UNIVERSITÄT BASEL

NANO

National Center of Competence in Research Nanoscale Science

SNI SWISS NANOSCIENCE INSTITUTE

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Workshop in Basel: Is nano toxic?

Safety and risks in the nanosciences and nanotechnology were the subject of a workshop that was held by the Swiss Nanoscience Institute (SNI) in Basel on 9 February 2007. Scientists from various Swiss research institutions presented their latest findings on this subject area. They made it clear that certain nanomaterials definitely entail risks, but that further research is needed. However, the nanosciences and nanotechnology also offer enormous opportunities, which also need to be further researched and applied.

More than a hundred interested participants from science and industry attended the half-day event at the SNI, University of Basel. Students, assistants and professors were all keen to hear how the experts assess the safety and risks of different nanomaterials. The SNI had invited scientists from all over Switzerland to offer their scientific insights into this field. The SNI, too, is set to start research projects on the safety of nanomaterials in the future. Discussions are currently ongoing as to which partners may deliver useful results in addition to existing projects.

In summary, it can be said that industrially manufactured nanoparticles and carbon nanotubes are finding their way into cells and organelles. In various cell culture systems, the nanomaterials presented show different degrees of toxicity depending on the material tested and the test system. But scientists today know very little about the long-term consequences of these particles in the cells of a body. Researchers therefore now need to investigate the mechanisms of the toxicity found, to submit certain materials to discriminating analysis and to pursue studies over many years. Only research in interdisciplinary teams will show us which nanomaterials carry a risk potential and how we can protect ourselves from these risks. At the same time, scientists should not neglect the enormous opportunities of nanotechnology. including in medicine. As some presentations at this workshop showed, nanotechnology can serve to keep other risks in check, such as adverse effects of medicines, and to determine the toxicity of conventional medicines.

Summary of individual presentations:

Prof. Peter Gehr from the University of Berne kicked off the series of lectures. He reported on the work of his team on a cellular system that simulates the surface of the airways. This acts like a self-cleaning system of the airway filter upstream of the gas exchange region – the body's largest port of entry for nanoparticles. In general, particles that enter the lungs are transported to the interior of cells to render them harmless. Using the test system presented here, it is now possible to study the route which the particles take and the way in which the various cell types (macrophages, dendritic cells, epithelial cells) behave. Larger particles (1 µm) are taken up by certain cells, the dendritic cells and macrophages, through phagocytosis. This leads to the formation of a marker substance for inflammation (tumor necrosis factor-α) as a result of individual particle types. Nanoparticles (0.078 µm) can be detected in macrophages and dendritic cells. However, they enter the cells by means of a hitherto unknown mechanism. Signs of inflammation are not observed after uptake. The distribution of inhaled and deposited nanoparticles in the lung is not a random process. In animal studies, Gehr showed that, 24 hours after exposure, the nanoparticles were to be found especially in the fine capillaries. Nanoparticles do not only enter the cells of the lung surface. Gehr also presented studies of red blood cells. These do not take up any microparticles, but nanoparticles can be detected in the interior of the cell. Within other cells, e.g. in macrophages, they then also penetrate organelles such as mitochondria, as well as the cell nucleus. However, it is not yet possible to assess what effect nanoparticles that have penetrated the cells might have on health. But they might induce oxidative stress in the cells.

Dr. Peter Wick from Empa in St. Gallen was also unable to offer any conclusions on the long-term effects of nanomaterials. Together with his research group, he is studying the toxicity of carbon nanotubes (CNTs) in cell culture systems. Carbon nanotubes have a lot of outstanding properties, such as enormous strength coupled with minimal mass. Amongst other things they are used to make materials in aeroplane construction lighter and more stable. The production of CNTs is set to multiply in the next few years, so information on their toxicity is hugely important. Wick's group has manufactured CNTs of varying quality from raw materials and tested them with different cell culture systems. The scientists found that CNTs are absorbed and not broken down by the cells. CNTs in the cells probably cause oxidative stress and thus exert a toxic effect. Different test systems have shown different rates of absorption and thus also different cytotoxicity. Wick stressed that it is now important to study the precise mechanisms underlying these effects.

