

# Nanomaterial Toxicity Testing in the 21<sup>st</sup> Century: Use of a Predictive Toxicological Approach and High-Throughput Screening

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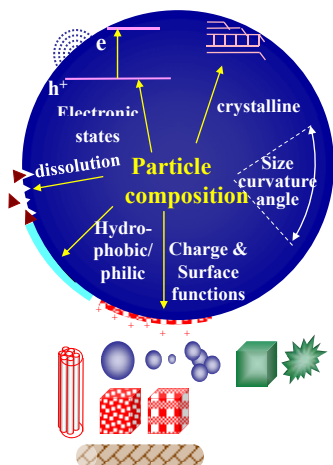
Director of the NSF- and EPA-funded Center for the Environmental Implications of Nanotechnology (UC CEIN)

Director of the NIEHS-funded Center for NanoBiology and Predictive Toxicology

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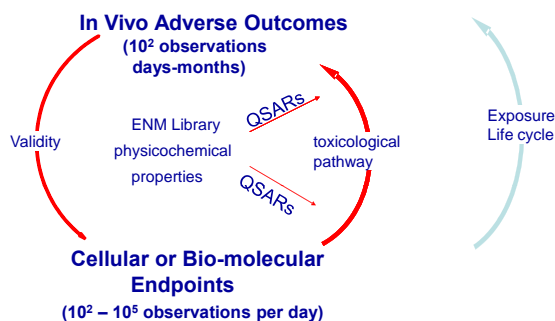
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Large number of materials with novel physicochemical properties



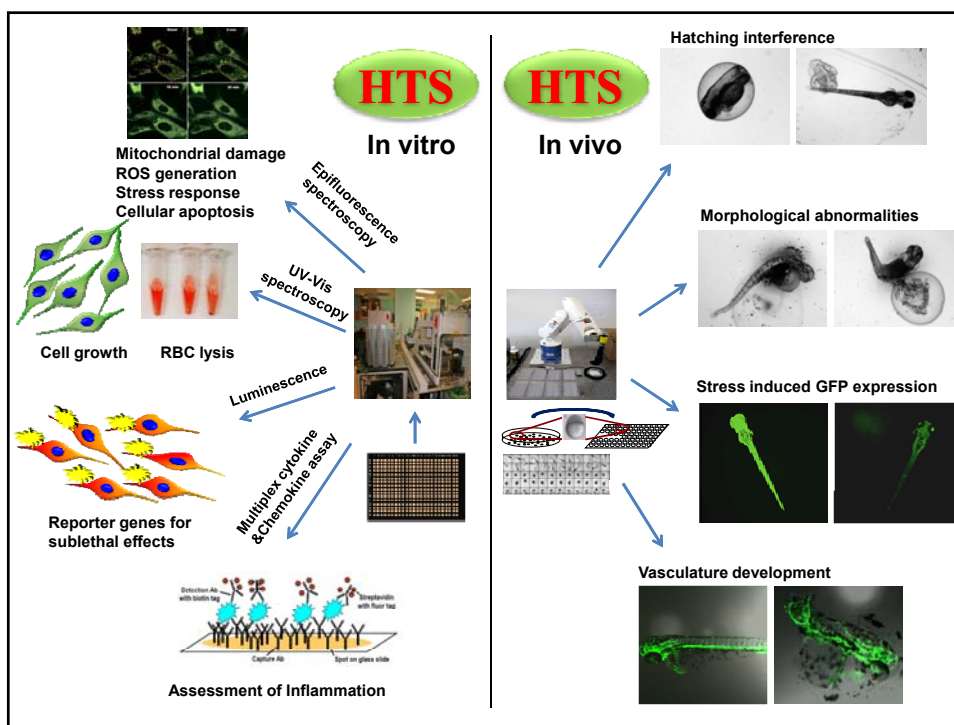
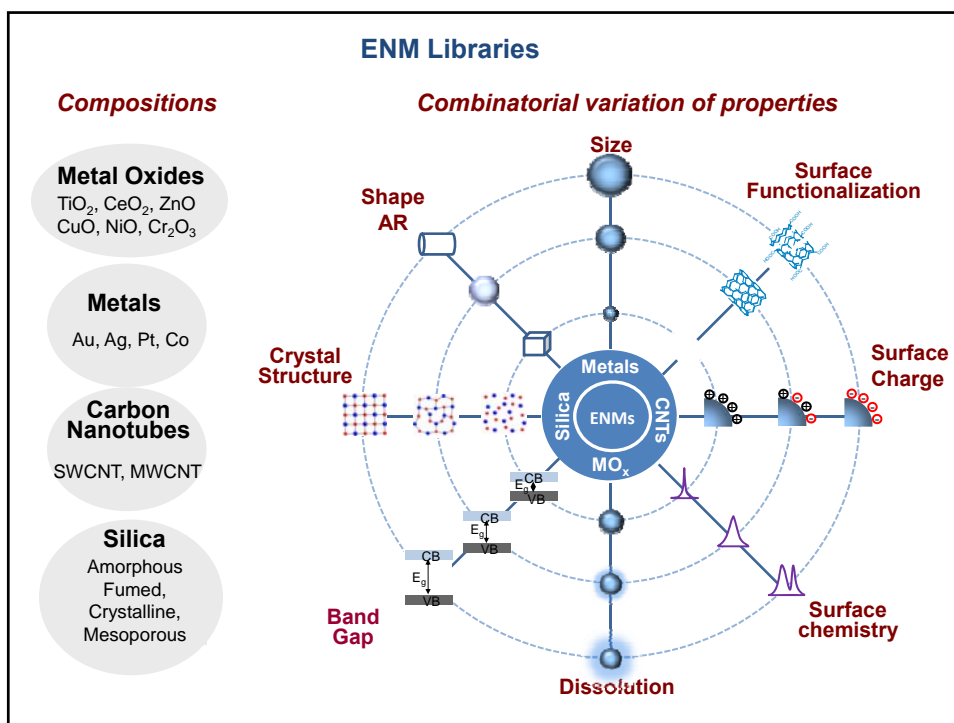
**US National Academy of Science Report (2007)**

- Wide coverage of toxicants
- Robust scientific platform for screening
- Predictive tests utilizing toxicity mechanisms
- High throughput screening
- Connectivity to *in vivo*

