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# **Nanotechnology Characterization Laboratory: *Foundation, Operation, Scientific Output, and Peer Review***

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**Advanced Technology Program**



*<http://ncl.cancer.gov>*

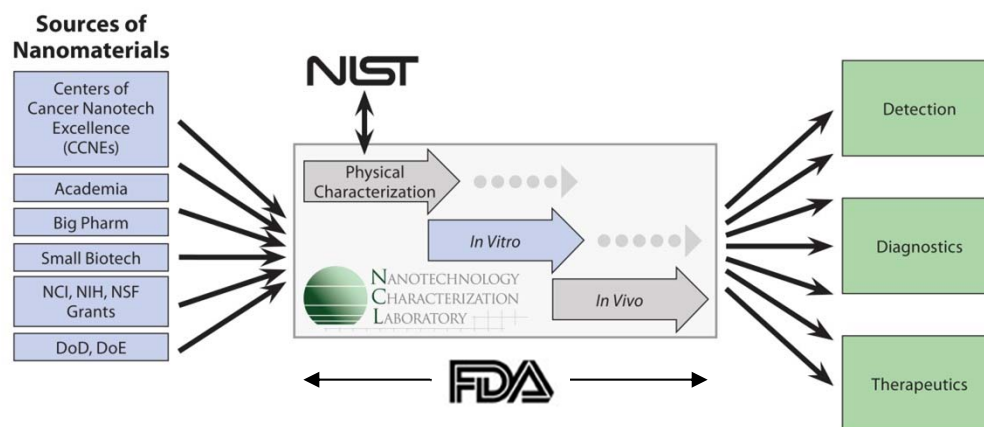


Frederick

# NCL – Background



- The NCL is a resource for in-depth characterization of nanomaterials to be used in new diagnostics and therapeutics. The data produced by the NCL facilitates translation of promising nanotech formulations to the clinic.
- The NCL was established in 2004 as an interagency collaboration among NCI, NIST, and FDA. Its budgets were included in Funding Plans (2005, 2010) of the Alliance for Nanotechnology
- Scott McNeil heads the laboratory.
- NCL performs preclinical characterization of nanomaterials, including:
  - physicochemical characterization
  - *in vitro* experiments
  - *in vivo* testing for safety and efficacy.



**90% of NCL's efforts support the extramural community.**

# NCL – Why It Was Established?

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- NCL was established in response to an NCI survey of investigators working in cancer nanotechnology. The PIs identified areas requiring additional support:
  - Standard assays for nanomaterials characterization
  - Hub for the data on different nanomaterials
  - Development of reference materials
  - Interdisciplinary expertise
- NCL is perceived as an objective entity, does not ‘compete’ with academic or industrial researchers
- Collaboration with NCL allows PIs to take advantage of “lessons learned” – sharing data on:
  - Trends in biocompatibility
  - Performance of different nanomaterials
  - Conduit to FDA strategies towards nanotechnology.

