## Description for the general public

Nowadays nanotechnology is at the forefront of science and technology research and development, mainly because of the unique physicochemical properties of nanoparticles (NPs). Unmodified nanoparticles (so called *first generation NPs*) possess unique features, different from their bulk (macro-scale) counterparts. It is often necessary to stabilize or functionalize such nanoparticles in order to extend their use and amplify their properties. Thus, modification of the surface of nanoparticles (creating so called *second generation NPs*, e.g. $Me_{mix}@MeO_x$, where $Me_{mix}$ is a bimetallic cluster, and $MeO_x$ are metal oxide NPs) is an important chemical challenge. As a consequence of the extraordinary properties (magnetic, mechanical, catalytic, electronic etc.) of modified nanoparticles, second generation nanomaterials offer promising and innovative applications. However, the same unique properties could result in as-yet-unknown risks to human health and the environment. Therefore, in the development of nanotechnology, the attention should be focused both on the promise of new possibilities and opportunities, and on the responsibility of industry to guarantee the safety of their products for workers, consumers and the environment. The conventional (i.e., experimental) risk assessment approaches, ensuring safe use of newly developed materials in the rapidly-developing field of nanoscience, are often expensive and time-consuming. Computational methods for the comprehensive risk assessment of NPs have been established for first generation nanoparticles. In the case of second generation nanoparticles, the risk assessment supported by computational approaches is at a very early stage of its development. Thus, the advancement of computational methods, complimentary to the experiments, and sometimes even capable to replace the empirical testing is of high importance.

Comprehensive computational (*in silico*) methods are an alternative for time-consuming experimental studies, allowing us to determine the influence of NP's structural features on their cytotoxicity *in vitro.* One of the approaches to risk assessment, listed by many international organizations and regulations (e.g. REACH in Europe), is the quantitative structure – activity relationship modeling (nano-QSAR). Nano-QSAR methods are based on the assumption that the differences in the biological activity (so called "endpoint", e.g. cytotoxicity) of compounds is determined by the variance in their chemical structure (expressed in the form of so-called "molecular descriptors"). Consequently, when values of the endpoint are available only for some of the compounds, it is possible to interpolate (predict) missing data with the help of an appropriate mathematical model. Unfortunately, because of the specific methodology, "classic" nano-QSAR techniques cannot be applied for risk assessment of nanoparticles with surface modifications, since they lack in:

1) methodology for building molecular structures of second generation nanoparticles;
2) appropriate descriptors, able to express specific characteristic of the "nano" structure for modified (second generation) nanoparticles;
3) quantitative structure-activity modeling procedures to screen large numbers of second generation NPs (so called $nanoQSAR_{mix}$);
4) nano-$QSAR_{mix}$ model(s) for $TiO_2$-based NPs modified with bimetallic clusters

**The main goal of the project is to determine how specific interactions between bimetallic nanoclusters and the surface of $TiO_2$ influence their *in vitro* cytotoxicity – using a combination of experimental and computational modeling**. In addition, **the project aims at verifying whether computational (*in silico*) methods could be used to support the risk assessment of metal oxide nanoparticles modified with bimetalilic clusters – so called *second generation* nanoparticles** ($Me_{mix}@MeO_x$ NPs). The specific objectives of the project include (i) development of methodology of molecular structure constructions represents second generation NPs; (ii) development of structural descriptors appropriate for second generation nanoparticles; (iii) development of quantitative structure cytotoxicity relationship modeling method for second generation nanoparticles and nano-$QSAR_{mix}$ models for modified $TiO_2$ NPs.

**The aim of this project is to verify the hypothesis** that computational chemistry and chemoinformatics can provide a viable approach complementing experimental research for such complex systems as $Me_{mix}@MeO_x$. The application of comprehensive computational approaches would allow us to reduce of number time-consuming and expensive experiments. In addition, we will be able to determine the influence of nanostructural features on $Me_{mix}@TiO_2$ cytotoxicity and discover possible mechanisms of toxicity. The cytotoxicity will be determined through an *in vitro* model of mouse fibroblast cell lines (Balb/c 3T3 cells) and normal human keratinocytes (NHK). As the case of study for second generation of NP will be used: metal oxide NPs ($TiO_2$) and metal NPs (e.g. Au, Ag, Pd, Pt). These group are in highest priority because they are commonly used in nanotechnology e.g. such as environmentally friendly photocatalys in degradation of pollutants.