The importance of lung cell research with regard to evaluating the health impact of UFP

UFP (ultrafine particles < 0,1 µm) are generally just one of the components of air pollution. Although the harmful effects of UFP are widely acknowledged, the question is how to determine the impact of this component. According to Evelien Frijns, VITO, which has extensive experience in nano research, can now offer part of the solution.

The Flemish Institute for Technological Research (VITO) conducts research where lung cells that are grown *in vitro* are exposed to harmful particles in the air, but also to inhalable medication. Inhalation of harmful particles can lead to damaged and dead lung cells, loss of function or inflammatory reactions. In establishing the correlation between the effect, the type of particle and the particle size, it is now possible to accurately evaluate the effects. Based on inhalation studies, we know that the smallest particles penetrate the deepest into the lungs and, from there, can be absorbed into the bloodstream.

Nano research as a guide for UFP

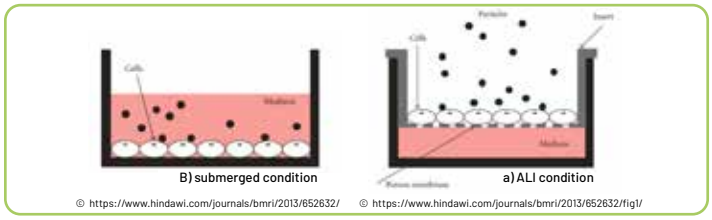
Nanomaterials are designed to facilitate a specific industrial application. Nanoparticles may be used to make a material lighter, in the aerospace industry, for example, to make a material more conductive or to give it a moisture-repellent quality, etc. VITO is specialised in nano research, which includes determining the exposure of employees to nanomaterials and evaluating their impact on the environment and health and thus assessing safety and sustainability. The key question is whether a nanomaterial poses a health risk during the production, processing or use of these materials.

'Nanoparticles are the same size as UFP particles and are measured with the same devices. That is precisely why this can be helpful for UFP research', says Evelien Frijns. 'To determine the health effects of nanoparticles, we use techniques such as lung cell research. Three-dimensional lung cell cultures are exposed to nanoparticles and the health effect on the lung is then determined. The technique used is the same as the one that is used for determining the impact of UFP on lung cells.'

ALI - Air Liquid Interface: non-animal testing method for direct testing of inhalable substances

Traditional animal experiments to determine harmful effects of airborne substances after inhalation require large numbers of laboratory animals, specialised facilities, expertise, time and financial resources. Moreover, these tests cannot be directly translated to human cases. There is a need to develop relevant, alternative methods for studying the potential hazards of these substances and reducing the number of laboratory animals. There is also a need for non-animal testing methods for drug research. These alternative methods use isolated tissues or cultured cells (in vitro testing).

The first in vitro inhalation studies were performed with submerged lung cells (see figure 'submerged') to which the substance to be tested was added. Although this method is still widely used for in vitro pulmonary toxicity studies, the results are not particularly comparable with human inhalation of a substance. To address this, exposure systems have been developed in which lung cells are exposed to substances in the air, which is known as the 'air-liquid interface' (ALI) exposure method (i.e. cells are grown on a membrane, nourished by a medium beneath them and brought into contact from above with substances in the air)(see figure Air Liquid Interface)



VITO has an 'ALI' platform with four different exposure systems: three commercial systems from VITROCELL® and a system called 'NAVETTA' (Frijns et al 2017), which has been developed and patented together with the international research partner Paris Lodron University of Salzburg (PLUS). These ALI exposure systems, combined with a generation and characterisation platform and a set of biological assays, can be used to screen the health effects of, for example, airborne (nano/ultrafine) particles, consumer products (e.g. electronic cigarettes), chemical substances, (exhaust) gases, vapours and pharmaceuticals. The biological assays can consist of various end points such as determination of cell viability/cytotoxicity, oxidative stress, inflammatory response, membrane integrity and mucociliary clearance. The efficacy of pharmaceutical products or vaccines administered via the respiratory tract can also be investigated using the ALI exposure method. This could include, for example, rapid screening, determining the absorption and permeation of inhalable components or testing for effectiveness.

• Frijns E *et al. 2017. A Novel Exposure System Termed NAVETTA for In Vitro Laminar Flow Electrodeposition of Nanoaerosol and Evaluation of Immune Effects in Human Lung Reporter Cells.* Environmental Science & Technology, 51 (9), DOI:10.1021/acs.est.7b00493

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Evelien Frijns (MSc.) obtained a Master's degree in Physical Geography at the University of Amsterdam in 2002. From 2002 to 2007 she worked as a consultant at a consultancy and engineering firm. Since 2007 she has been working as an aerosol researcher at VITO and has developed expertise in measuring human exposure to (ultra) fine particles and nanoparticles in the air. She conducts research indoors, at workplaces, in offices, schools and homes, as well as outdoors, in cities, around industrial sites and airports. In test chambers she conducts research into the release of these particles from products or processes. Since 2014, she has also been involved in research on exposing lung cells to aerosols to determine toxic effects at the cellular level.

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