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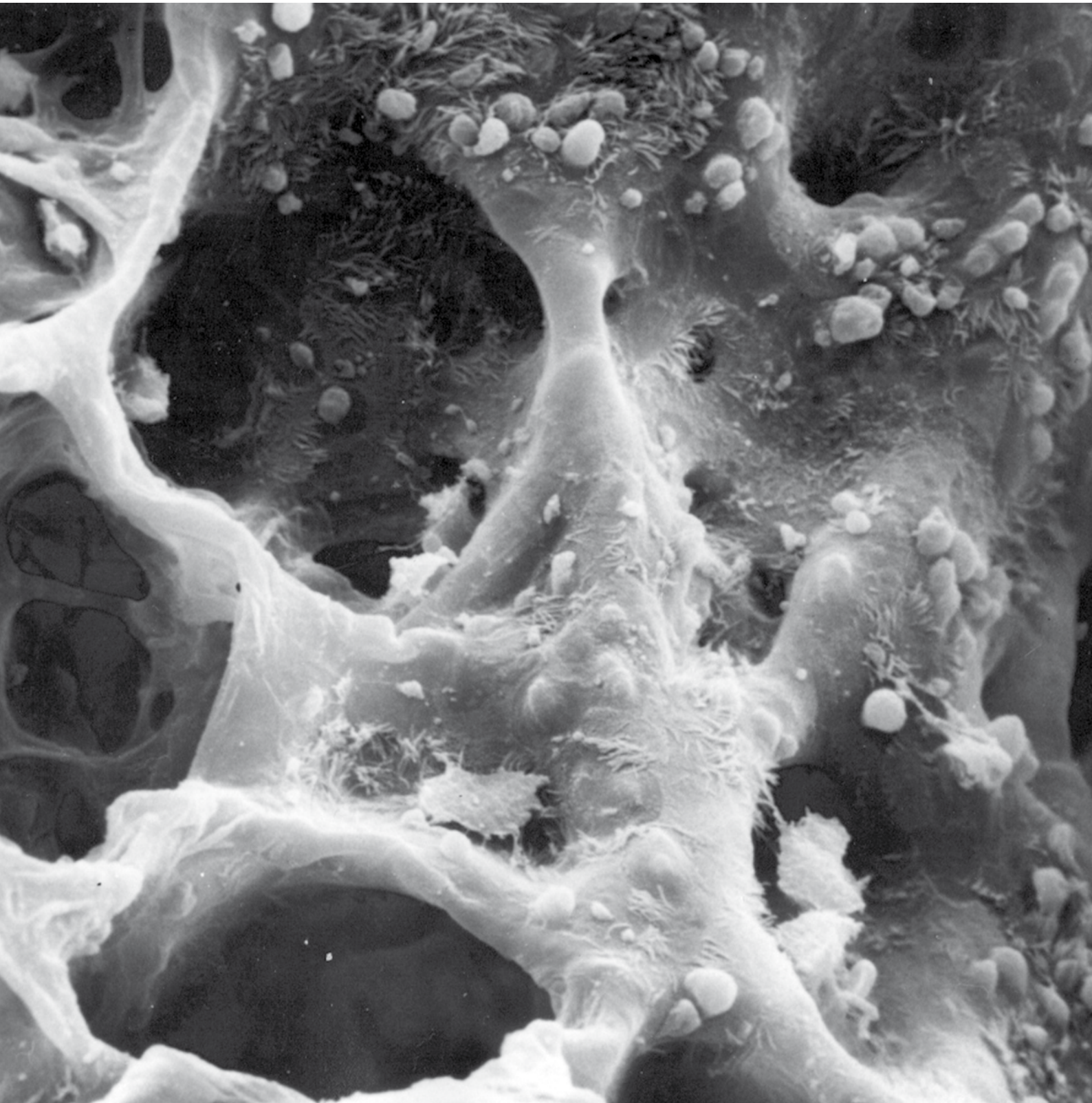
Toxicology and Experimental Medicine

Crime Scene in the Lung: Air pollutants and how they pose a risk to health

Toxicological evaluations of low solubility particles using image analysis



Crime Scene in the Lung: Air pollutants and how they pose a risk to health

Toxicological evaluations of low solubility particles using image analysis

Research on contamination of humans and of their environment due to emissions and chemicals, process the toxicological questions as well as to provide important medication research impetus: in the inhalation toxicology department of the Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM), Dr. Bernd Bellmann is predominantly occupied with the health-related effects of airborne substances. Microscopy and digital image analysis are valuable tools in his investigations.

