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Empa researchers develop test procedures for cell cultures

Tracking down possible dangers of nanoparticles

Our world is becoming a better place thanks to nanotechnology. That at least is the promise of marketing directors in the nanotechnology industry. Still, there are possible risks posed by these small particles to humans and the environment, and these risks have not as yet been fully evaluated and studied. Empa researchers want to help. In a research project titled „Nano Risks", an Empa team developed intercellular tests which can quickly and in a relatively simple manner measure the toxicity or „poison level" in biological cells. Preliminary results show that not all nanoparticles are the same in their effect and impact.

Since the start of the „nano age", heretofore unimagined possibilities present themselves to material scientists. Nanoparticles, that is infinitesimal small particles with a diameter of a few nanometers, often just a few molecules thick, show differing chemical and physical properties than bigger particles of the same material. Thus, for the first time, novel materials with specially designed characteristics can be produced. Dirt repellant shirts, non burning frying pans, scratch free surfaces, better computer hard disks and more effective sun protectors – the nanoproducts range is indeed impressive. But how does the human organism react to these small particles? And what possible effects have nanoparticles on cells and tissues? Since nanoproducts are similar in size to a cell's protein molecules, they can easily penetrate a cell's membrane and be absorbed. But what happens then to the cell? Many questions and few answers remain.

Peter Wick, Arie Bruinink and their colleagues at Empa decided it is high time to dedicate their research efforts to these „nanotoxicity" questions. „Should these novel materials be mass produced, it is imperative that we determine if the use of these new physical-chemical products will have unexpected adverse impacts on humans", declared cell biologist Wick.

Cellular cultures as laboratory guinea pigs for toxicity testing

The goal of the Empa researchers was to develop a quick and relatively simple test for an initial evaluation of nanoparticles' toxicity, without resorting to animal experimentation. Ideal candidates for such investigations are cellular cultures often used in toxicity tests of various chemicals. „However, we had to conclude rather quickly that this sort of test is not that simple when it comes to nanoparticles testing", related Wick. The problem is that these small particles bind themselves to each other very fast. „As we introduced the nanoparticles into cellular food solutions, we got clumps as big as a whole cell rather than individual particles", recalls Wick. „Thank god we have wonderful materials scientists here at Empa“, he continued, who helped the biologists with several „tricks“, suspending the nanopowdered particles in cellular food solutions and then examining them in an electron microscope. This allowed the Empa researchers to determine exactly in what form and size the nanoparticles exist in the cell. In the meantime, they also succeeded in separating the nanoparticles from each other according to their size and form. „Many of the previous studies of the toxicity of nanoparticles were conducted by biologists who were not fully convinced, as we were at first, about the eventual form in which these particles react within the cell. This is good biology but poor material science“, according to Wick. If you simply introduce nanoparticles into the cell, one can never be sure which of these particles in which form are responsible for the observed effect.

Not all nanoparticles damage cells equally

Following their materials science „homework“, Wick and his colleagues at Empa have examined the toxic effects of seven important industrial nanoparticles on cells. These ranged from the harmless Siliconoxide used as a food additive for a long time in such items as ketchup, to Titanium and Zincoxide used in cosmetics, and to Ceroxide and Zirconoxide, materials employed in the production of electronics. For comparisons sake asbestos fibers whose toxic effects on cells are well known and researched were also tested (asbestos fibers, whose average length is around ten micrometers, and whose diameter is around one micrometer, are not, however, actually considered nanoparticles). The researchers also used as laboratory „guinea pigs“ two kinds of cells regularly used in toxicity testing: human lung cells and mice fibroblasts. The cells metabolism, their division rates and speeds as well as the cell’s observed appearance under the microscope were used by the scientists as criteria for the relative health of the cell. The conclusion of the study, which will be published in the next editon of the scientific journal „Environmental Science and Technology“: „Not all nanoparticles are equally toxic“.