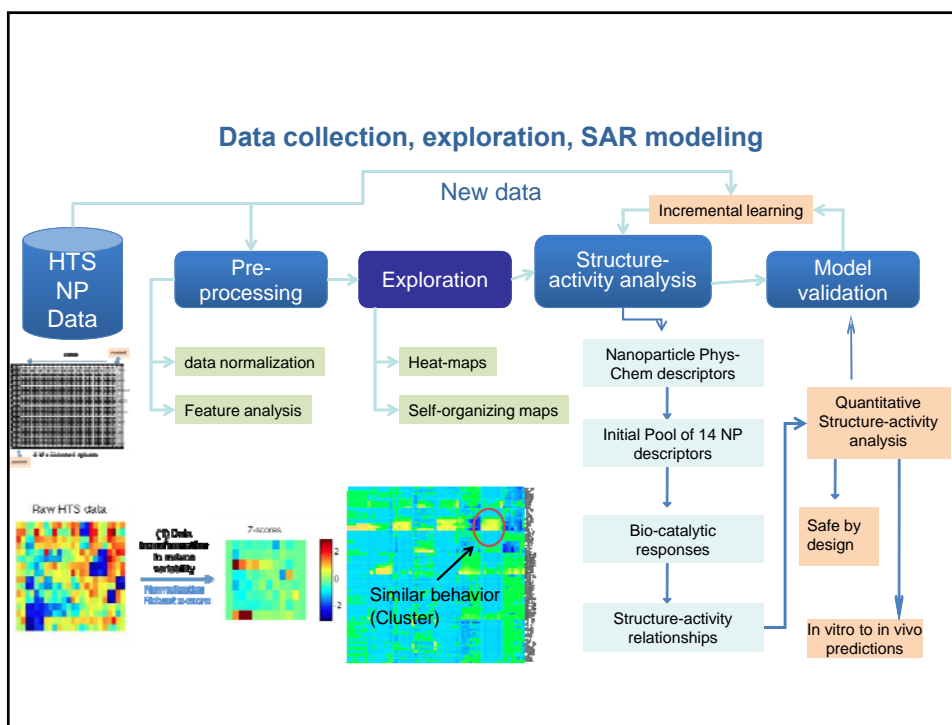
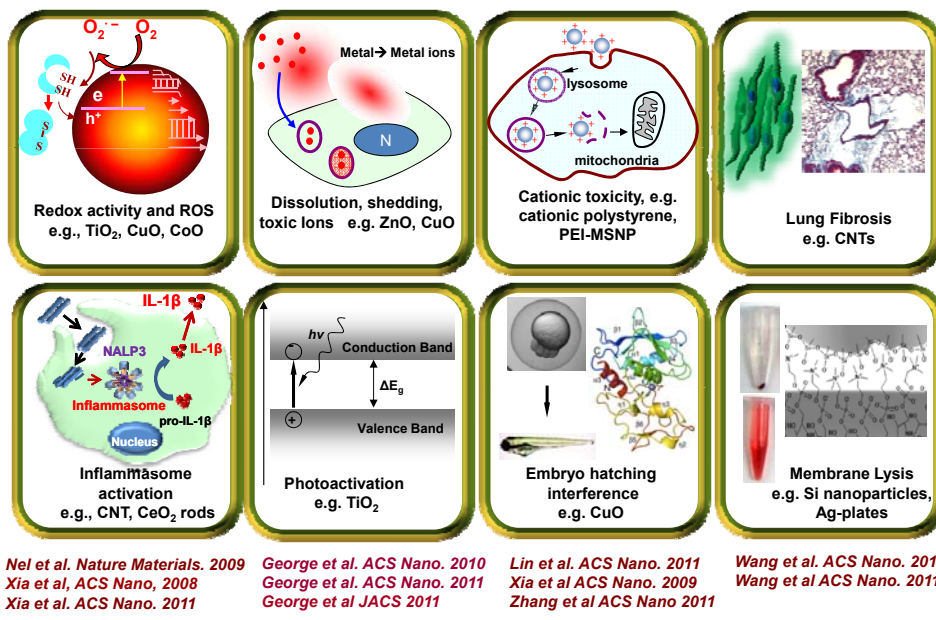


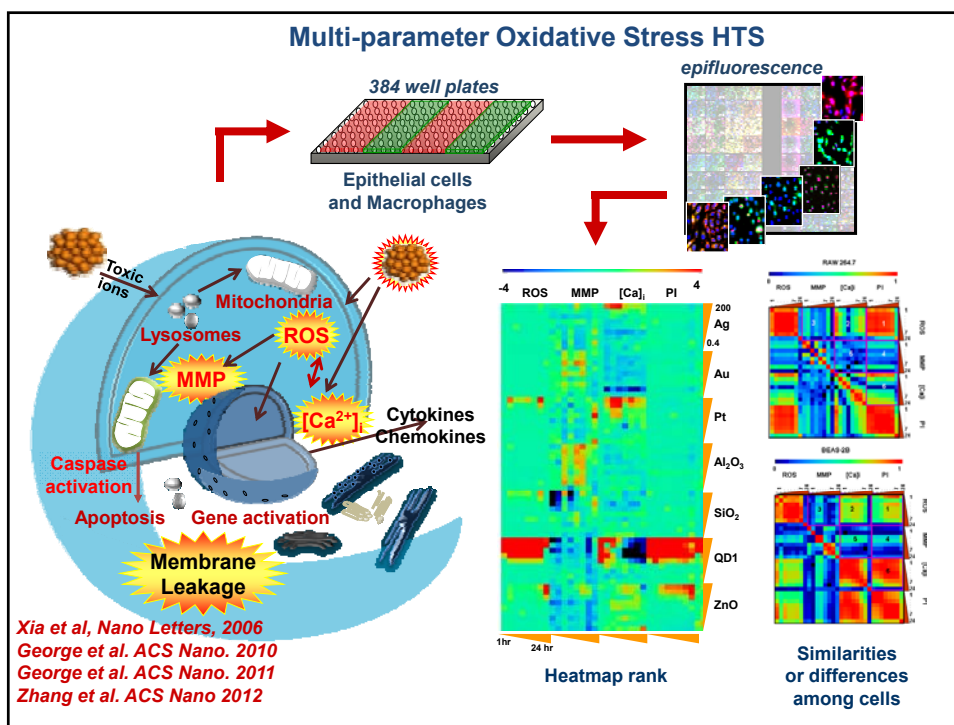
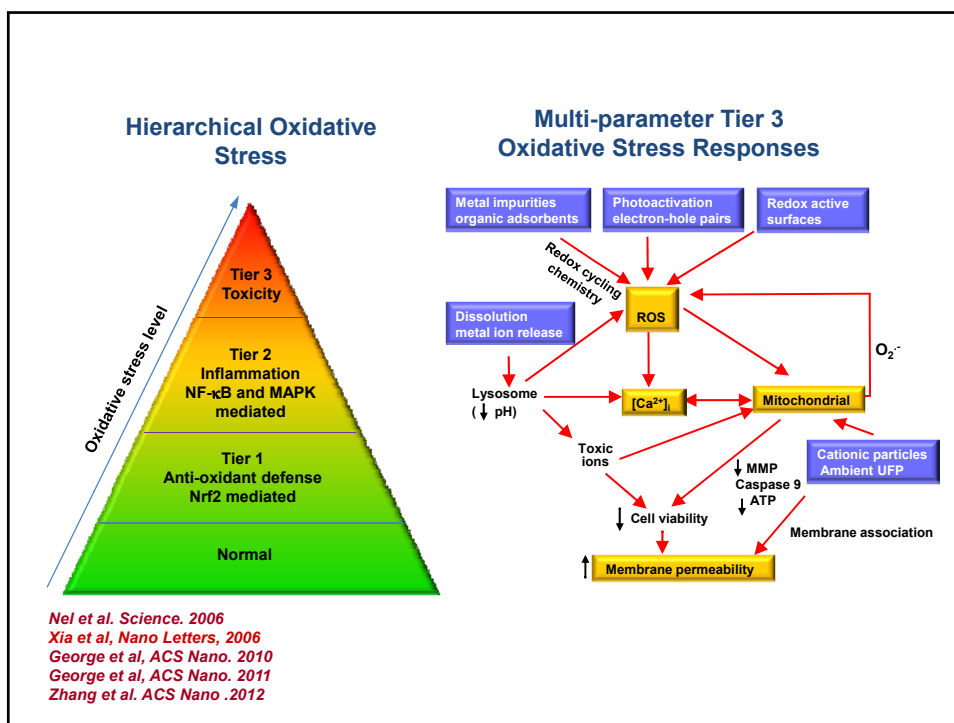
Meng et al. ACS Nano. 2009  
Nel et al. Accounts Chem Res, 2012

