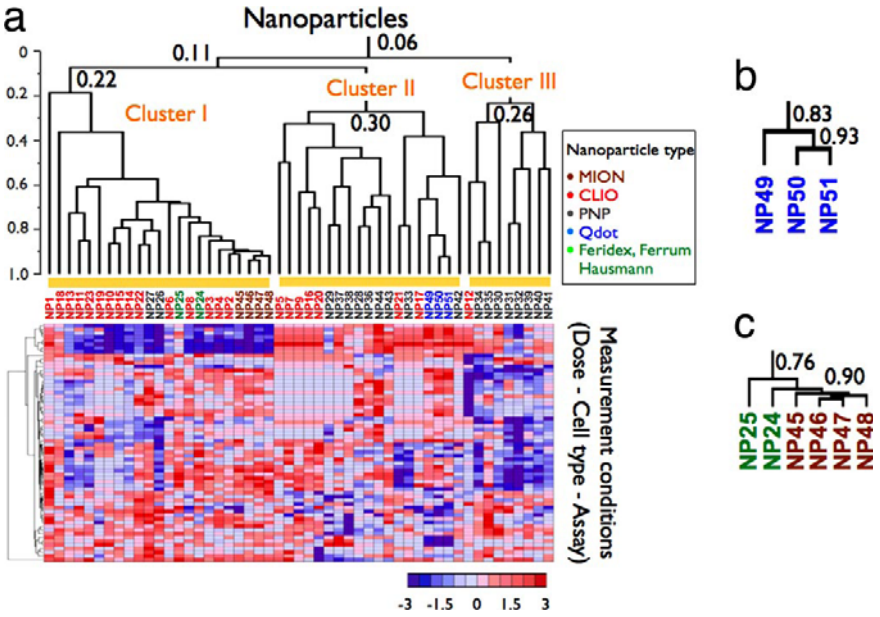
High-Throughput Screen for Nanoparticle Toxicity

Understanding the biological activity of nanomaterials is essential for determining the potential for biomedical application, and for assessment of occupational and environmental risks that the materials may pose. However, widespread *in vivo* testing of all candidate materials early in their development lacks feasibility. To address this problem, Shaw and colleagues have developed a multi-dimensional screen to analyze *in vitro* nanomaterial activity in a generalizable systematic fashion. The screen employs multiple assays that reflect different aspects of cellular physiology; apoptosis, mitochondrial potential, reducing potential and ATP concentration. The screen also uses multiple cell types that reflect tissues particularly relevant for evaluation of agents administered intravenously; endothelial and smooth muscle cells from the vasculature, monocytes which take up many nanoparticle imaging agents, and hepatocytes (reflecting the importance of hepatotocity of biomaterials). In addition, each material was tested at four different concentrations over a range typically used *in vivo*.



a) Heat map depicting hierarchical clustering of biological activity in the data set, represented by Z scores. Numbers adjacent to nodes indicate correlation values for the node.

b) Dendrogram of a subcluster containing all three quantum dots.

c) Dendrogram of clustering of two nanoparticles approved for human use (green) and four MION-based nanoparticles

Clustering of the data identified nanomaterials with similar patterns of biological activity across a range of biological properties; the use of multiple assays and cell types was significantly enriched the biological activity profiles. The detailed structure-activity profiles obtained showed instances where the activity profiles were dominated either by core composition or by surface modifications. Testing of a subset of nanoparticles in mice showed that nanomaterials with similar activity profiles *in vitro* had similar effects on monocyte number *in vivo.* The results suggest that using a multidimensional screen *in vitro* may be useful in optimizing the design of safe nanomaterials for clinical use.

Shaw S.Y., Westly E.C., Pittet M.J., Subramanian A., Schreiber S.L., and Weissleder R. *Proceedings of the National Academy of Sciences USA* 105(21)7387-7392, May 27, 2008.

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