# Accomplishments

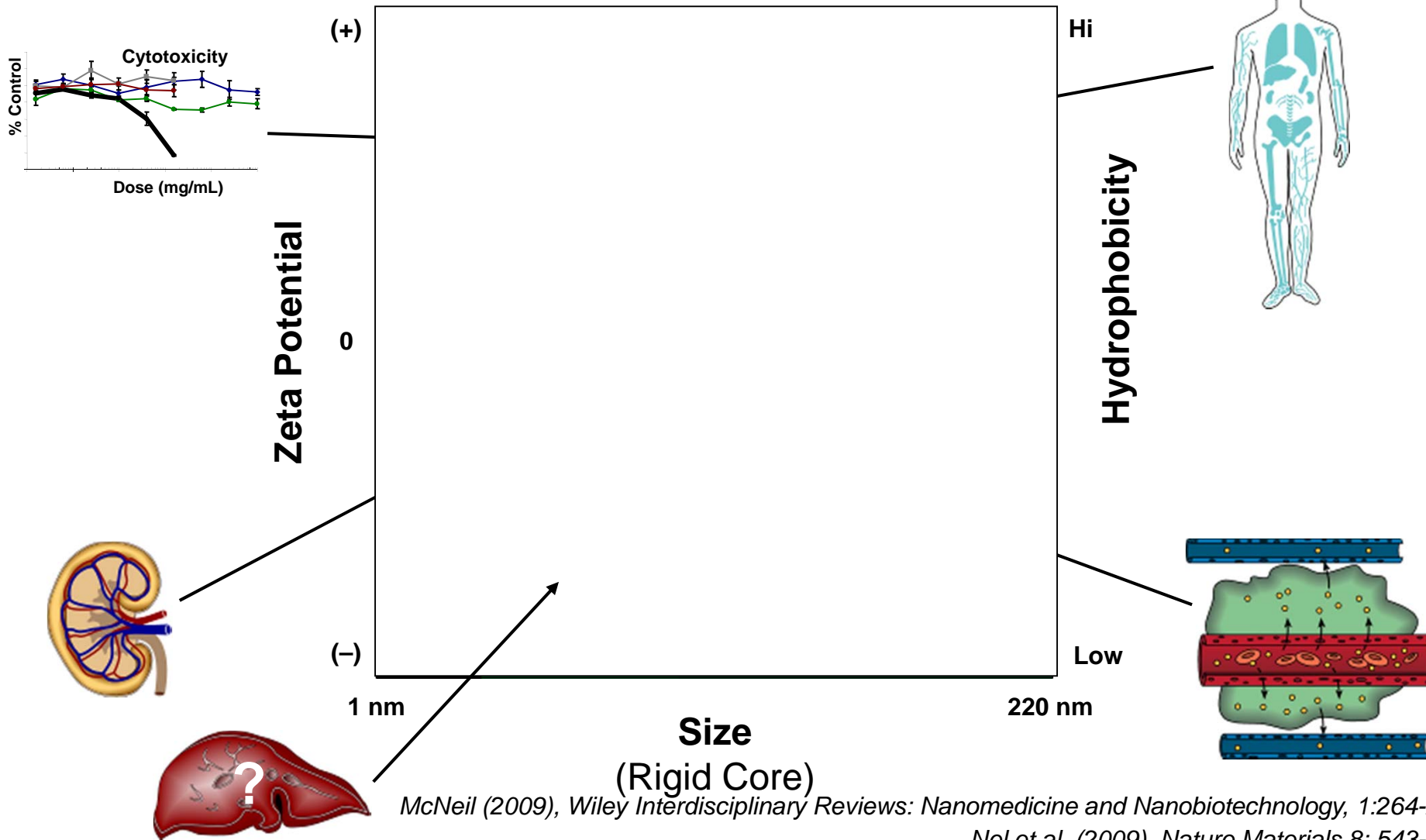


- NCL has characterized more than 250 candidate nanotech formulations, 5 of which are in clinical trials, many more in pre-IND stages.
- Each year of operations:
  - ~20 animal studies
  - ~10 publications
  - over 900 pages of data for collaborators in reports
  - ~10 new materials transfer agreements (MTAs)
- NCL collaborates and supports other institutes and agencies:
  - provides support for NIEHS center grants on 'nanotechnology health implications research'
  - Collaborates on database developments; caNanoLab (NCI), nano-registry with NIBIB and NIEHS;
- Standards development and interlaboratory studies with ASTM & ISO. Reference material development with NIST.



