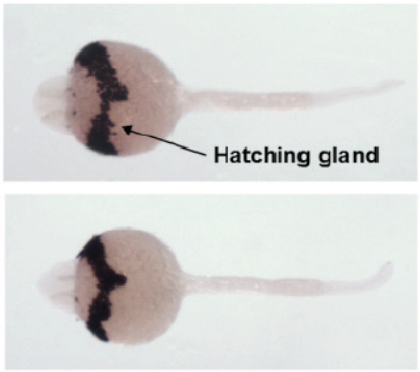
Dr. Andre Nel Delivers Truman Lecture on Nanobiology and Predictive Nanotoxicology

"Hopefully, by 2020, we won't think of the toxicity of a material as an afterthought, but rather as an integral part of the development of the material."

The closing thought of Dr. Andre Nel's President Harry S. Truman Lecture on July 24, 2012, formed the capstone to an amazing depth and breadth of material, spanning the range from band-gap physics through material chemistry to molecular, cellular, and whole organismal biology. The presentation ranged for example, from data indicating the receptor-mediated cytoskeletal rearrangement mechanism by which single cells can distinguish between silica nanorods and nanospheres to data obtained by screening nanomaterials for their ability to inhibit zebrafish embryo hatching as a toxicology screen.



Zinc oxide nanoparticles have the ability to interfere with the hatching of zebrafish embryos.

Predicting a "sea-change in medicine," with improved diagnosis, imaging, and treatment stemming from a "huge impact (of nanobiology) in the next decade," Nel deftly traversed virtual mountains of data on nanomaterial-biological interfaces and structure-activity relationships (SAR). These data illustrated, for example, how, at a mechanistic level, substances such as multiwalled carbon nanotubes (MWCNTs) could be viewed as "the new asbestos" in their ability to induce inflammation with fibrotic changes in lung alveoli (air sacs).

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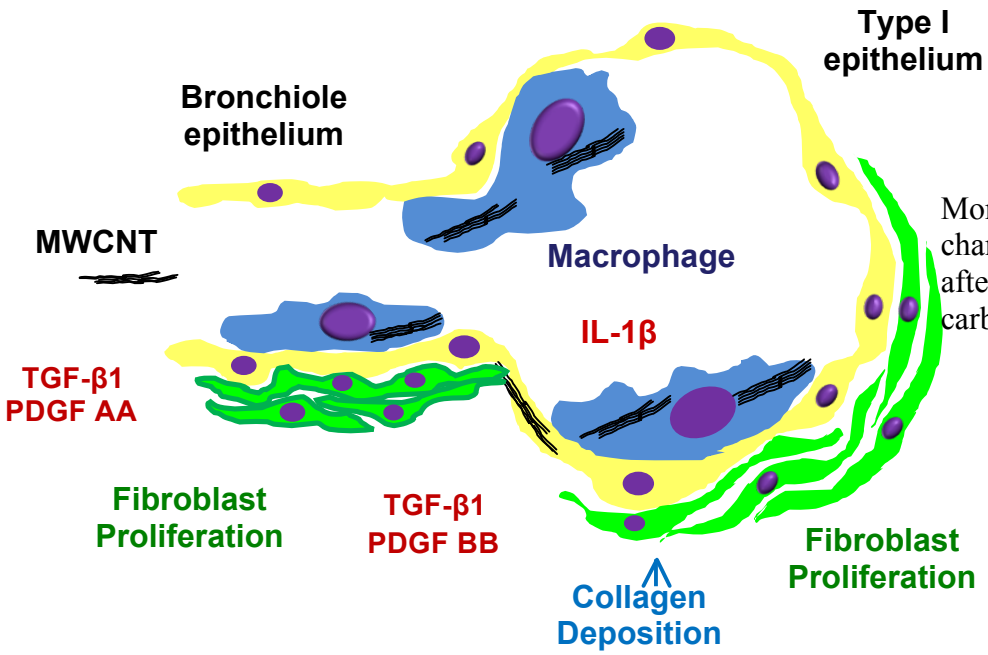

Morphological and biochemical changes occurring in lung alveoli after inhalation of multiwalled carbon nanotubes (MWCNT).

Then there was zinc oxide (ZnO), the culprit in "Metal Fume Fever," a syndrome occurring in welders that produced an oxidative stress reaction with flu-like symptoms. Nel described, in intimate cellular and molecular detail, how, after endocytosis in mouse epithelial cells and macrophages, the release of zinc ion (Zn^{2+}) into an acidic lysosomal environment led to secretion of a collection of inflammatory chemical messengers (cytokines), and he displayed huge data sets — obtained partially through robotic assay systems — that would account for this acute illness. Playing off this example, he ultimately evolved a description of a predictive toxicological capability, one that might allow future investigators and clinicians to forecast, in advance, which nanomaterials could be expected to have adverse physiological effects. Foremost among the parameters underpinning such "a system allowing predictions based on nanomaterial properties" was material band-gap energy as predictive of metal oxide toxicity. Another massive data set illustrated the general accuracy of this predictive capacity, particularly when nanomaterial dissolution characteristics were taken into account.

After a thorough discussion of the development of a multiparameter high-throughput screening assay for oxidative stress induced by nanomaterials, Dr. Nel discussed a ranking system for pulmonary (lung) toxicity based on nanomaterial structure-activity relationships, while emphasizing the difference in exposure to environmental toxicants based on an organism's trophic (feeding) level in food webs (e.g., bacteria, phytoplankton, herbivores, and carnivores).

Ultimately, Nel's presentation evolved to a discussion of cancer therapy and the potential role of nanomaterials in the treatment of drug-resistant cancer cells, which often determine the success or failure of chemotherapy and therefore, the longevity of a cancer patient's survival. He described a particular instance of such nano-therapeutics, in which co-treatment with chemotherapeutic drug and small inhibitory RNA (siRNA) was able to overcome drug resistance in a cancer cell line.

Returning to toxicology for one final passage before fielding questions, Nel proposed the need for a regression analysis models for quantitative structure-activity relationships (QSARs) for nanomaterial toxicity as a necessary goal for ultimately predicting the hazards of novel environmental nanomaterials, while expressing his hope that industrial entities would heighten their awareness of material toxicity as a fundamental concern in their operations.

Taken as a whole, the presentation's many journeys into the intricacies of the research of Nel and his colleagues form a body of data boldly exhibiting both the opportunities and the dangers associated with the proliferation of nanomaterials research and development. Clearly, the future will be graced with novel nanomaterial applications, but there will likewise undoubtedly be challenges to human health that must be taken into consideration over the course of this revolution-already-in-progress.

Dr. Nel displays his Truman medallion, with Sandia Vice-president and Chief Technology Officer, Steve Rottler.


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"Safe Implementation of Nano-Technology
in Humans and the Environment"
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