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National Institute of Environmental Health Sciences

Grand Opportunity (GO) Program: Engineered Nanomaterials Environmental Health & Safety

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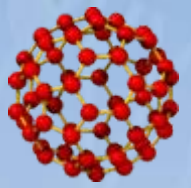
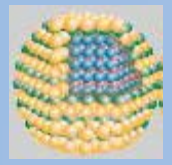
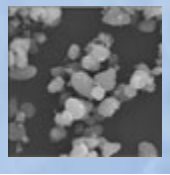
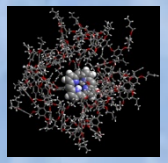
Engineered Nanomaterials (ENMs)

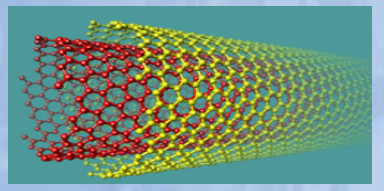


- Nanomaterials are two or three dimensional assemblies of molecular building blocks in nanoscale (1-100 nm) with well-defined structures.
- This extremely small size leads to unique properties: large surface area, high reactivity, great strength and small mass.
- Tunable nature of optical, electrical and magnetic properties.









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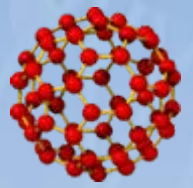
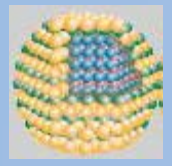
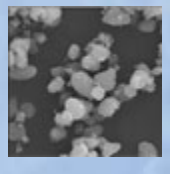
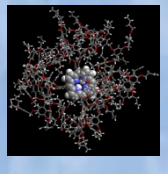
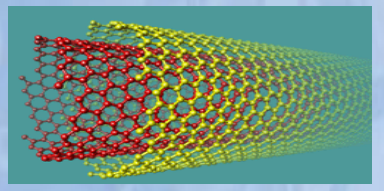


- Carbon-based (fullerenes, SWNT, MWNT)
- Inorganic or metal oxides (TiO2, ZnO, CeO),a
- Metals (Au, Ag, Fe)
- Quantum dots (Cd-sulfide/selenide)
- Surface modifications can lead to thousands of variants









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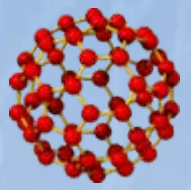
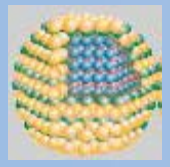
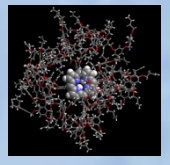
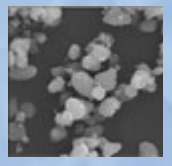
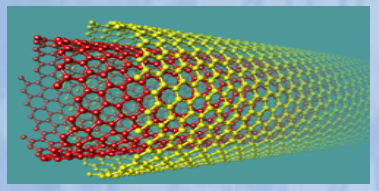


- Diverse industrial applications
  - Electronics, pharmaceuticals, biomedicine, cosmetics, construction, environmental remediation
- Global demand for nanomaterials & nano-devices is projected to be ~$3 trillion by 2015
- Unanticipated exposure and unknown health consequences









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NIEHS- Nano Health Program

- National Nanotechnology Initiative (NNI) in 2001
- NIEHS started extramural research program on health implications ENMs in 2004
- NIEHS issued RFA in 2006 (NCI, NHGRI, NIGMS, NIDCR, USEPA & NIOSH)
- NNI Environmental Health & Safety strategy document in 2008

NIEHS Nanotechnology Team:
David Balshaw, Heather Henry, Sri Nadadur
Sally Tinkle, Nigel Walker

Nano EHS- Challenges

- Nano size range is below barrier cutoffs for portals of entry, can lead to unintended routes of exposure
- Lack of human exposure data
- Lack of production information & use of specific ENMs
- Fundamental mechanisms of biological interactions of nanoscale materials is not known

