



# LUND UNIVERSITY

Nanotoxicological studies in the Air-Liquid Interface using engineered metal NPs – Protein corona, gene analysis and dose response

Svensson, Christian; Ameer, Shegufta; Pagels, Joakim; Cedervall, Tommy; Kåredal, Monica; Ludvigsson, Linus; Broberg Palmgren, Karin; Meuller, Bengt; Messing, Maria; Rissler, Jenny

2013

[Link to publication](#)

*Citation for published version (APA):*

Svensson, C., Ameer, S., Pagels, J., Cedervall, T., Kåredal, M., Ludvigsson, L., Broberg Palmgren, K., Meuller, B., Messing, M., & Rissler, J. (2013). *Nanotoxicological studies in the Air-Liquid Interface using engineered metal NPs – Protein corona, gene analysis and dose response*. Abstract from European Aerosol Conference (EAC) 2013, Prague, Czech Republic.

*Total number of authors:*

10

## General rights

Unless other specific re-use rights are stated the following general rights apply:

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

## Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117  
221 00 Lund  
+46 46-222 00 00

# Nanotoxicological studies in the Air-Liquid Interface using engineered metal NPs – Protein corona, gene analysis and dose response

C.R. Svensson<sup>1</sup>, S. Ameer<sup>2</sup>, J.H. Pagels<sup>1</sup>, T. Cedervall<sup>3</sup>, M. Kåredal<sup>2</sup>, L. Ludvigsson<sup>4</sup>, K. Broberg<sup>2</sup>, B.O. Mueller<sup>4</sup>, M.E. Messing<sup>4</sup>, J. Rissler<sup>1</sup>

<sup>1</sup>Ergonomics and Aerosol Technology, Lund University, Lund, SE 221 00, Sweden

<sup>2</sup>Occupational and Environmental Medicine, Lund University, Lund, SE 221 00, Sweden

<sup>3</sup>Biochemistry and Structural Biology, Lund University, Lund, SE 221 00, Sweden

<sup>4</sup>Division of Solid State Physics, Lund University, Lund, SE 221 00, Sweden

Keywords: Nanoparticles, Air Liquid Interface, Characterization, Toxicology

Presenting author email: Christian.Svensson@design.lth.se

There is an ongoing discussion whether traditional toxicological methods are sufficient to evaluate the risk of inhalable nanoparticles. Since the use of manufactured nanoparticles is increasing, the need for toxicological data is great. There is also an increased interest in metal nanoparticles for targeted drug delivery. This has led to the emergence of Air-Liquid Interface toxicology. Here aerosol NPs are administered directly from air and deposited upon cellular cultures, or relevant media, providing a more realistic in vitro environment for toxicological studies, especially for lung deposition – one route of exposure that has been pinpointed as important in risk assessments.

This work takes on a holistic approach towards the toxicology of metal NPs. The NPs are characterized in aerosol phase with regards to both mass, size and morphology. The NPs are then deposited onto cellular cultures or into physiological media using a commercialised deposition chamber, *Nano Aerosol Chamber In Vitro Toxicity* (NACIVT), a chamber based on the work by Savi (2008). When deposited into cellular media, blood serum or into lung fluid the NPs characteristics in solution can be studied using several methods. By using UV-Vis spectroscopy the relative degree of agglomeration is determined and by using dynamic light scattering and particle tracking analysis the hydrodynamic size is determined. Upon deposition onto cellular cultures, both primary and standardized cell lines, endpoints of varying sensitivity is investigated to determine the NP effects. Cellular viability and cytotoxicity is determined using standard assays. Protein expression from the cells will be investigated in the surrounding media, cytokines, interleukins etc. In addition state of the art gene analysis techniques will be employed, both towards a whole genome perspective and single genes. The rationale is that as particles may not be directly terminal towards the cells, they still react in characteristic ways expressing various genes.

One type of NP that will be used is agglomerate and sintered silver (AgNP) generated by a spark discharge system, described by Mueller (2012). The system is capable of generating aerosols of a variety of different metal particles with different shapes properties. The aerosol is generated polydisperse as agglomerates, by using a sintering furnace the agglomerates can be compacted to varying degrees. This results in metal NP aerosols with the varying total surface areas, while retaining the same total mass.

In order to characterize a sintered AgNP aerosol it was connected to a laminar flow diluter (model 3302, TSI Inc.) and the NACIVT was coupled in parallel with a TEOM and an SMPS system. The dilution system allowed for a stable dilution up to 15 times. Also AgNP was deposited in the NACIVT on silicon surfaces for electron microscopy and determination of deposition efficiency, Figure 1A.

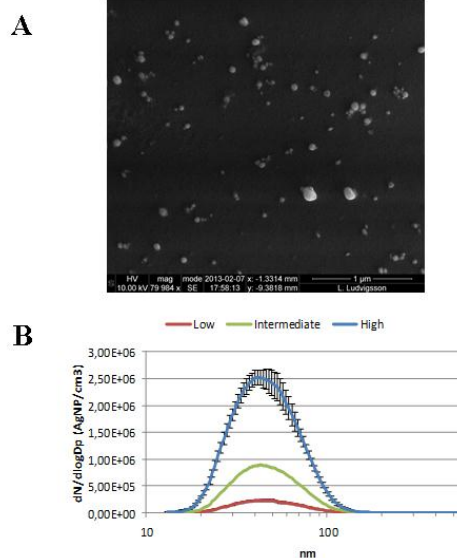


Figure 1. A) Sintered AgNPs deposited onto a SEM grid in the nacivt chamber. B) Average SMPS scan of sintered AgNP at three concentrations tested.

The cell exposures were performed at three concentration levels, exposing the cells placed in the NACIVT chamber during one hour. The SMPS system scanned the size distributions continuously, shown in Figure 1B, The AgNP aerosol was stable during the events and deposition efficiency approximately 15-20%. By TEOM the mass concentrations with std was 1520(180), 467(97) and 99(20) μg/m<sup>3</sup>.

In conclusion a stable aerosol of AgNP agglomerates was generated for exposure of cells during 1h duration, with endpoints including state of the art gene analysis and standard assays.

This work was supported by the Nanometer Structure Consortium at Lund University (nmC@LU) and the Swedish research council FAS through project 2009-1291 and the FAS-centre METALUND Savi, M. (2008). *Environ. Sci. Technol.* **42**, 5667-5674 Mueller, B.O. (2012). *Aerosol Sci. Technol.* **46**, 1256-1270