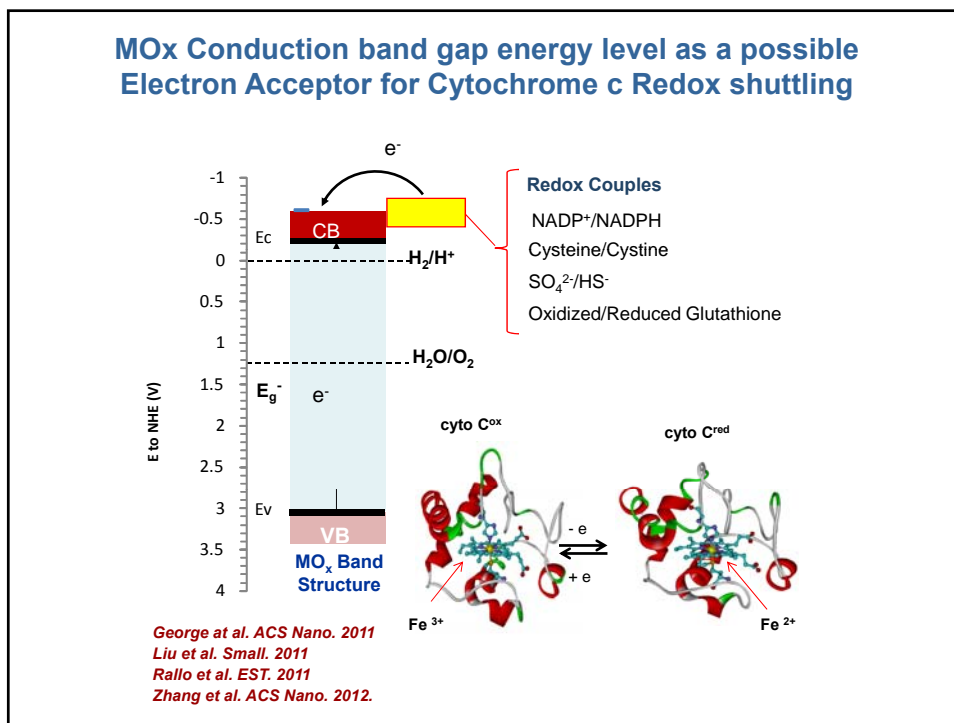
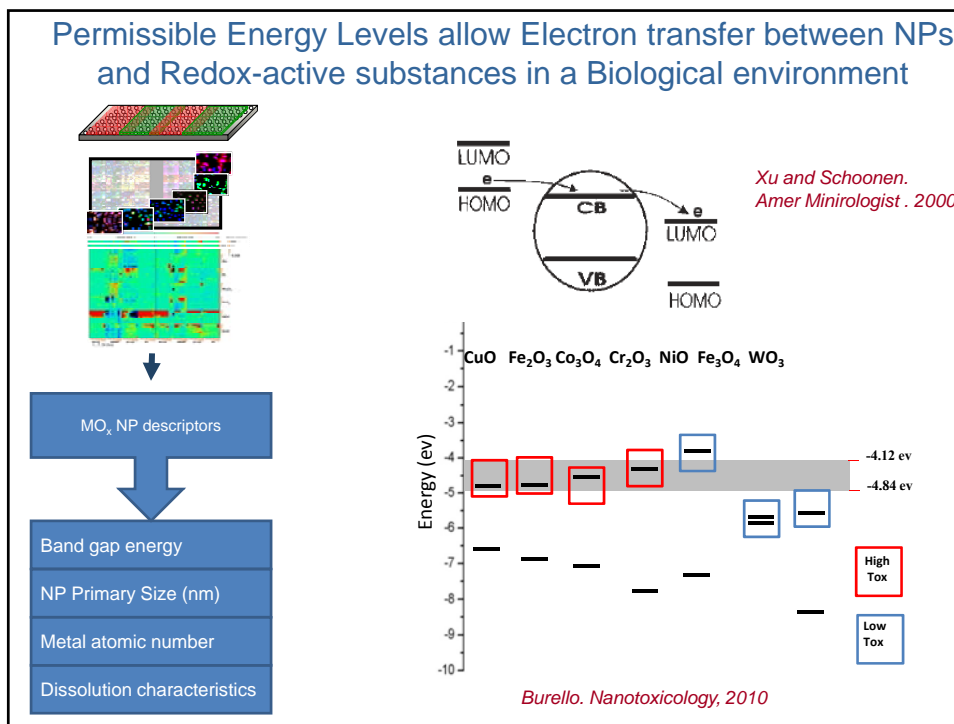
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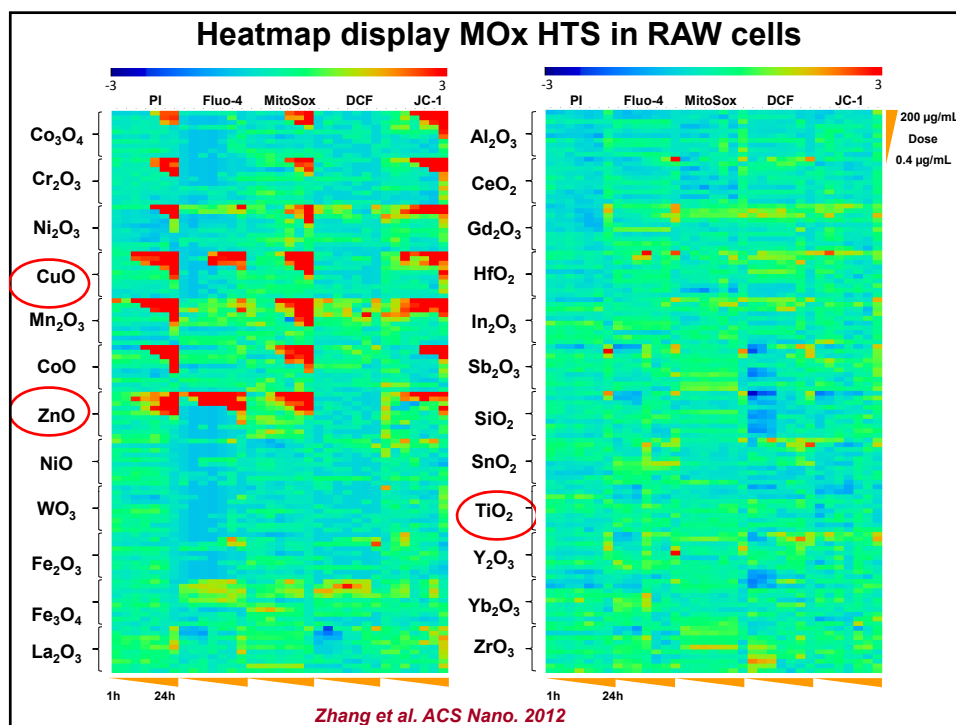
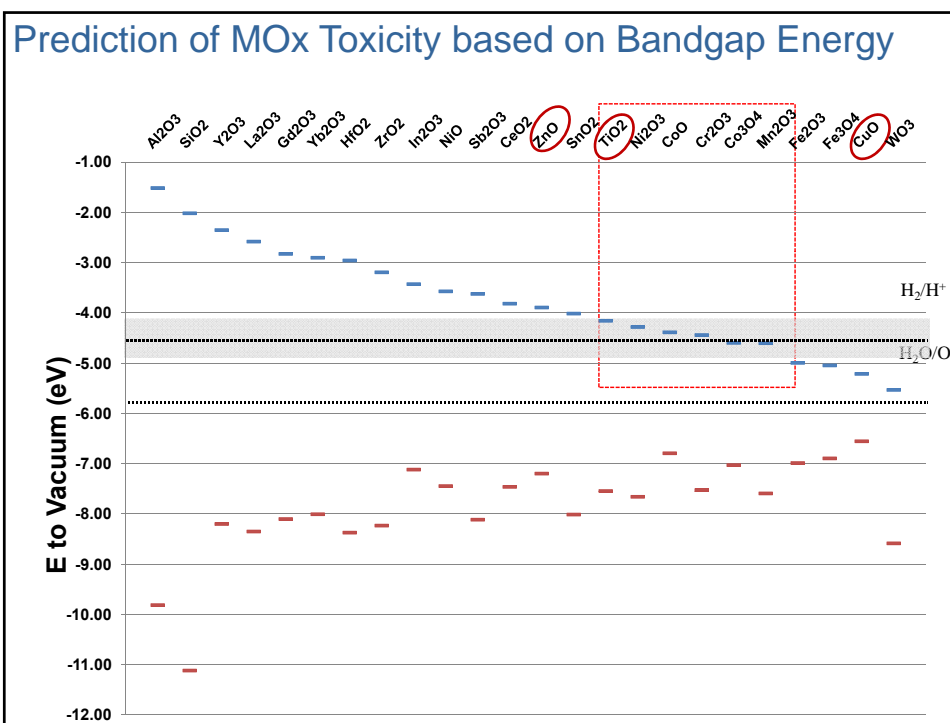