Prof. Laszlo Forro from the Swiss Federal Institute of Technology (EPF) Lausanne is working on the toxicity of carbon nanotubes (CNTs) in collaboration with Prof. Schwaller (Histological Institute Fribourg) and Dr. Pasquier (Cytopath Labor in Geneva). This team is using a colour reaction to examine how many cells die off as a result of treatment with purified carbon nanotubes. In his studies the addition of CNTs led to the death of about 50% of cells within the study period of four days (concentration 0.2 mg/mL). But there were substantial differences between the various nanotubes: multi-walled nanotubes were less toxic than those with a single wall. The toxicity increased as a result of surface oxidation. Carbon black has proved especially toxic – this is made up of tiny soot particles which have been used for many years in car tyres to confer wear-resistance and good adhesion.

In the lecture by **Dr. Martin Kuster**, Head of Occupational Health at Novartis, it became clear how important it is to initiate and complete studies that allow conclusions to be drawn on the effective impact of nanoparticles throughout the body. He feels that many nanoparticles have to be classified as problematically for the time being, because they cannot be metabolized by the body. For him and his work as a doctor, however, it is essential to know the longer-term effects. Only then can effective precautions be taken.

PD Dr. Patrick Hunziker from the University of Basel steered the interest of the audience in a different direction. He illustrated how nanoproducts and nanotechnology may be able to solve some fundamental problems in medicine. As a practising physician in an intensive care unit, he is witness every day to the fact that diseases such as arteriosclerosis, which leads to myocardial infarction and stroke, start at the cellular level. But he does not have sufficiently refined instruments and treatment methods at his disposal to engage in optimally effective diagnosis and treatment that is both low in side effects and low on costs before the disease actually develops. Carriers of medicines in nanoscale dimensions now promise more targeted use of medicines for the treatment of diseased cells and organs. However, unlike the nanoparticles mentioned above, these carriers are not solid objects, but act as "envelopes" in which a suitable active ingredient can be packed and conveyed specifically to the focus of disease. Ongoing experiments show that the dose of medication needed and any side effects can be reduced using this method. In support of these efficacy studies, the scientists place great value on better understanding the interplay between such medicine carriers and living cells and organisms and thus identifying toxicity problems at the earliest stage. On this subject, Hunziker pointed to some experiments that have so far yielded highly promising results.

Dr. Christof Fattinger, from Discovery Enabling Sciences at Hoffmann-La Roche, also focused rather on the opportunities than the risks of nanotechnology. He demonstrated how toxic effects can be studied using nanotechnology. Together with the IBM Research Laboratory in Rüschlikon, his team has developed a test system that allows a large number of parameters to be tested simultaneously in the tiniest blood, serum or tissue samples. This system, for example, enables the concentration of tumor necrosis factor-α to be measured, as a result of which conclusions can be drawn on inflammatory processes in the body. Pointers to disease processes or potential toxic side effects of medicines can thus be obtained at an early stage and with far fewer animal experiments. Nanoanalytical methods based on "gene chips" are already being used today in human diagnostics in order to adjust the treatment of certain diseases immediately and precisely to the needs of the patient and thus also to avoid unwanted side effects.

The **Swiss Nanoscience Institute (SNI)** developed from the National Center of Competence in Research (NCCR) "Nanoscale Science" and constitutes a priority program of the University of Basel. It combines basic science with application-orientated research. In various projects researchers focus on nanoscale structures and aim at providing new impact and ideas to the life sciences, to the sustainable use of resources, and to information and communication technologies. The University of Basel as the leading house coordinates the NCCR network of universities, federal research institutes, and industrial partners, which is a research instrument of the Swiss National Science Foundation, and the Argovia-network, which is financed by the Swiss Canton of Aargau. With the establishment of the SNI the University of Basel continues to secure the internationally acknowledged position as a centre of excellence in nanoscale sciences.
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