:
http://www.fda.gov/MedicalDevices/default.htm

Use of DNA Barcoding in Regulatory Science

A DNA barcode is a short gene sequence used to identify species taken from a standard position in the genome – nucleotides identify the species

DNA Barcodes Invariable Across Life Stages, Processed Parts, Genders



What's in a Name?

Species Identification Matters

- Basic research on evolution, ecology
- Endangered/protected species
- Agricultural pests/beneficial species
- Disease vectors/pathogens
- Invasive species (e.g., in ballast water)
- Environmental quality indicators
- Managing for sustainable harvesting
- Consumer protection, ensuring food quality

Current FDA Barcode Projects

- Fish
- Dirty 22 (insects and rodents)
- Plants
- Bushmeat

Creating the Reference Library

Required Barcode Elements

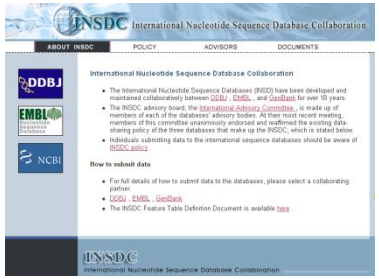
- Taxonomic identification to species
- Voucher specimen ID in standard format
- Name of barcode region (gene)
- Country/Ocean/Sea of origin
- Length, quality, 2 trace files
- Forward/reverse primer sequences, names

Identified Museum Specimens

Extract and Amplify DNA

Sequence DNA

Publish Reference BARCODE Record



Assay Development Using Barcode Database

Difficulty in using traditional barcoding for identification of species food and feed

- Samples contain multiple sources of DNA including multiple animals as well as filth such as feathers, feces, and insects
- Samples are degraded (cooked, processed, or neglected)

Microarray Assay

- 40-80k species in single assay
- Ability to analyze cooked, processed, or mixed samples

Case Study

- Real- Time PCR Assay
  - Develop assay in 2-3 days
  - 3-4 species in single assay
  - Ability to analyze cooked, processed, or mixed samples
  - Results in ~1 hour

In the "not-so-distant" Future

CVM would like to collaborate to develop a hand held device that has the ability to extract DNA, amplify DNA, and identify a species (using PCR, probes or sequence)!

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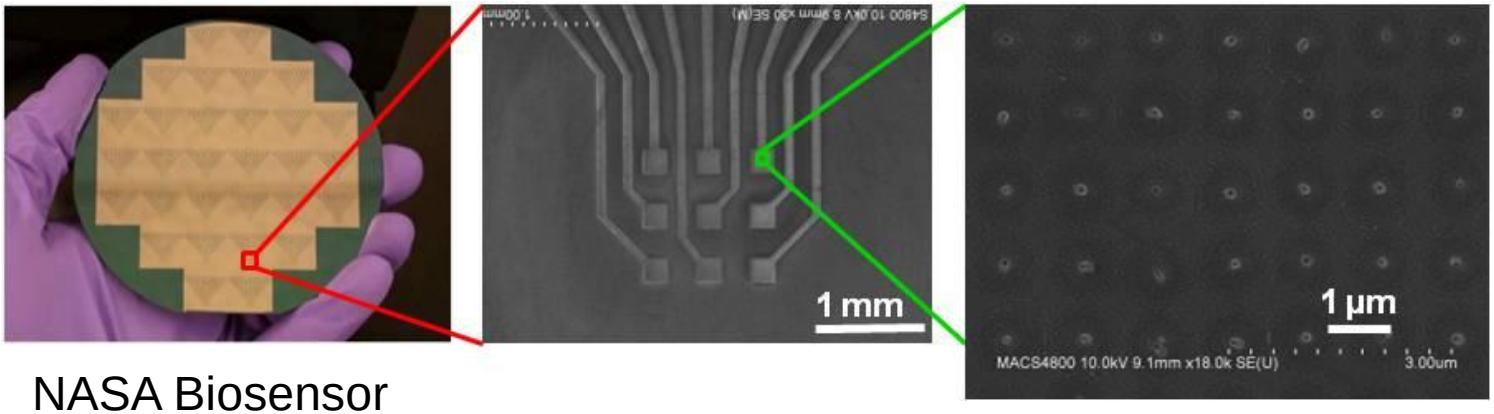
U.S. Food & Drug Administration
Center for Veterinary Medicine

National Aeronautics and Space Administration

The NASA Ames Nanotechnology group focuses on nanomaterials and application development in sensors (chem, bio, rad), miniaturization of instrumentation, electronics, optoelectronics (detectors), energy storage devices, e-paper, e-textile and related areas.