Nano EHS- Challenges

- Conflicting data from simple in vitro cell viability assay(s)
- A remarkable range of toxic effects were reported for carbon nanotubes both from *in vitro* and *in vivo* studies.
- *Lack of physicochemical characterization information*
- Dose metrics for ENMs
  - Conventional mass-related metrics may not be informative
  - Physical (size, surface area, structure) and chemical properties dictate their biological interactions

Nano EHS- Challenges

- Experimental evidence from in vitro and in vivo studies
  - Comprehensive physical and chemical characterization of ENMs
  - Standardized protocols for reliable and reproducible assays
  - Data validation across different laboratories

Goals of Nano GO Program

- Develop reliable and reproducible methods to assess exposure and biological response/toxicological endpoints for ENMs.
  - *In vitro* and *in vivo* models that can reliably predict biological response and reproducible across the labs using well characterized ENMs
  - Methods that are standardized and adaptable to predict ENMs exposure from different routes and in diverse media.
- Develop guidelines for ENMs environmental health effects and safety.
- Coordinated and integrated research efforts can be accomplished through consortium approach.

Nano GO Schedule

- RFA announcement: March 29, 2009
- Information Meeting: April 24, 2009
- Letter of Intent Receipt: April 27, 2009
- Application Receipt: May 27, 2009
- Review Panel – Dr. Sally Eckert-Tilotta
- Peer Review: July 21-22, 2009
  - 42 applications were submitted
  - 15 applications were not discussed
  - 27 discussed and scored (range of scores: 20-65)
  - 10 applications funded

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Nano GO: Funded Applications

Principal Investigator	Title
Witzmann, Frank	Characterization Methodologies & Proteomics to Assess Carbon Nanotube Exposure
Orr, Galya	Tying Distinct Nanoparticle Properties to Cellular Interactions, Fate and Response
Vulpe, Christopher	Integrated nanoparticle characterization and toxicity assessment
Crandall, Edward	Interactions of engineered nanomaterials with lung alveolar epithelium
Nel, Andre	Predictive Toxicological Paradigms to Establish Inhalation Toxicology Models
Bonner, James	Lung Toxicity of Carbon Nanotubes in Models of Pre-Existing Respiratory Disease
Worden, Robert	Bio-mimetic Microsystem for High Throughput Evaluation of Engineered Nanomaterials
Holian, Andrij	Defining physical characteristics of bioactive nanomaterials
Elder, Alison	Hazard Assessment and Risk Estimation of Inhaled Nanomaterials Exposure
	Detection of engineered nanomaterials in drinking water, food, commercial

Nano GO: Funding Overview

ENMs proposed:

- Metal oxides (TiO2, Mn, Ag, ZnO- native and functionalized)
- Carbon (fullerenes, quantum dots, SWNT, MWNT- pristine and functionalized (carboxylated/nitrated/sulfonated/PVP polymer)

- In vitro culture systems
  - Animal (epithelial, endothelial, dendritic, macrophages, fibroblasts)
  - Human primary (epithelial, endothelial, fibroblasts, keratinocytes)
  - Microfluidic-2D high content screening system
  - Acellular & biosynthetic fluids

Nano GO: Funding Overview

- In vivo models
  - Allergic asthma (OVA sensitized), inflammation (LPS)
  - Knockouts (cathespin B, IL-1R)
- Biological response processes
  - Pro-inflammatory, oxidative stress, cytotoxicity, intracellular trafficking, internalization, fate, cell proliferation, DNA damage, etc.
- Exposure metrics and ENMs levels
  - Workplace real-time assessment of ENMs
  - In body fluids and drinking water

Nano GO Program

- First meeting of the Nano GO grantees is scheduled for October 20th at NIEHS
- Nano Challenge grantees (three) are also invited to attend
- Develop Framework for coordination on:
  - Selection of type(s) of ENMs
  - ENM physicochemical characterization efforts
  - Material, protocol, and data sharing scheme,
  - Set milestones

