More efficient risk assessment for nanomaterials

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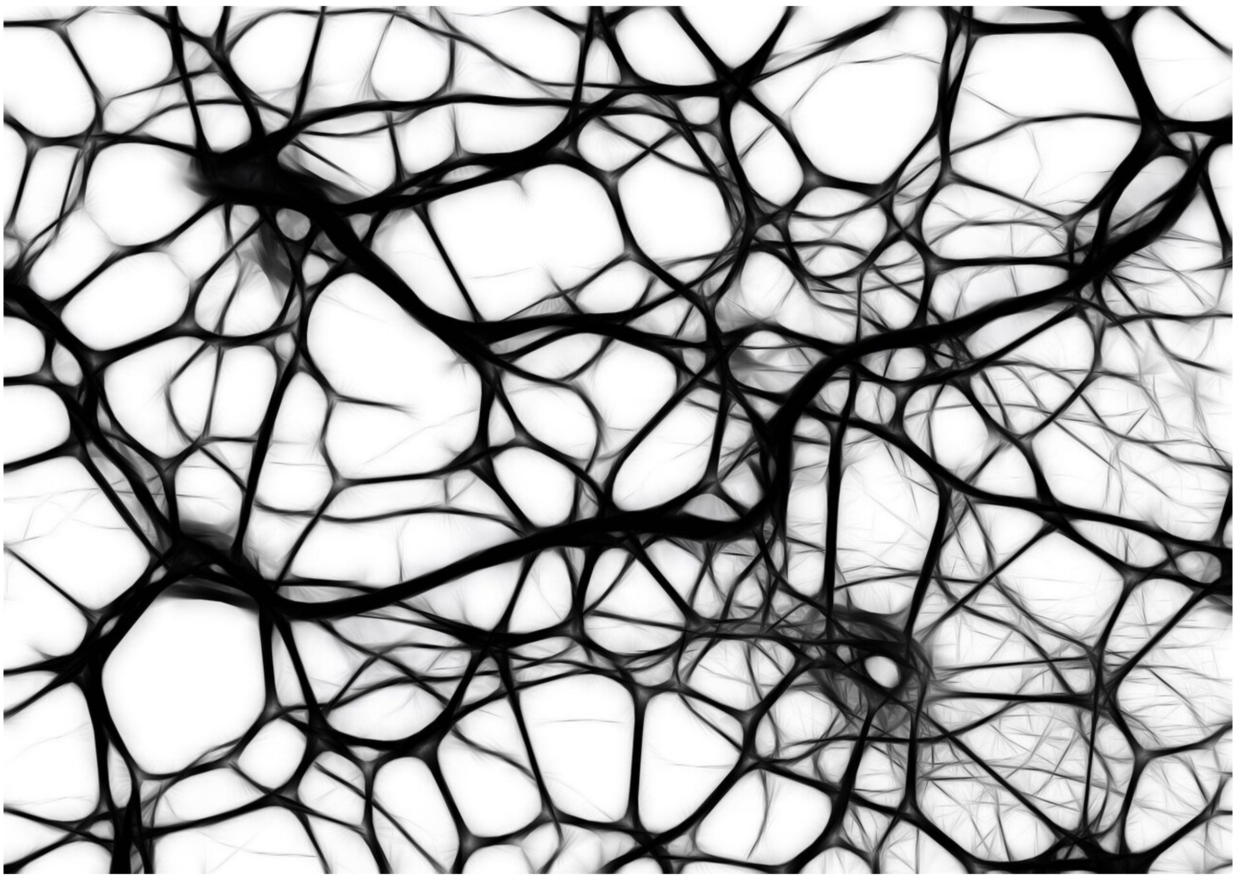

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Nanotechnology is booming, but risk assessment for these tiny particles is a laborious process that presents significant challenges to the German

Federal Institute for Risk Assessment (BfR). To find more efficient test methods, researchers at the Helmholtz Centre for Environmental Research (UFZ) in cooperation with BfR scientists took a closer look at the biological effects. Their results have been published in the journal Particle and Fibre Toxicology.

From dyes to construction materials, and from cosmetic products to electronics and medicine, nanomaterials are found in many different applications. But what are these materials?

"Nanomaterials are defined purely by their size," explains Dr. Kristin Schubert from the Department of Molecular Systems Biology at UFZ. "Materials between one and 100 nanometers in size are referred to as a nanomaterials." To help envisage their diminutive size: One nanometer is just one millionth of a millimeter. Since nanomaterials are so small, they can easily enter the body, for example through the lungs, skin or gastrointestinal tract, where they can cause adverse effects. Just like conventional chemicals, nanomaterials must therefore be tested for potential health risks before they can be industrially manufactured, used and marketed.

Currently, testing is carried out for each nanomaterial individually. And since even the smallest changes—for example, in size or surface characteristics—can affect toxicity, separate tests are also needed for each variant of a nanomaterial. "Risk assessment for nanomaterials is sometimes difficult and very time-consuming," says Dr. Andrea Haase from BfR. "And the list of substances to be tested is getting longer every day, because nanotechnology is growing to become a key technology with wide-ranging applications. We therefore urgently need to find solutions for more efficient risk assessment."

How can nanomaterials be appropriately classified into groups? Are there similarities in their effects? And what material properties are associated with these effects? In their recent study, researchers at UFZ and BfR and industry representatives set about answering these questions. "We focused on the biological effects and examined which molecules and signaling pathways in the cell are influenced by which types of nanomaterials," says Schubert.

Through in vitro experiments, the researchers exposed epithelial cells from rats' lungs to different nanomaterials and looked for changes within the cells. To do this, they used what are known as multi-omics methods: they identified several thousand cell proteins, various lipids and amino acids, and studied important signaling pathways within the cell. Using a novel bioinformatic analysis technique, they evaluated huge volumes of data and came to some interesting results.

"We were able to show that nanomaterials with toxic effects initially trigger oxidative stress and that in the process certain proteins are up- or down-regulated in the cell," explains Schubert. "In future, these key molecules could serve as biomarkers to detect and provide evidence of potential toxic effects of nanomaterials quickly and effectively." If the toxicity of the nanomaterial is high, oxidative stress increases, inflammatory processes develop and after a certain point, the cell dies.

"We now have a better understanding of how nanomaterials affect the cell," says Haase. "And with the help of biomarkers we can now also detect much lower toxic effects than previously possible." The researchers also identified clear links between certain properties of nanomaterials and changes in the cellular metabolism. "For example, we were able to show that nanomaterials with a large surface area affect the cell quite differently from those with a small surface area," says Schubert. Knowing which parameters play a key role in toxic effects is very useful. It means that nanomaterials can be optimized during the manufacturing process, for example through small modifications, and hence toxic effects reduced.

"Our study has taken us several large steps forward," says Schubert. "For the first time, we have extensively analyzed the biological mechanisms underlying the toxic effects, classified nanomaterials into groups based on their biological effects and identified key biomarkers for novel test methods." Andrea Haase from BfR is more than satisfied: "The results are important for future work. They will contribute to new concepts for the efficient, reliable risk assessment of nanomaterials and set the direction in which we need to go."

More information: Isabel Karkossa et al. An in-depth multi-omics analysis in RLE-6TN rat alveolar epithelial cells allows for nanomaterial categorization, *Particle and Fibre Toxicology* (2019). DOI: 10.1186/s12989-019-0321-5

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