The group has a number of sensor technologies in development, with Technology Readiness Levels from 3 to 5-6 with potential applications to NASA, other agencies and industry.

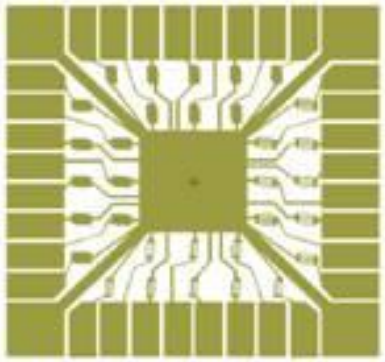


NASA Biosensor

NASA Ames – Nano Chem Sensor (TRL 5-6)

(Government Invention of the Year Award 2012)

- Electronic nose with a powerful pattern recognition algorithm
  - 1 cm x 1 cm chip
  - 32-256 sensor elements
  - Carbon nanotubes, oxide nanowires
  - Gas and vapor detection

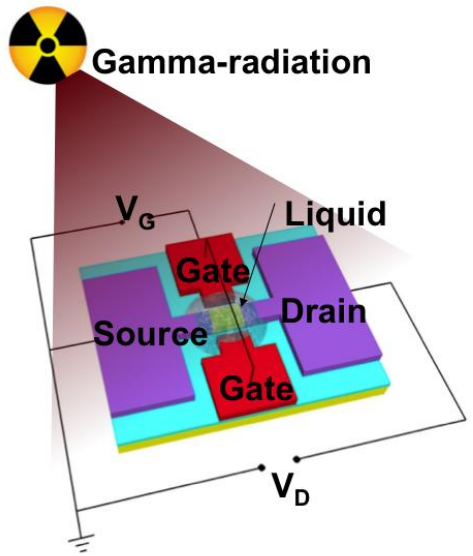


- Rigorously tested
  - ISS air quality monitoring in 2009
  - Field tested for CO detection by Los Angeles Fire Department
  - Munitions monitoring by US Army AMRDEC
  - Hydrazine leak detection by Kennedy Space Center
- Integration into smart phone platform
  - 30 iPhone sensor prototypes delivered to DHS in 2012
  - Simultaneous test in DC, TN and CA
  - Cl_2 and NH_3 detection
  - Networked multiple, geographically distributed sensors

NASA Ames – Nano Radiation Sensor (TRL 3)

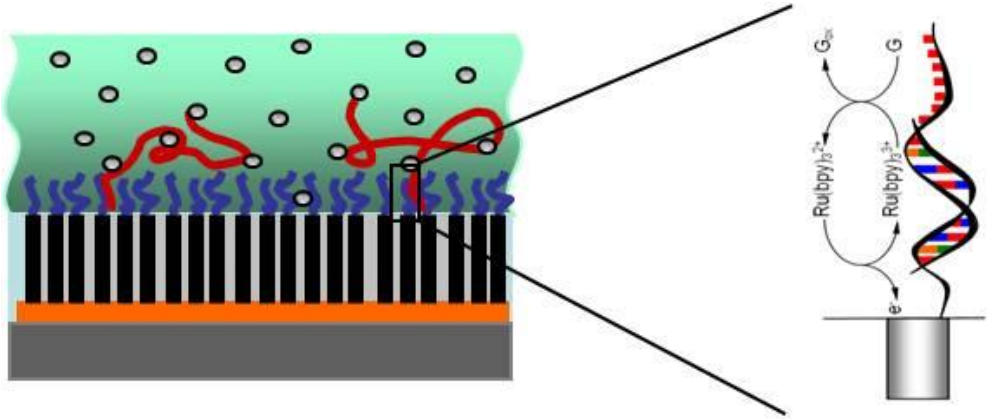
- Adapt chemsensor chip with radiation-responsive nanowires
  - Ge, ZnTe, CdTe, $Zn_xCd_{1-x}Te$, Ni and other oxides
- Develop a 2-in-1 Chem+Rad nanosensors