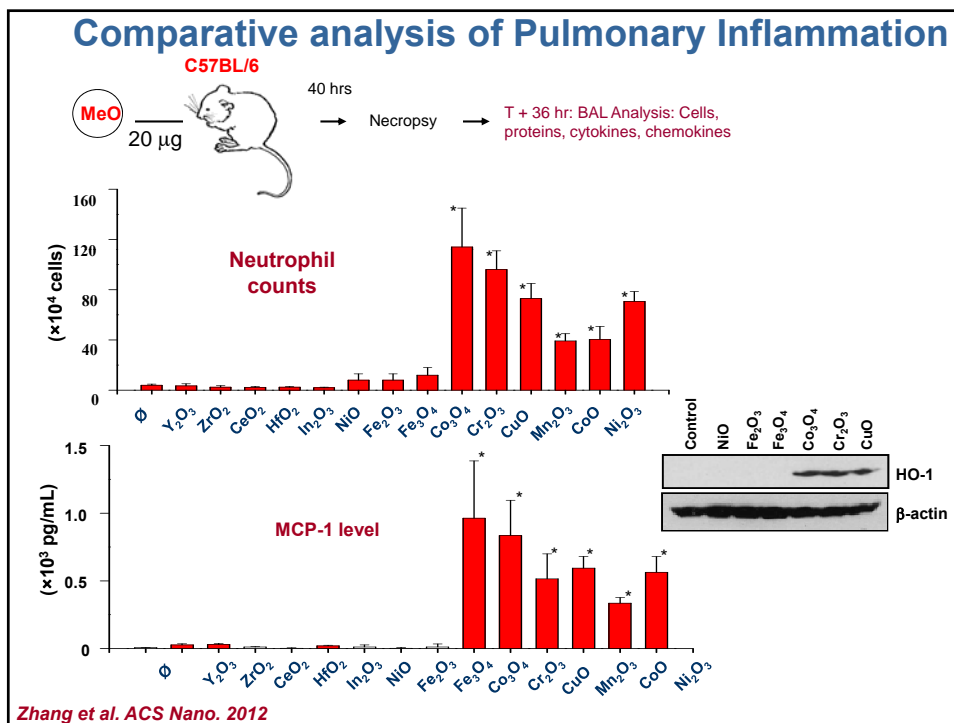
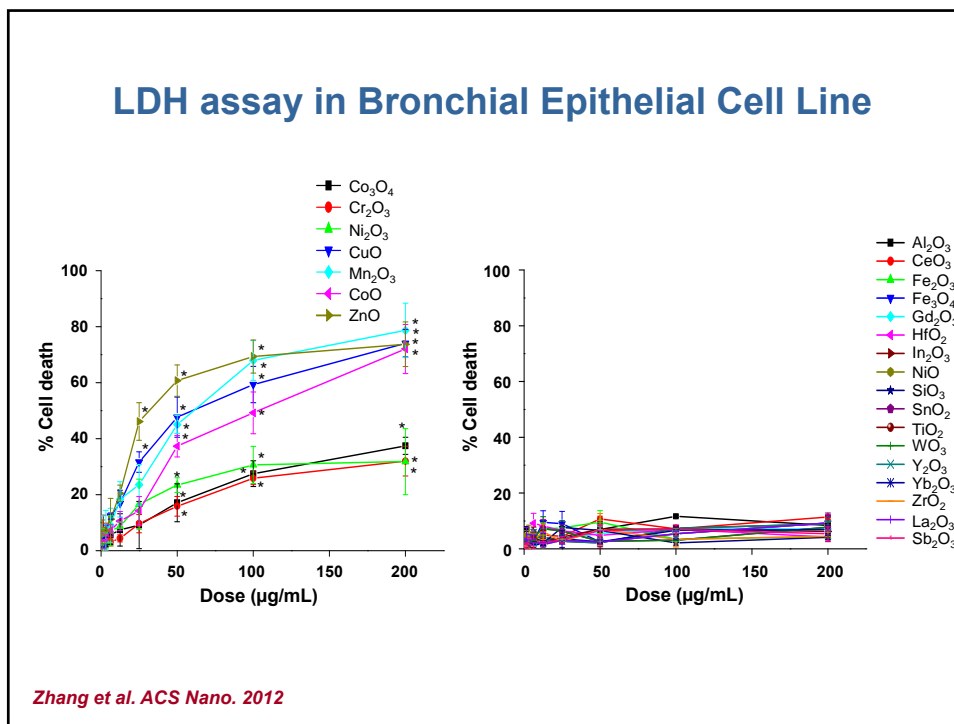
## Mechanistic Toxicological Pathways in Cells that can be used for HTS & Predictive Toxicological Modeling

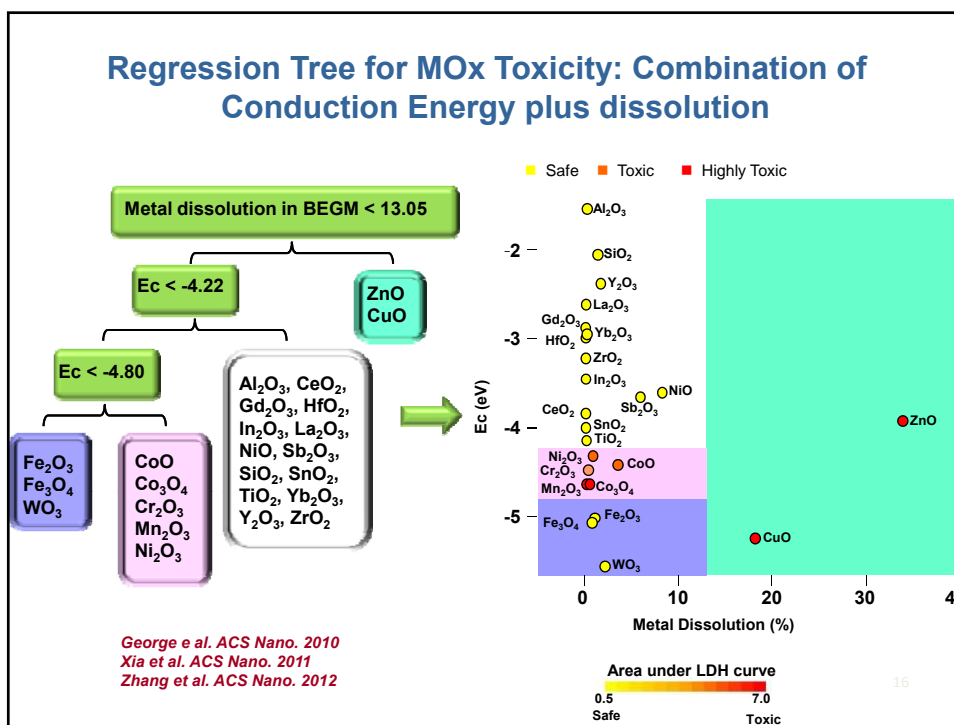
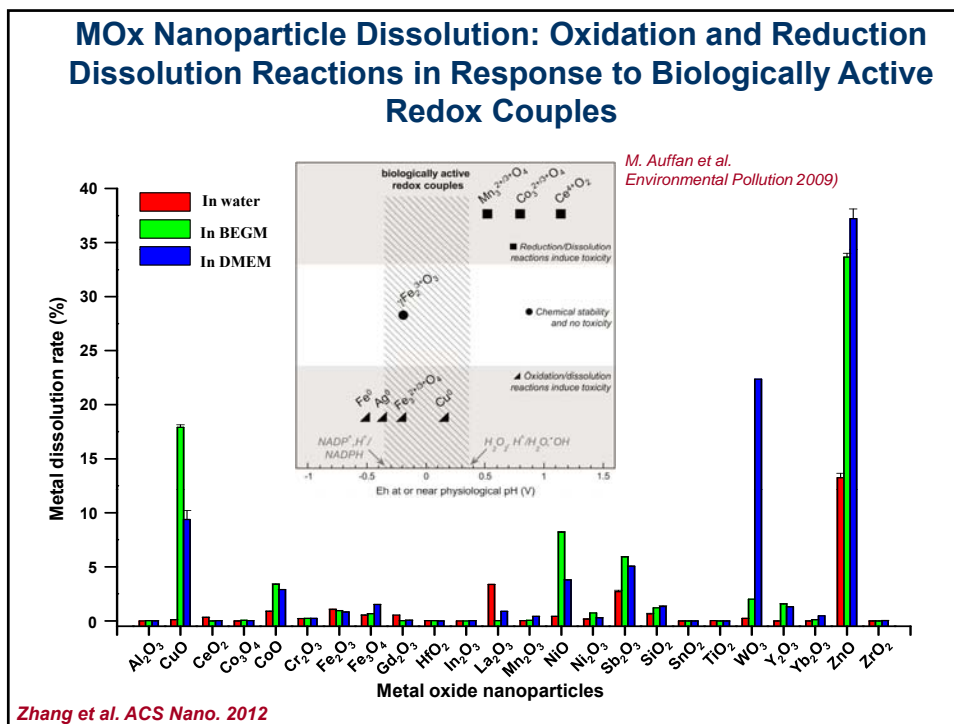