# Nanoparticle Biocompatibility

## Nanoparticle Biocompatibility

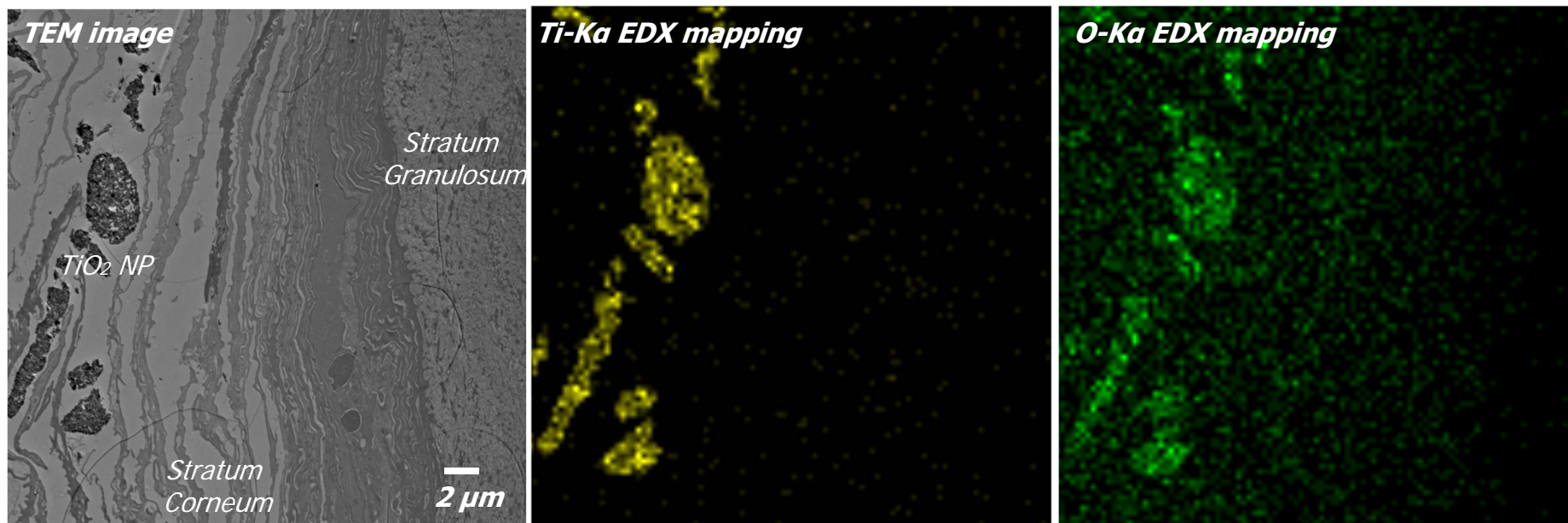


McNeil (2009), *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*, 1:264-271.

Nel et al. (2009), *Nature Materials* 8: 543-557.

Cover of *Advanced Drug Delivery Reviews*, June, 2009.

# Dermal Penetration of TiO<sub>2</sub> In Sunscreen Formulations



Studies on minipigs skin using:

- Transmission Electron Microscopy (TEM)
- Energy Dispersive X-ray (EDX)
- No penetration beyond stratum corneum
- No elevated titanium levels in lymph nodes and liver

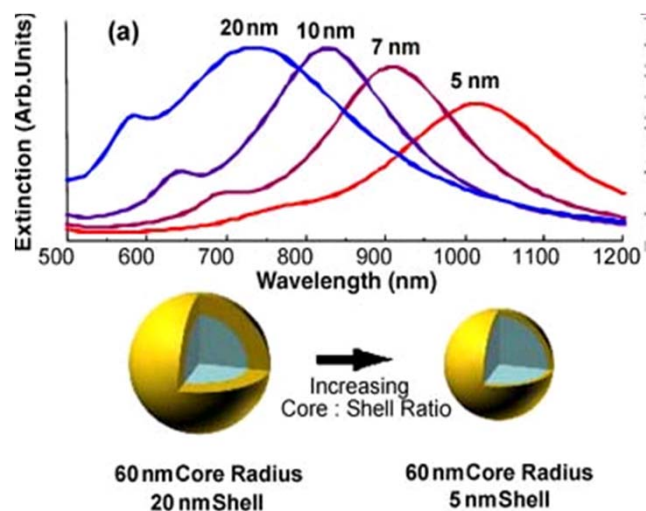
***TiO<sub>2</sub> Particles were detected only in stratum corneum***

*Patri, A. et. al. J. Appl. Tox. (2009) 29, 662-672.*

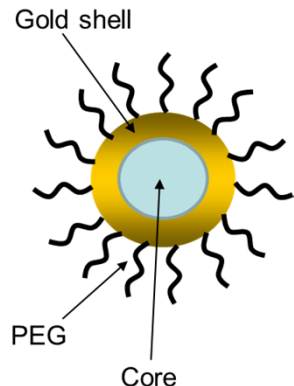
*Sadrieh, N. et. al. Toxicol. Sci. (2010) 115, 156-166.*



# Studies of Gold Nanoshells



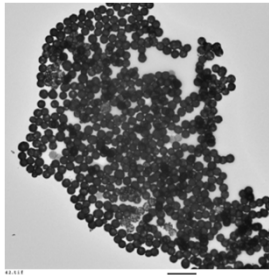
- Evaluation of two different batches of gold nanoshells, the first batch was ~6 months older than the 2<sup>nd</sup>;
- In tox studies, 1<sup>st</sup> batch caused extensive toxicity, 2<sup>nd</sup> batch was largely benign.



**Batch 1** : Extensive pigmentation in liver, spleen, lungs, ovaries, muzzles, granulomous lesions in lungs.

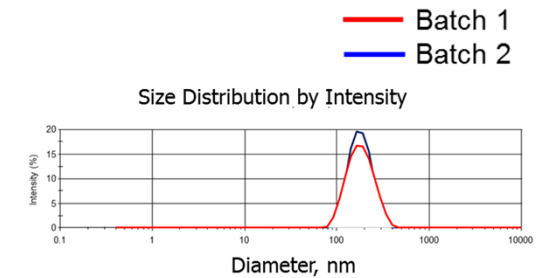
**Batch 2**: Few, statistically insignificant, mild lung lesions

# Mechanism of Toxicity – Gold Nanoshells

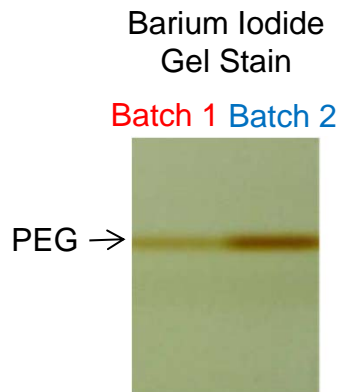
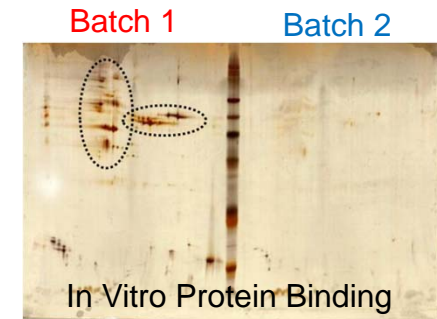


Batch 1 and Batch 2 appeared identical by TEM.