- Alternative platform: vertical CMOS transistor, silicon technology
  - Replace SiO_2 dielectric with liquid gel
  - Dielectric property changes upon exposure to radiation
- Construct Radiation nose (r-nose)
  - Different liquids have different responses
  - Identify individual radiation threats along with energy levels
  - Demonstrated gamma ray detection with a suitable gel



NASA Ames – Nano Biosensor (TRL 4-5)

- Affinity based sensor, with probe pre-selected for target
- Nanoelectrode array sensor
  - Carbon nanofibers 50 nm diameter on silicon substrate
  - DNA, antibody, protein, aptamer probes on nanofiber tip
  - Electrical impedance measurement
  - Fabrication on 6” wafers
- Sensitive detection of ricin, biomarkers for heart disease shown
- Multiple applications – threat detection, lab-on-a-chip, environmental monitoring, food quality control



Defense Threat Reduction Agency – Mission & Interests

DTRA safeguards the United States and its Allies from global WMD threats by integrating, synchronizing and providing expertise, technologies, and capabilities across all operating environments – it is a defense agency, a combat support agency, and a national asset for countering weapons of mass destruction.

Sensors for radiation, biological and chemical weapons, high yield explosives

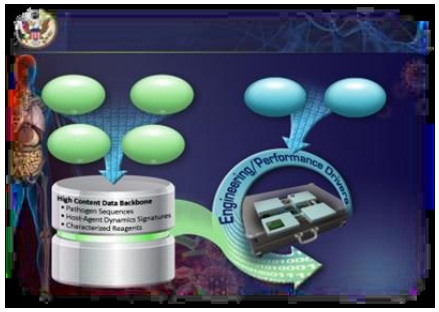
Research to explore novel nano-scale phenomenology for sensing or detection applications

- Sample preparation and handling
- Matrix effects
- Sensing elements

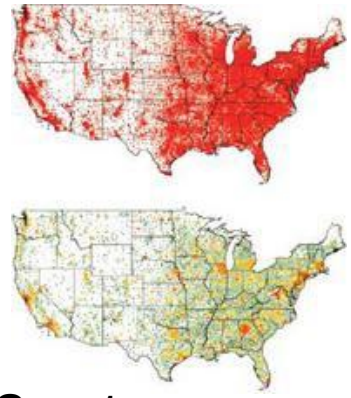
Chem-Bio Defense Program: Chemical & Biological Technologies

Manages and integrates development, demonstration, and transition of timely and effective chemical and biological defense solutions for DOD, while serving as focal point for science and technology expertise

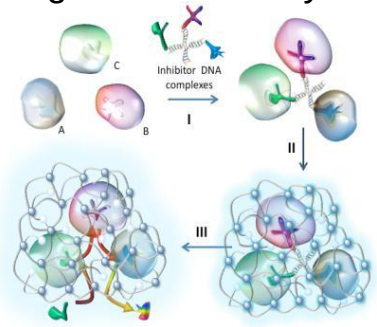
Biological Diagnostics …provide high quality data closer to the point of need