The Empa team could devise a kind of a „range of toxicity“ scale between asbestos and Siliconoxide: While Ironoxide and Zincoxide particles appeared to impair human lung cells, Tricalcium phosphate (used in medical implants) exhibited similar toleration properties as Siliconoxide. Titaniumoxide, Ceroxide and Zirconoxide caused a temporary enlargement of the cell but are clearly less toxic than asbestos. Alltogether, the human lung cells showed a definite greater sensitivity to nanoparticles than mice fibroblasts. „Lung cells are therefore better suited for these kind of toxicity studies“ according to Wick, „and our goal is to develop a cellular culture testing method which comes closest to animal experimentation“. Hence the Empa researchers intend to examine now various kind of cells among which are three kinds of lung cells as well as freshly isolated chicken nerve cells.

Carbon nanotubes: more toxic when they clump together

In a not yet published study, Wick and his colleagues examined carefully carbon nanotubes. In contrast to nanoparticles, nanotubes became more damaging to cells when they clumped together in a larger needle like form. „These agglomerates, similar in form and toxicity to asbestos fibers seem therefore to be unfavorable“, said Wick.

Next, Wick wants to understand what exactly happens inside a cell when nanoparticles are introduced into it. He is therefore analyzing the activities of thousands of genes with the aid of so called DNA chips. „We can thus see the effect these nanoparticles have on the cell, i.e. which genetic codes are turned on and off“, informed Wick.

„NanoRisk“ study examines also the impact of nanotechnology on society as a whole

The results of Wick’s studies – coupled with data from various animal experimentations and research analyses about the diffusion of nana particles in the environment – are also used by researchers from Lorenz Hilty’s Laboratory of Technology and Society at Empa, to carry out a risk assessment study of nanoparticles and nanotubes. The researchers analyze published studies of nanotoxicology and consult with experts in order to evaluate the validity of these studies. Thus far it appears that there exist few significant research studies in this field, and some of these even show conflicting conclusions. Such results may have come about by not completely analyzing the properties of the nanoparticles used in the various experiments, so that the researchers conducting them may not have been fully aware of, or familiar, with the form and size of the particles they studied.

In the second phase of their risk assessments studies, the Empa researchers will examine the practical application of nanotubes as it relates to their fabrication, the manufacturing of nanoparticles containing products and the eventual disposition of such products. The goal of these „lifecycle“ analyses is to obtain exact data about releasing nanoparticles in varying quantities into the environment, in order to devise possible precautionary strategies.

Further information

Dr. Peter Wick, Lab. of Materials-Biology Interactions, peter.wick@empa.ch, phone +41 71 2747684
Prof. Dr. Lorenz Hilty, Lab. of Technology and Society, lorenz.hilty@empa.ch, phone +41 71 2747345
Dr. Michael Hagmann, Section of Communications, michael.hagman@empa.ch Tel. +41 44 8234592

The pictures and the PDF version of the study which will be published in „Environmental Science and Technology“ can be ordered from Martina Peter; martina.peter@empa.ch Tel.+41 44 8234987