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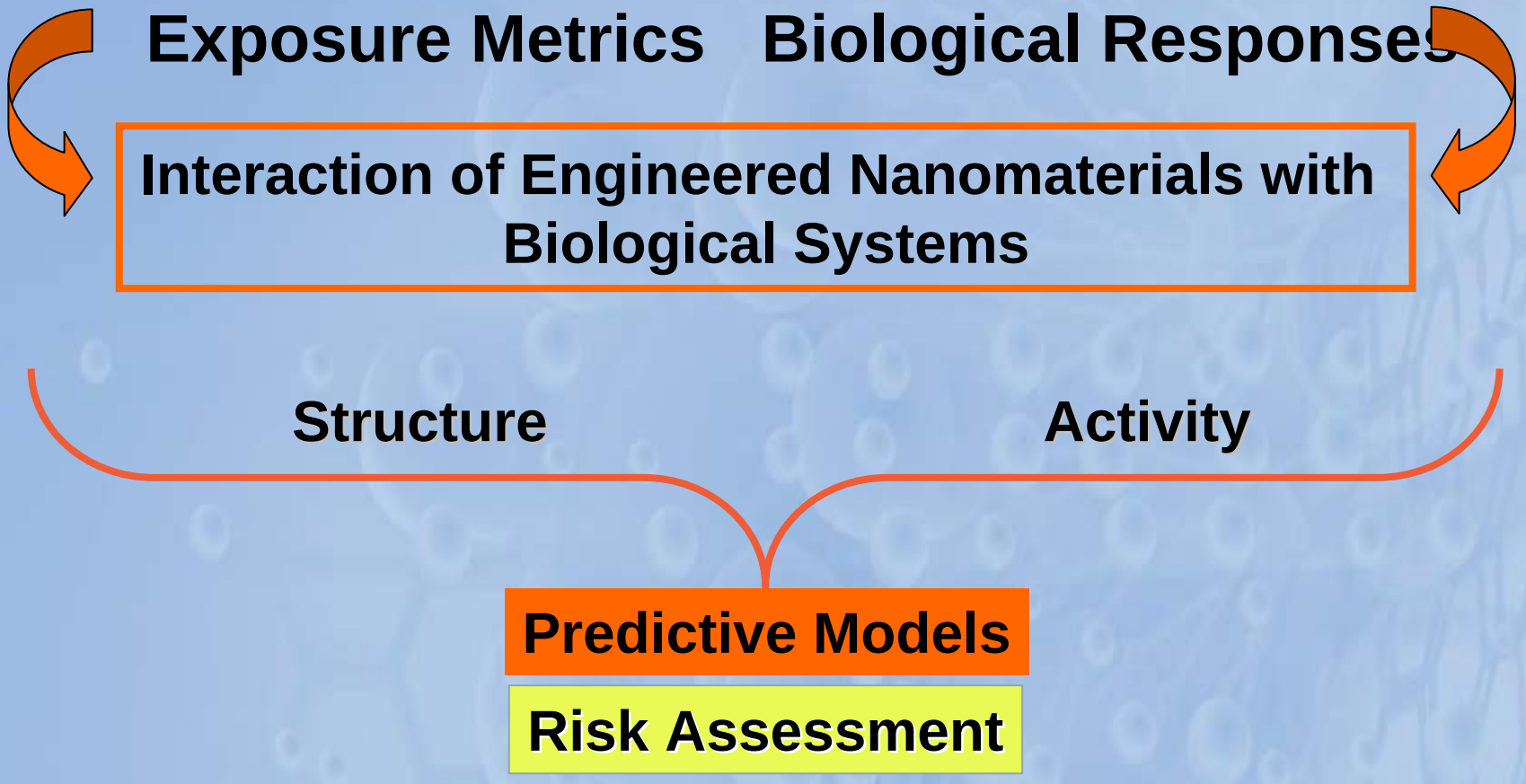

Thanks to Council Reviewers

- Dr. George D. Leikauf
- Dr. Sem H. Phan
- Dr. Jerald L. Schnoor