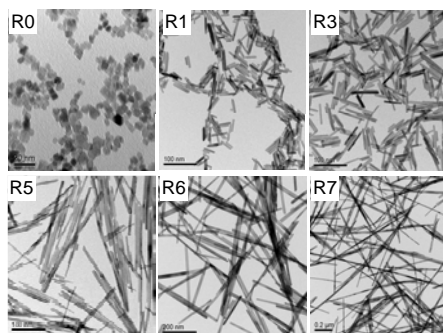
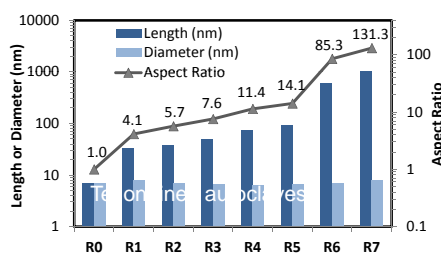
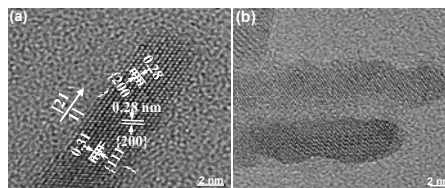
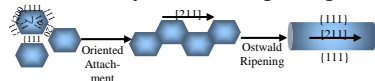






## Synthesis of a Ceria Nanowire Library to Study shape-dependant toxicity

- Synthesized by hydrothermal technique
- Aspect ratio can be finely tuned from 1 to >200
- Growth by oriented attachment followed by Ostwald ripening



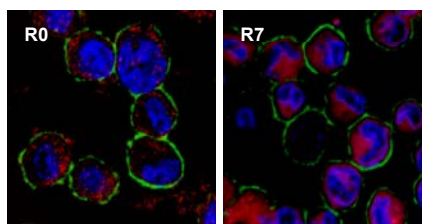
Ji, Xia, Wang, Nel, Zink ACS Nano 2012

## Ceria Nanowire Toxicity in THP-1

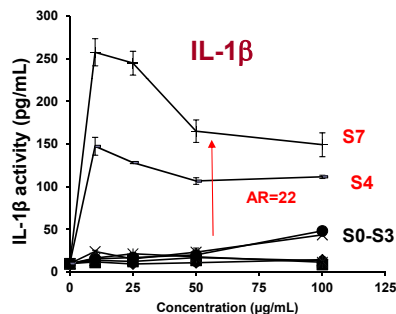
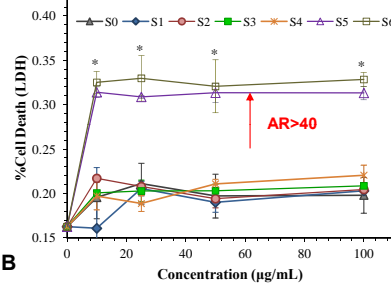


No  
Cathepsin B  
release

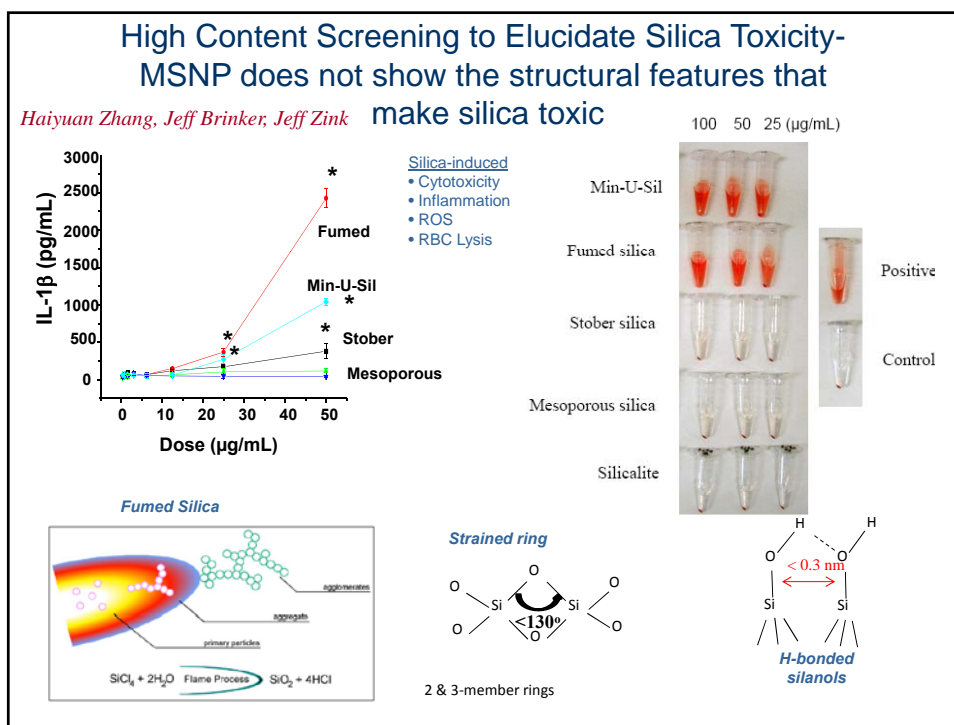
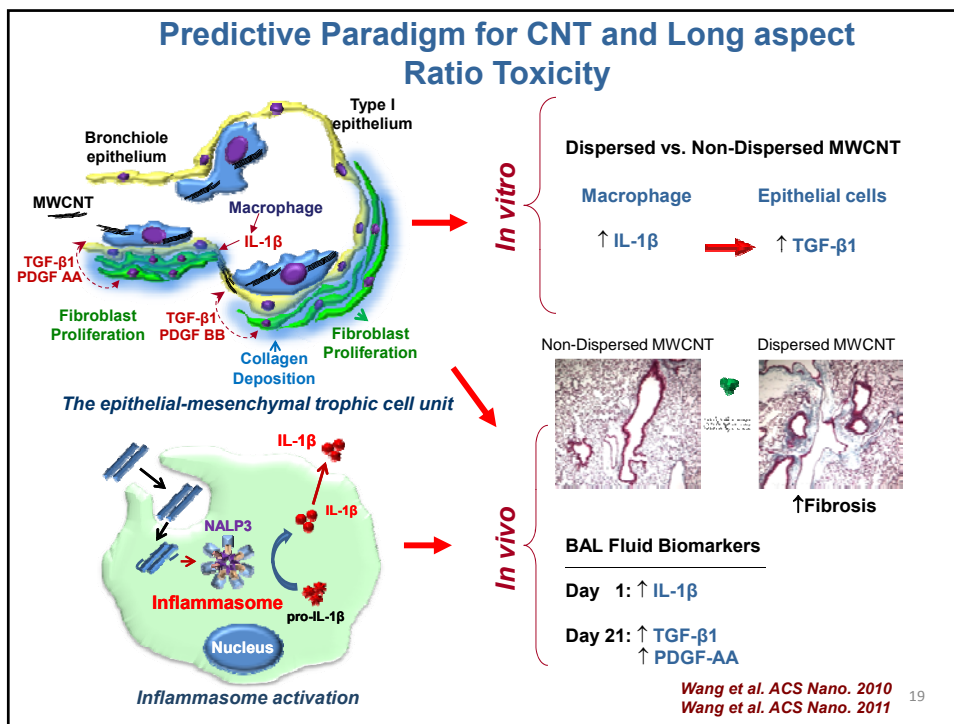
Cathepsin B  
release