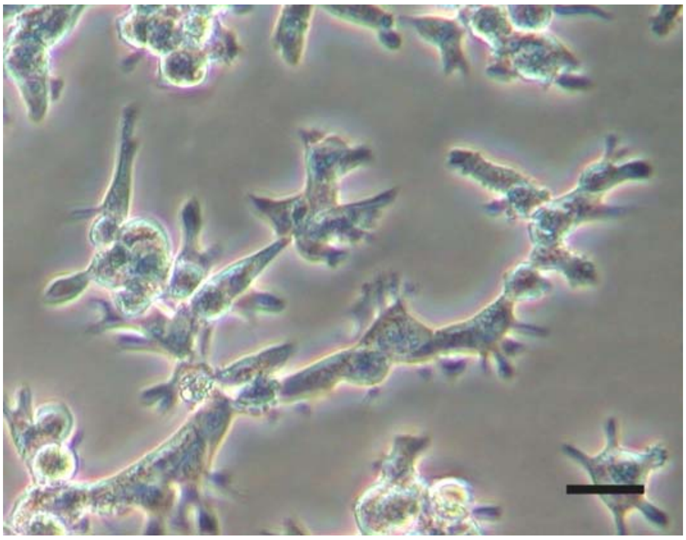

Abb1_SiO.jpg

Human lung cells were exposed to harmless Siliconoxide (SiO_2) nanoparticles for three days. The cells stick to the bottom and have a spindle like form. This is how a healthy cellular culture looks like. (the beam is about 20 micrometers long.)

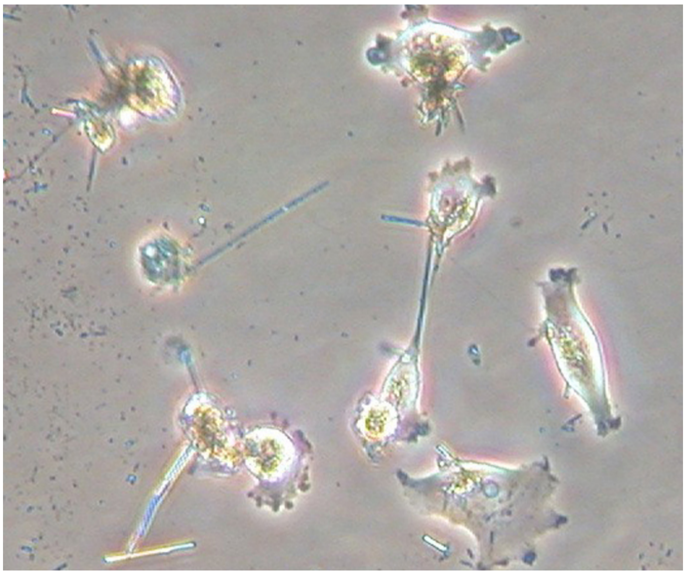

Abb2_Asbest.jpg:

Human lung cells were exposed to toxic asbestos fibers for three days. The cells which normally stick to the bottom and are long and stretched out start to round up and separate from the bottom – a signal of stress. Some cells, top left, are close to dying.

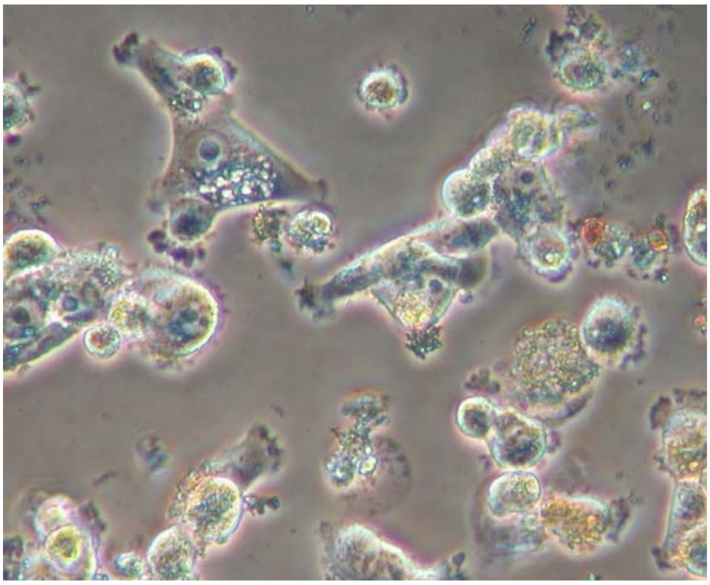

Abb3_Fe2O3.jpg

Human lung cells were exposed to Ironoxide (Fe_2O_3) nanoparticles for three days. Here too, the cells begin to round up and separate from the bottom, a first sign that Ironoxide particles are zytotoxic.