Example of reduction and replacement (Project 89-03, Geiser Kamber)

Cell culture systems for estimating the risk of inhaled (nano-) particles to replace inhalation experiments involving laboratory animals

Every one of us is exposed to particles in the air we breathe at work or in our free time. In order to determine the effects on our lungs of inhaled nanoparticles (1-100 nanometer ∅), Marianne Geiser and her research team at the Institute of Anatomy of the University of Berne developed cell culture systems that present a realistic image of the inner lining of the airways. These cell culture systems can be exposed to various particles in a specially developed aerosol chamber under realistic conditions in order to test their effects on the airways. Thanks to the test model, it is possible to avoid carrying out stressful inhalation tests on laboratory animals and to observe the effects direct on lung tissue.

The lungs are exposed principally to particles in the air surrounding us. The risks connected to the inhalation of nanoparticles during industrial processing and through consumer goods, in particular, are not yet known. Marianne Geiser and her research team at the Institute of Anatomy of the University of Berne developed cell cultures systems for determining the effects of inhaling nanoparticles on our health. These systems provide a realistic image of the highly specialised inner lining of the airways, i.e. the respiratory epithelium. The first cell culture systems were created from pig lungs. Today human cells, isolated from healthy donors as well as people with respiratory disease or impairment (smokers, people suffering from cystic fibrosis or asthma) are used for the epithelial cultures. These respiratory tract epithelia demonstrate a protective as well as self-cleaning function, react to known stimuli and can be kept in culture for months. By using these systems it is possible to carry out toxicity tests involving inhaled (nano-) particles in an efficient, economical and ethical way, as well as testing the effects of new therapeutic aerosols.

Apart from reproduction of the target tissue, a realistic test system requires a realistic application of the particles, i.e. the deposit of particles on the cell surface from inhaled air. For this purpose an aerosol deposit chamber for (nano-) particles was developed by Marianne Geiser and her colleagues at the University of Cambridge (UK), the North-West Switzerland University of Applied Sciences (Windisch) and the Paul Scherrer Institute (Villigen). The cultured cells were exposed to the aerosols in this chamber under conditions similar to those in the lungs. After various lapses of time following the exposure the effect of the particles on the cells was then determined. The subsequent analysis included on the one hand parameters that are important for the balance and functioning of the lungs, and on the other indicators for the formation of or influence on lung disease. The long life of the cell cultures and the stable conditions in the chamber enabled the researchers to use longer exposure times or repeated exposure.

The chamber is easy to transport, so that it is possible to carry out studies at the source of the particles, e.g. on a busy street or in a factory where products with nanoparticles are manufactured and packed. These NACIVT (nano aerosoldeposition chambers for in vitro toxicology, www.nacivt.ch) allow 24 cell cultures to be exposed to the particles simultaneously, which means that they can be used in routine testing.

The mechanical and biological testing unit will help us to understand the health risks of inhaled nanoparticles. The results of this project are expected to lead to national and international studies. The knowledge obtained will help to reduce the number of laboratory animals used for testing – a considerable step forwards in relation to the 3R principles.

http://www.forschung3r.ch/en/projects/pr_89_03.html

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