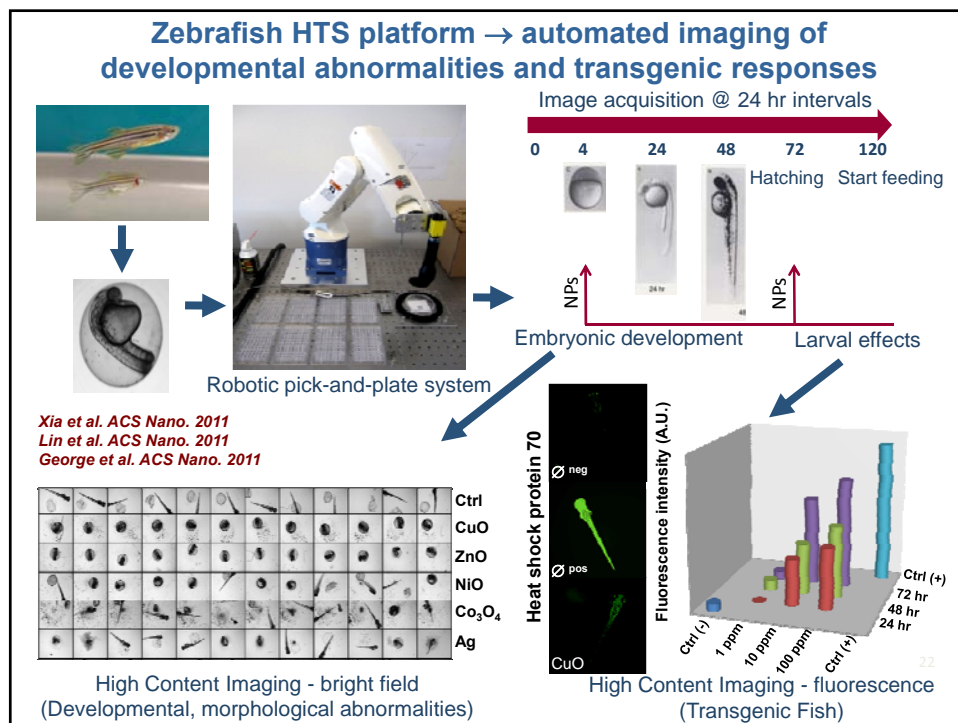
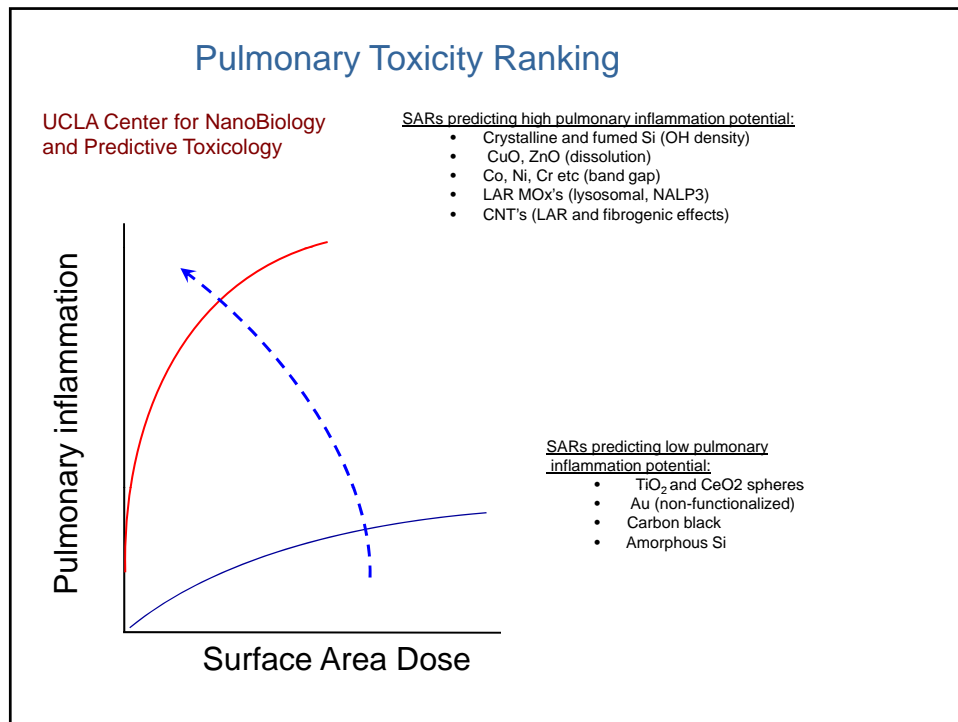


