Does size matter? Connecting materials and biological researchers to understand how nanomaterials interact with life.

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Significance

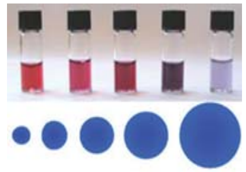
Have you touched a nanomaterial today?

- 3-4 new nanomaterial-containing products are released onto the market each week.
- There are over 1,300 consumer goods on the market that contain nanomaterials, including: foods, medicines, beauty products, electronics, and much more.
- By 2015, the market for nanotechnology could reach over one trillion dollars.

*The Project on Emerging Nanotechnologies, National Science Foundation

Nanomaterials can behave differently than their bulk forms.

- The chemical and physical properties of a material may be altered as it becomes smaller.
- For example, gold is relatively inert in its bulk form, but it can act as a catalyst when it is downsized to just a few nanometers. Gold even changes color at the nanoscale.



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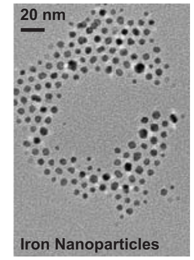
Nanomaterials have the potential to improve the welfare of humankind, but the effects of nanomaterials in humans, animals and on the environment are largely unknown.

We must understand the biological and environmental consequences of nanomaterials before they are widespread.



Our interdisciplinary approach will improve understanding of the effects of nanomaterials from genetic to whole-body levels.

The knowledge gained from these studies will be used to design and produce better, safer nanomaterials for potential applications in a wide variety of technologies including: energy, medicine, electronics, textiles, construction materials, and much more.

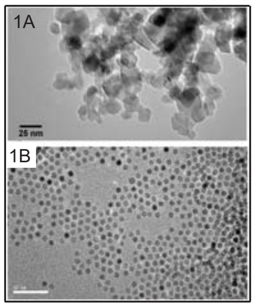
Fabrication → Experimentation → Predictive Capabilities

Fabrication

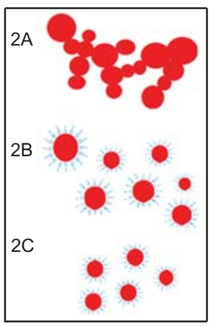
Size, shape, surface area, crystal structure and surface charge may all affect nanoparticles biocompatibility.

We must control these properties to understand nanomaterial interactions with biological systems.

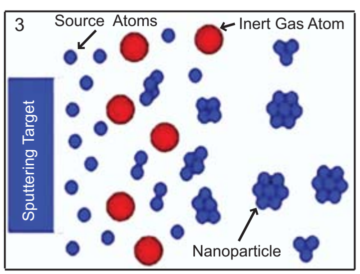
Many toxicity studies involve agglomerated particles with wide size distributions as illustrated in *Figure 1A*, but understanding nanomaterial toxicity requires more uniform particles, like those shown in *Figure 1B*.



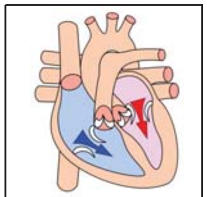
Surfactant assisted milling (SAM) and inert gas condensation (IGC) produce nanoparticles that are more uniform than those that are commercially available. Uniform nanoparticles allow us to determine how chemical and physical properties of nanomaterials affect their interactions with biological systems.



- SAM is a brute force method of breaking up powders into smaller particles using high-energy collisions.
  - Agglomerates in commercially available powders are broken into nanoparticles through collisions with the milling media.
  - Surfactant coats the constituent nanoparticles and prevents them from re-agglomerating, as shown in *Figure 2B*.
  - Size selection processes then produce a much more uniform set of particles, as seen in *Figure 2C*.
- IGC builds nanoparticles atom-by-atom as illustrated in *Figure 3*. This technique allows exceptional control over nanoparticle size and shape.