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The Fraunhofer ITEM in Hanover, Germany

The Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM) was founded in 1981 in Hanover, Germany and researches contamination of humans and of their environment due to emissions and chemicals. In order to process the toxicological questions as well as to provide important medication research impetus, core competences have been established in the natural sciences/biomedical sector. Today there are ca. 200 employees working in 4 business areas at the ITEM: in pharmaceuticals research, clinical respiratory system research, environmental toxicology and in testing and registering chemicals and biocides.

Focus on inhalation toxicology and consumer protection

In the inhalation toxicology department, Dr. Bernd Bellmann is predominantly occupied with the health-related effects of airborne substances. „The prime focus of our work is analyzing the potential dangers presented by chemicals and mixtures of gases or aerosoles as these occur at the workplace, inside indoor rooms and in the environment“, explains Dr. Bellmann regarding his tasks. One focus is investigating low soluble particles in environmentally relevant atmospheres and in accordance with the exposure occurring in respective workplaces. „This involves also investigating the toxicokinetics of particles in the lungs and the mechanism of toxic effects“, noted Dr. Bellmann further. The aim is to clarify the connection between the occurrence of air pollutants and their toxic effect on humans. As nanotechnology becomes ever more prevalent, today‘s primary focus are on the predominantly fine and ultrafine particles in dimensions less than 0.1 µm. This is a topic of tremendous significance due to the fact that consumer protection and health protection are becoming more and more relevant for marketing purposes.

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The objective of the Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM) which was founded in 1981 is researching contamination of humans and their environment due to emissions and environmentally relevant chemicals resulting from human activity.

The respiratory tract in focus

One central research target for the department of inhalation toxicology is the respiratory tract. The focus is on substances absorbed via inhalation. „Mineral and organic fibers as well as low soluble particles are what we are primarily occupied with“, stated Dr. Bellmann. This involves determining the toxicity and carcinogenicity of potential pollutants. The scientists use the results for evaluating the health risk in accordance with occupational and environment-related exposure.

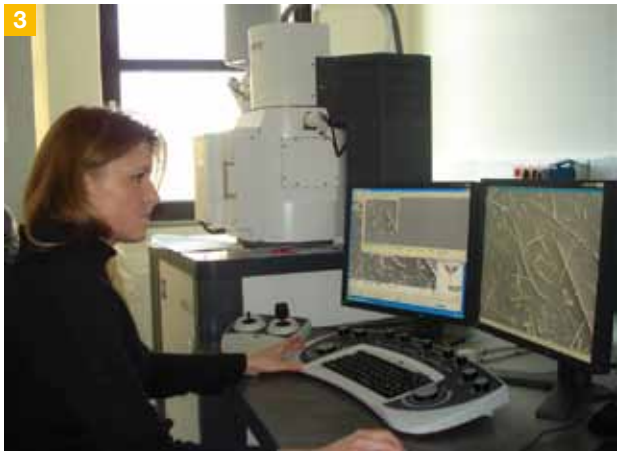
Dr. Bellmann‘s team has a wide variety of methods and instruments at their disposal for the toxicological investigations. The fiber and particle analysis includes electron microscopy techniques and image-analysis procedures. The images of the scanning-electron microscope (SEM) are automatically transferred to Scandium, the Olympus Soft Imaging Solutions imaging platform. All critical acquisition parameters such as XY calibration and the stage coordinates of the microscope are associated with the images. The software offers numerous interactive measurement procedures and statistic options thus providing for direct and precise fiber measurement. These image-analysis techniques are used by Dr. Bellmann and his team for investigating rock wool and glass wool fibers.

In order to conduct these routine measurements in a uniform fashion and to adapt them to the requirements of their own measurement requirements, a special measurement routine was developed by the Fraunhofer Institute. This program is contained within the Scandium program environment, is written using Imaging C, controls the workflow and aids the operator in following this measurement directive. Before the actual fiber measurement, a standardized measurement grid is drawn on the image. This measurement grid facilitates the subsequent selection of fibers to be measured for the operator. The selected fibers are shown on the image and their length is measured interactively. The thickness of these selected fibers is then automatically recorded by the measurement routine. This value, automatically obtained by the software, is displayed on the image clearly magnified to make it easier to monitor. It can also be interactively corrected at any time.

