Title:
Comparison of diverse nanomaterial bioactivity profiles based on high-throughput screening (HTS) in ToxCast™

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Abstract Body:

Most nanomaterials (NMs) in commerce lack hazard data. Efficient NM testing requires suitable toxicity tests for prioritization of NMs to be tested. The EPA's ToxCast program is screening NM bioactivities and ranking NMs by their bioactivities to inform targeted testing planning. 62 samples of Au, Ag, CeO_2, $Cu(O_2)$, TiO_2, SiO_2, and ZnO nanoparticles, their ion and micro counterparts, carbon nanotubes (CNTs), and asbestos were screened for 262 in vitro bioactivity/toxicity endpoints. Cellular stress and immune response were primarily affected. NM's core chemical composition was more important than size for bioactivity. Similar profiles between NMs and their ion counterparts suggested ion shedding as a key factor in NM bioactivity. Immune response profiles of 6 CNTs were distinctive from the profile of 3 asbestos. Potential bioactivity targets that were not directly measured were suggested by reference profiles similar to our data, e.g. similar profiles of a microtubule stabilizer and our nano-TiO_2. Dividing endpoints into 10 function domains, we developed a ToxPi-based ranking for *in vitro* bioactivity. Ag, Cu, and Zn samples were ranked as high *in vitro* bioactivity due to their activities in more domains and at lower concentrations than other samples. Our assays may be not very sensitive to inhalation effects, but our data and prioritization approach can be used for various purposes. We showed that HTS assays can identify affected cellular functions, predict targets, and may be useful for ranking NMs for specific purposes. *This abstract does not necessarily reflect EPA policy.*

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