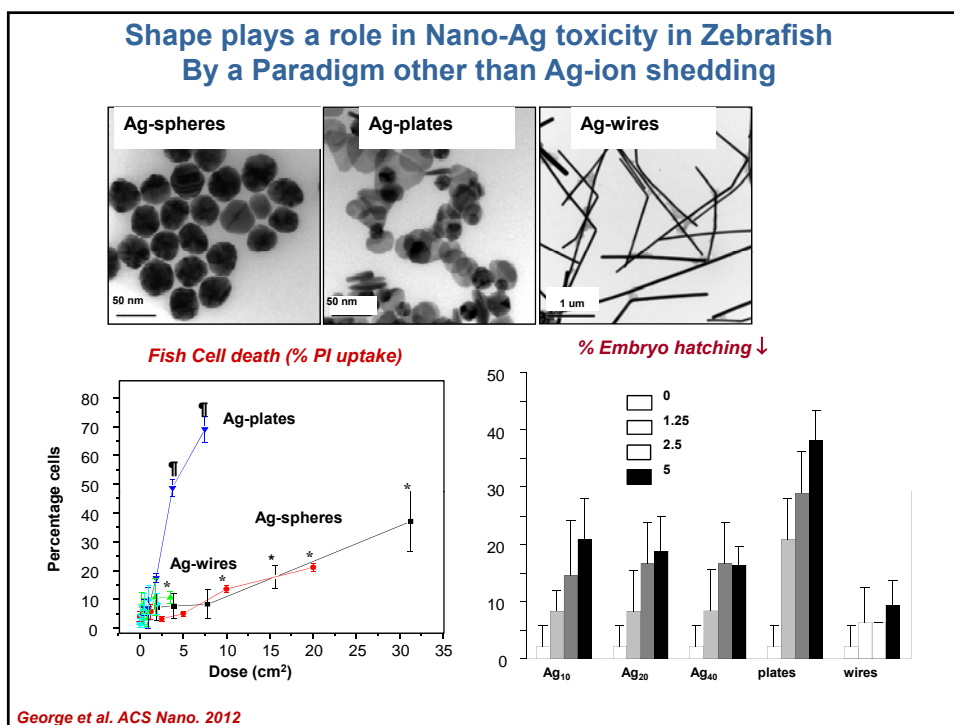
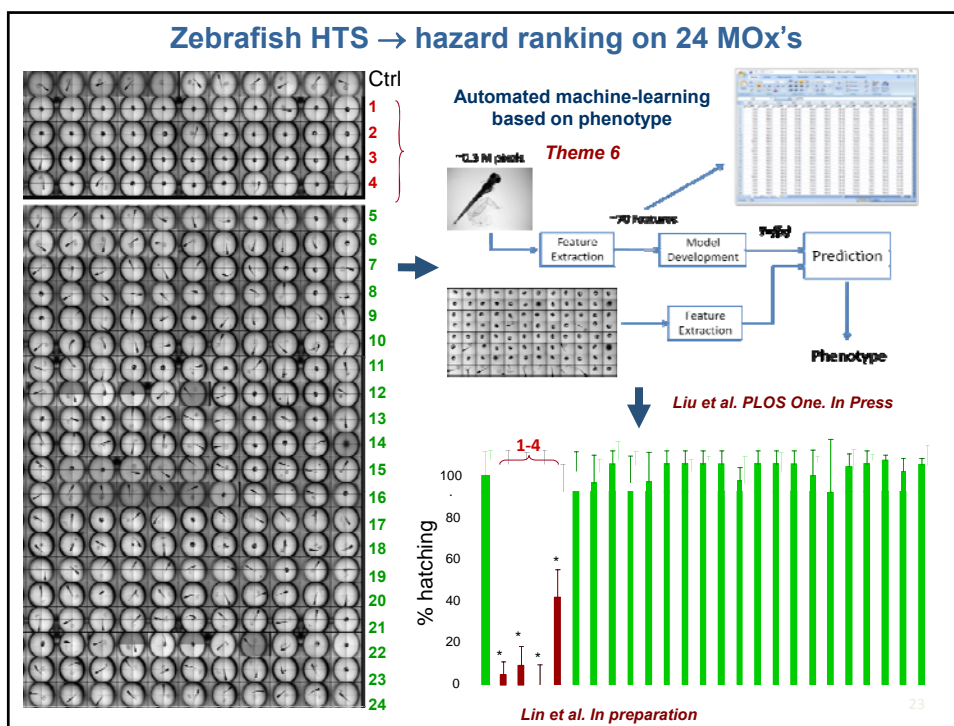
### PI uptake - cytotoxicity

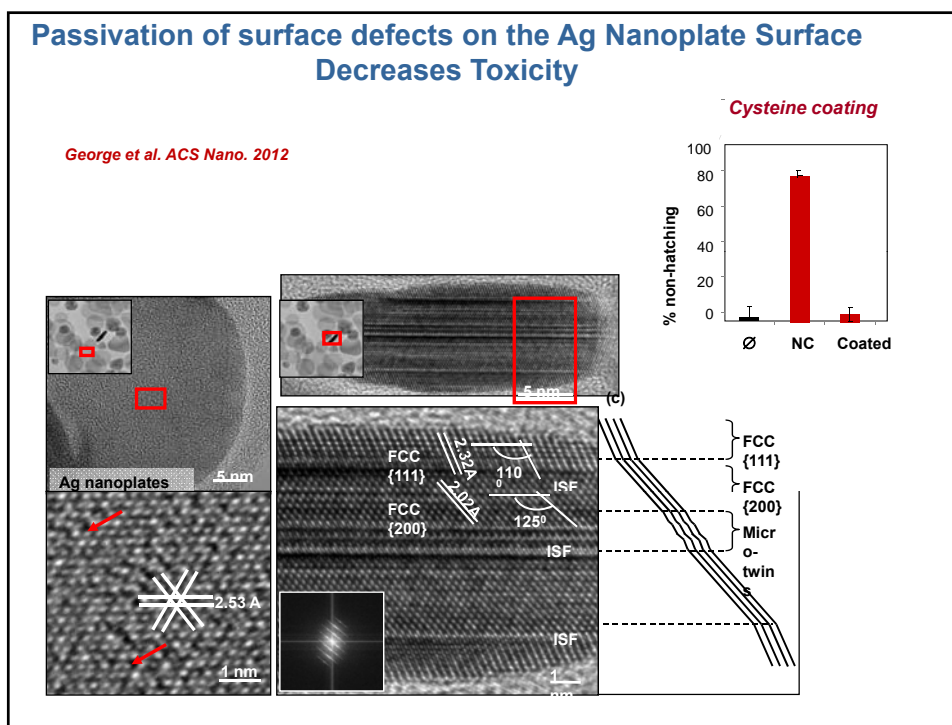
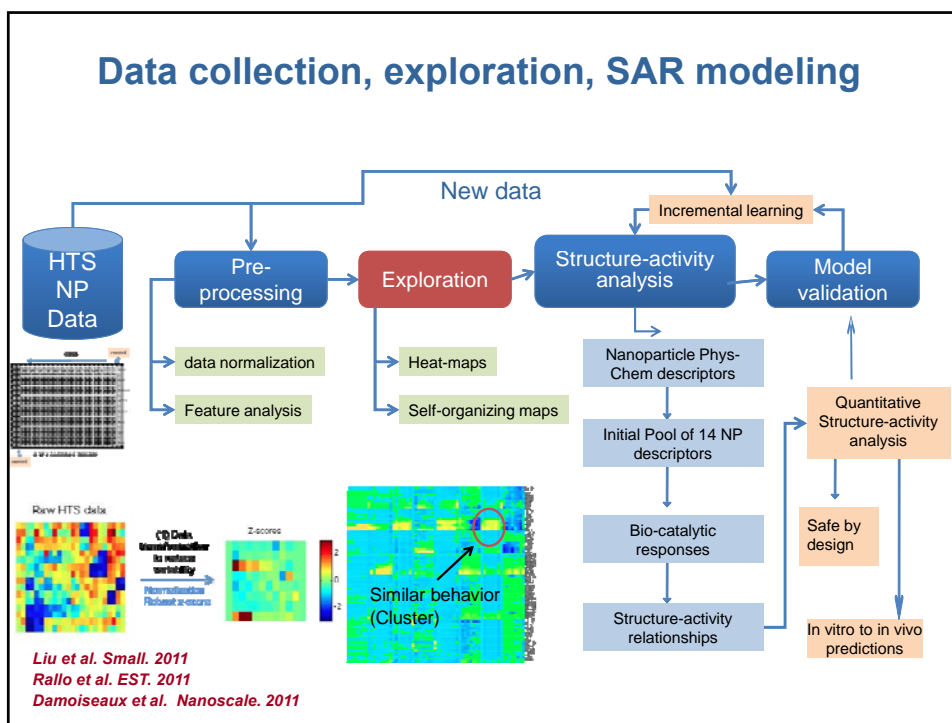