This means that the individual results and relevant statistics of the measurement are available at any time. The investigations demonstrate that newly developed biosoluble rock wool fibers change and ultimately dissolve when in the lung over a longer period of time. The biological processes in the lung modify glass fibers as well. The originally straight fibers are bent or rolled after being in the lung for a longer period of time. Biosoluble glass fibers are largely dissolved after being in the lung 3 months.

Nanotoxicology

Research currently is focusing on more and more nanoparticles at the Fraunhofer ITEM. The „Nanotoxicology“ research project is looking at the biological and toxicological effects and specific mechanism of action of inhaled nanoparticles with regard to their chemical and physical properties. These include, eg, material composition, size, shape and charge. Intercellular and intracellular accumulation and distribution of nanoparticles, the cytotoxicity of nanoparticles and a consideration of cell vitality are all topics to be investigated systematically within the framework of respiratory tract research. These research efforts aim at gaining insight into nanoparticle-specific biological effects. Understanding these



Electron microscopes with integrated image analysis are used at the Toxicology and Environmental Hygiene department of the ITEM for investigating rock wool and glass wool fibers.

effects can be helpful in comprehending and illuminating the biological and toxicological mechanisms of action. Due to the expertise available, the inhalation toxicological aspects are at the forefront of these investigations. This work also involves employing image-analytical techniques to determine distribution characteristics, for example.

Conclusion

Inhaling the tiniest particles can result in massive health problems because biological processes in the lung permanently alter the structure of the fibers inhaled. What it is that happens exactly and how dangerous these substances are is what Dr. Bellmann and his team are investigating at the Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM) in Hanover, Germany. The image-analytical solutions of Olympus provide assistance in this analysis at the department of inhalation toxicology. This results in better and safer products for all of us.

ACKNOWLEDGEMENT

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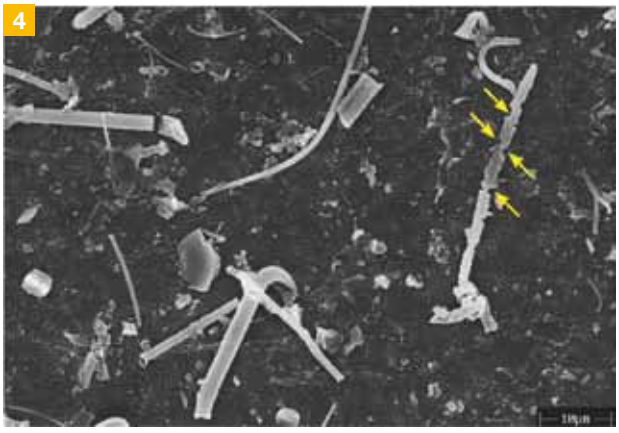
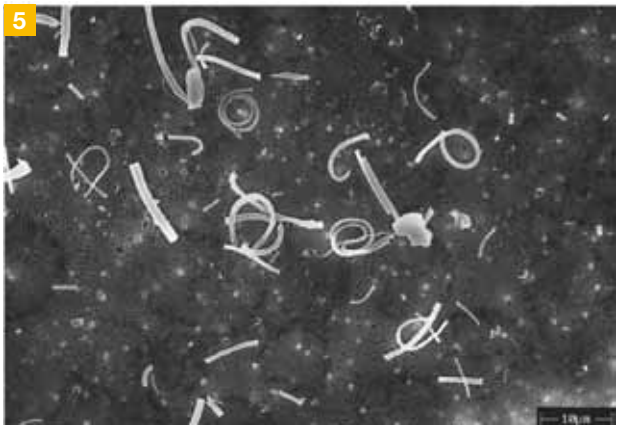
Image courtesy: ITEM Hannover, Olympus Soft Imaging Solutions GmbH, Nikita Golovanov



Rock wool fibers after being in the lung for a long period of time. The changes in the fibers are clearly visible: surfaces of some of them have gone from smooth to roughened (see arrows).



Glass fibers are also subject to biological processes within the lung: the fibers which had originally been straight, become bent or rolled after being in the lung for a longer period of time.

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