Linking nanomaterial physico-chemical properties with cellular uptake and toxicity

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Nanotechnology is one of the key technologies of the 21st century. Already by now, many products containing manufactured nanomaterials (NMs) have entered the market. Most industrial applications are based on just a few NM types, mostly metals and metal oxides. However, by varying size, shape or surface chemistry a large number of variants can be produced. Variations of physico-chemical parameters can result in altered cellular uptake and NM toxicity. Therefore, each NM variant has to be tested and assessed individually, in a case-by-case approach. Considering time and costs of toxicological testing as well as the high number of possible endpoints this approach seems not feasible. Thus, there is an urgent need to understand in more detail how specific physico-chemical properties influence NM cellular uptake and toxicity.

In the context of several projects we have systematically investigated how different physico-chemical properties such as size and surface charge influence cellular uptake and toxicity for different NMs including several SiO2 and nanosilver variants. For instance we could show that size has a strong influence on NM uptake. In general, smaller particles were taken up more efficiently, resulting in a higher number of particles per cell while larger particles resulted in higher cellular NM mass per cell. Most of the toxicological endpoints investigated so far (i.e. cytotoxicity and oxidative stress) correlated better to available NM surface than to total available mass. Toxicity was mostly dependent on chemical composition while NM surface modification could modify toxicity. Currently, we focus on understanding NM toxicity on a mechanistic basis by applying systems biology approaches such as proteomics and metabolomics.

Taken together, this knowledge will be used to establish NM grouping principles allowing for a more targeted testing and a more efficient risk assessment of NMs. Grouping approaches can then be used in several regulatory frameworks, most importantly within REACH, to derive data on novel NM variants by considering structural similarity and available date for similar NM types.