Biosurveillance …obtain timely & accurate insight on current & emerging risks

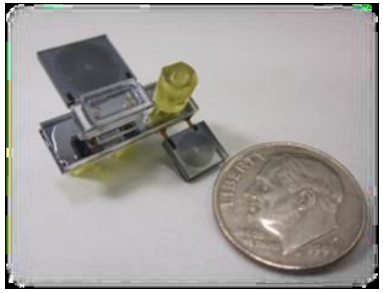


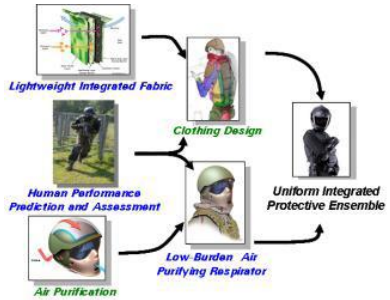
Nanogel-Coated Enzymes



Basic Research
… emphasizes innovation & discovery

Medical Countermeasures
…advancements in regulatory S&T of agile flexible manufacturing and rapid enhanced product development …new avenues of treatment against CB threats





Physical Sciences
… demonstrate integrated capabilities and advanced technologies

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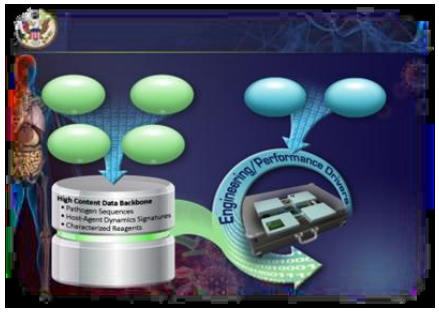

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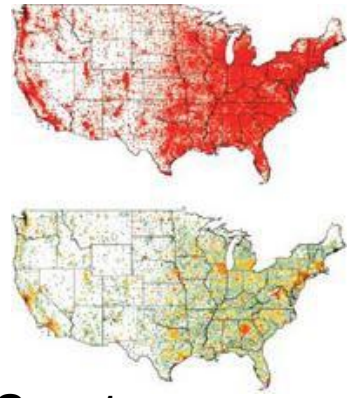
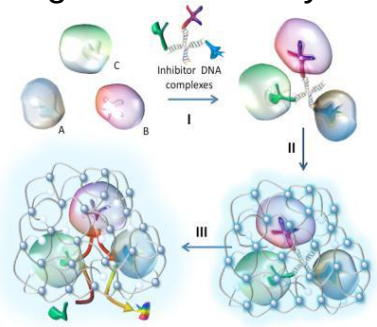


Nanogel-Coated Enzymes



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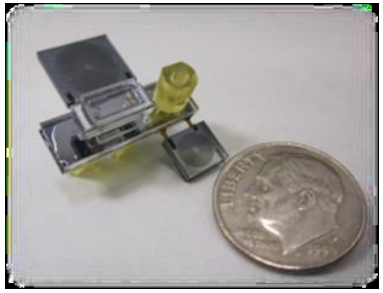

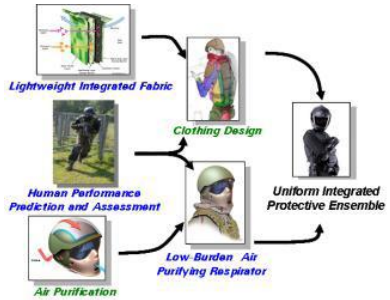

Physical Sciences
… demonstrate integrated capabilities and advanced technologies

USDA-NIFA Nanotechnology Program

Support innovative ideas and fundamental sciences to develop nanotechnology enabled solutions for food security, improved nutritional value, enhanced food safety and biosecurity and increased protection for natural resources, the environment, and agricultural ecosystems.

- Nanoscale-based sensing mechanisms and smart sensors for reliable and cost-effective early detection of insects, diseases, pathogens, chemicals, and contaminants;
- Monitoring physiological biomarkers for optimal crop, animal productivity;
- Minimally invasive field survey tools for agricultural production;
- Precision agriculture technologies including applications of agricultural chemicals and water resources;
- Risk assessment include characterization of hazards and exposure levels, transport and fate of nanoparticles or nanomaterials in crops, soils, etc.

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The NSI member agencies have a variety of resources to support development of nanosensors and research into nanomaterials.

We are looking for partners to develop nanotechnology enabled sensors and models, methods and materials to track and understand the path and disposal of engineered nanomaterials in the environment.

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