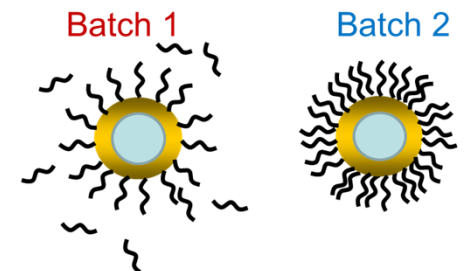
- NCL performed extensive characterization: the two batches seemed identical by physicochemical characterization.



- NCL *in vitro* characterization revealed a difference in protein binding. Batch 1 binds more protein than batch 2.



- NCL determined the difference in protein binding was due to a difference in PEG coating – the PEG was dissociating over time. NCL developed a “lot release” PEG gel assay.



Less PEG → Distribution to the Lung and other organs



# NCL – Oversight and Peer Review

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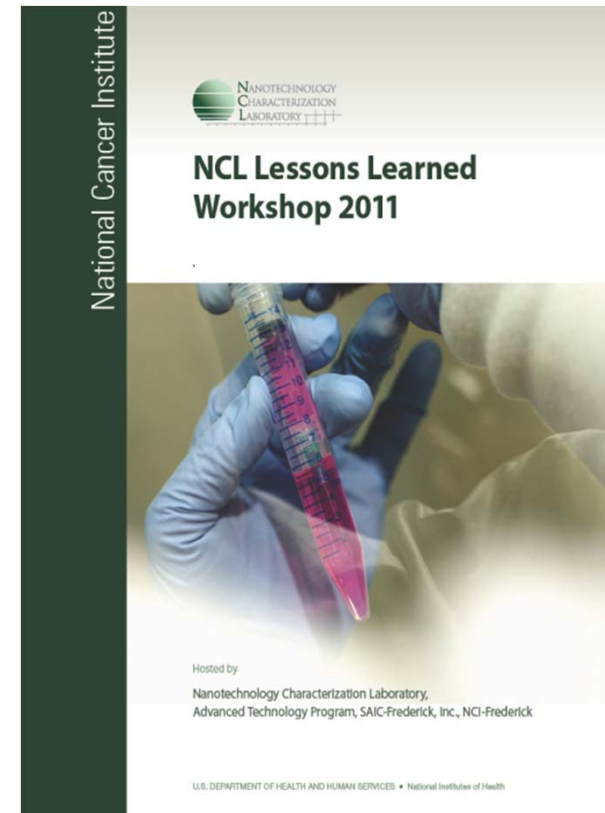


- Scientific Oversight Committee (SOC) made up of scientists from NCI, NIST, FDA and EPA provides oversight to the laboratory's operation;
  - SOC meets annually in Frederick to review the laboratory's progress and discuss future directions.
- Extramural inputs from nanotechnology leaders and consultants: e.g., Andre Nel, UCLA; Martin Philbert, U. Michigan; Günter Oberdörster, Rochester U.;
- Input from CCNEs, extramural investigators from academia, industry, and government.

# Lessons Learned Workshop



- NCL communicates the “lessons learned” from NCL characterization to the research community:
  - Annual 2-day workshop at NIH
  - Shorter 1-day seminars at FDA and universities.



# Review of Incoming Projects

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- NCL receives applications every quarter from extramural community – academia, industry, and government;
- Committee reviews applications based on:
  - **Demonstrated efficacy *in vitro* and/or in animal models**
  - Advantages over existing cancer therapies or diagnostics
  - Existing characterization data
  - Inherent toxicity or environmental concerns
  - Proposed path to clinical trials
- In 2010-2011, NCL received 42 white paper applications. More than half were accepted. Rejected applications either didn't show an advantage over existing formulations or were self-limiting (for example lack of stable process to produce material).

# Summary

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- NCL has become highly respected national resource for evaluation of nanomaterials to be used in new diagnostics and therapeutics;
- It supports extramural community as an independent and objective resource;
- NCL will be a key player in establishing relationships with industry within future ATRF;
- Several NIH institutes and other agencies approached NCL to collaborate and learn about its operational model.

# NCL Extramural Collaborators