Experimentation



Stiff heart muscle can't relax and fill normally.
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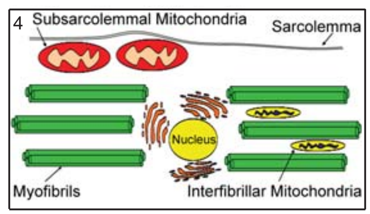
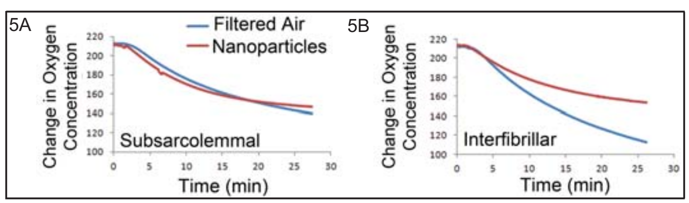
After nanomaterial exposure using WVU and the National Institute of Occupational Safety and Health's unique inhalation chambers, we use echocardiographic techniques to examine heart function.

- These non-invasive techniques assess how nanomaterial exposure in the lung affects the heart.
- Nanoparticle exposure impairs disatolic function: the heart must work harder to pump blood after nanoparticle exposure.

The heart needs energy to circulate blood, so we next examined the mitochondria, whose main function is to supply energy to heart cells.

- A heart cell contains two types of mitochondria, as shown in *Figure 4*. The subsarcolemmal mitochondria are located near the cell membrane, and the interfibrillar mitochondria, which help fuel contraction, are located between myofibrils.
- Nanomaterial exposure did not affect the functioning of the subsarcolemmal mitochondria, as illustrated in *Figure 5A*, where the oxygen consumption of the exposed and control samples was relatively the same.
- The interfibrillar mitochondria's ability to produce energy was reduced. *Figure 5B* shows that oxygen consumption of the nanoparticle-exposed sample decreased.
- This means that the nanomaterials we breathe affect how efficiently mitochondria produce energy needed for our hearts to pump blood.

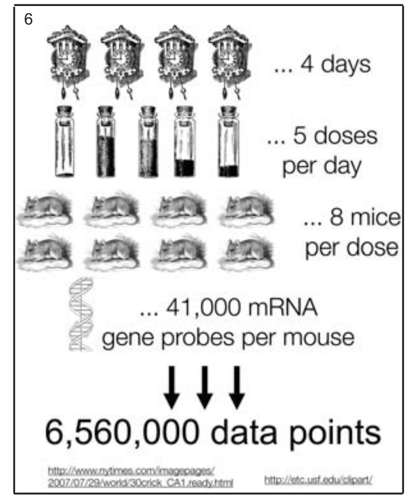


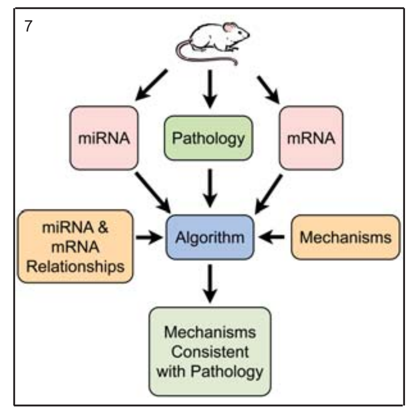


Predictive Capabilities

We collect data from tens of thousands of genes at multiple times and doses as seen in *Figure 6*.

- From this wealth of data, we can predict cellular mechanisms that may be affected by nanoparticles.
- We develop computer algorithms (*Figure 7*) that relate quantitative pathology scores (from lung inflammation and fibrosis) to mRNA and miRNA data to extract underlying functional patterns from gene expression data.
- We use the resulting patterns and prior knowledge of gene involvement to identify cellular mechanisms significantly related to the original pathology scores. These mechanisms identify frequently occuring genes as potential biomarkers.
- Unlike most existing techniques, our system uniquely uses pathology information, multi-dimensional gene expression data, and prior knowledge of gene involvement to identify mechanisms activated by nanoparticle exposure.





Conclusion

Fully realizing the potential of nanomaterials to solve important problems in medicine and energy requires understanding how materials interact with life. Our IGERT connects biological and materials scientists to determine how physical and chemical properties of nanomaterials affect biology. This information can then be used to engineer nanomaterials with these properties in mind.

Acknowledgements

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