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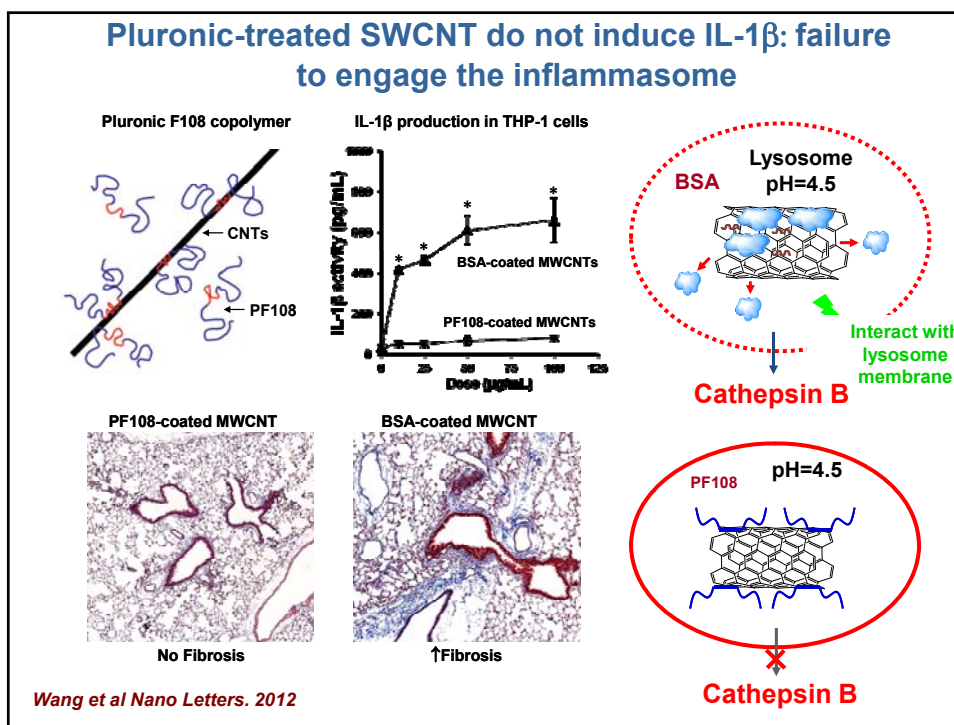
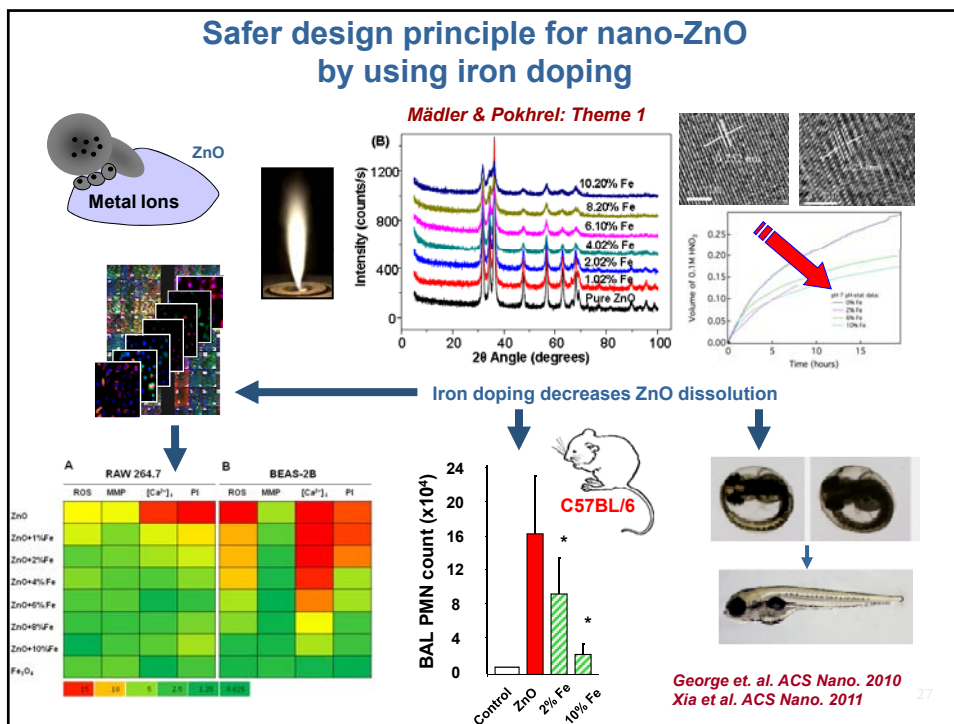
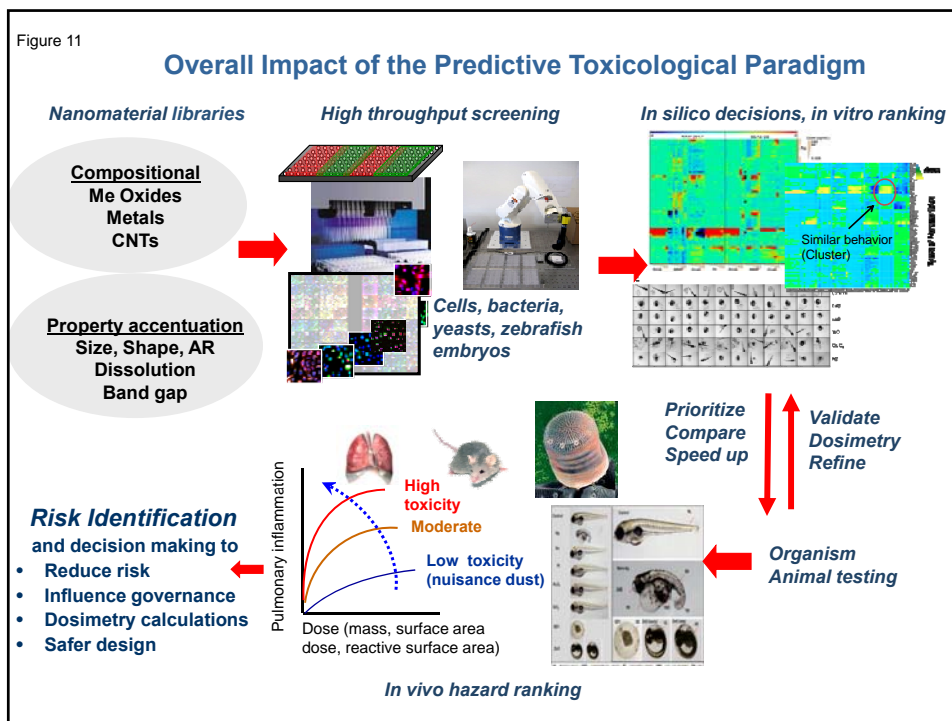
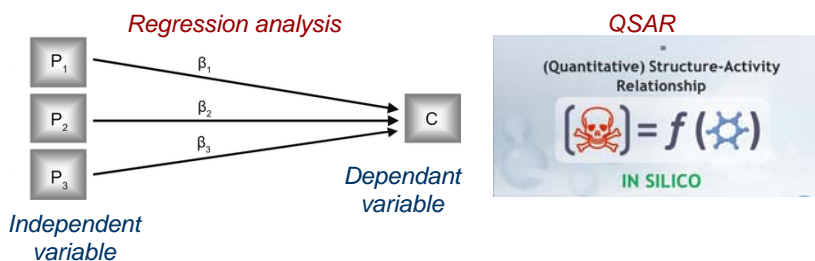


Figure 11



## Quantitative Structure-Activity Relationships in Nanomaterial Toxicity



**Quantitative SARs (QSARs)** are regression analysis models in which fundamental material physicochemical descriptors are employed to generate quantitative models for correlating and predicting injury responses resulting from exposure to ENMs. Fundamental descriptors are essential since dependable variables (most proximate physicochemical properties associated with injury) may be determined by a series of independent variables in a hierarchically structured matrix. The ultimate goal of QSAR models is to predict the activity of new ENMs and also establish the range of ENM descriptors suitable for the design of safe ENMs.

Liu et al. *Small*, 2011  
Rallo et al. *EST*, 2011

