BB3R Newsletter

Berlin-Brandenburg research platform BB3R – Issue 14 June 2020

BB3R introduces: Working Group of Prof. Luch

Research at the Department of Chemical and Product Safety at BfR comprises nanomaterial biokinetics and the development of methods for *in vitro* toxicity testing. Mass spectrometric techniques are being developed for nanomaterial quantification and visualization in different test systems.

In a chronic inhalation study with rats exposed to nano-CeO_2, a dose-dependent linear increase in lung burden was observed. The tissue burden was found to decrease in the following order: lung > lymph nodes > bone > liver > bone marrow. The application of time-of-flight secondary ion mass spectrometry (ToF-SIMS) confirmed the presence of non-homogenously distributed CeO_2 agglomerates within lung tissue (Figure 1, Tentschert et al. 2020).

With regard to 3R, *in vitro* systems are evaluated for the investigation of nanomaterial agglomeration behavior and membrane penetration. Different lung cell lines were compared in terms of their suitability for toxicological testing of nanomaterials at liquid–liquid and air–liquid interfaces. Investigation of transepithelial resistance and tight-junction immunohistochemistry confirmed the formation of a functional barrier for *in vitro* cultivated human alveolar epithelial and human umbilical artery endothelial cells similar to the *in vivo* situation (Leibrock et al 2019).

Mass spectrometric imaging has revealed a three dimensional (3D) distribution of nanomaterials within biomolecular agglomerates. Furthermore, intra- and extracellular biomineralization of gold ions by human alveolar A549 cells was shown to generate partially embedded long aspect ratio fiber-like Au nanostructures (Figure 2, Singh et al. 2020).

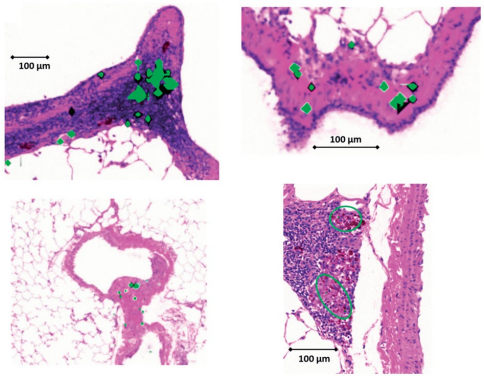

Figure 1. Applying ToF-SIMS analysis CeO_2 NP agglomerates were correlated with histopathological light microscope images. (A–D) show overlay pictures (500 mm _ 500 mm) consisting of ToF-SIMS signal for CeO_2 NP (green) and their corresponding histopathological images. CeO_2 NPs are associated with the BALT (bronchus-associated lymphoid tissue); (a total of 36 pictures was analyzed at the 24-month time point).

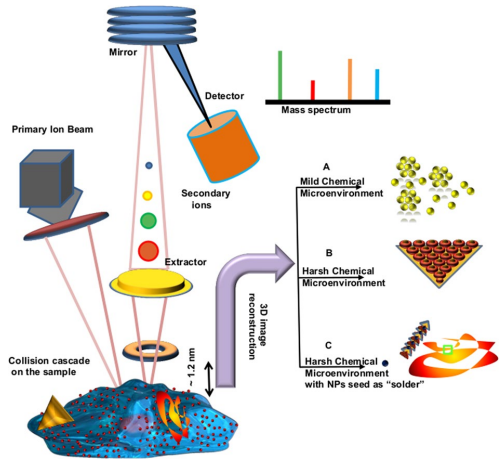

Figure 2: Schematic overview of the workflow of the 3D biomolecular imaging of de novo biomineralization of ionic gold into anisotropic (0, 1 & 2D) nanostructures. Left panel shows the collection of secondary ions by the detector after the primary ion beam impacts freeze dried A549 cells with embedded anisotropic gold nanostructures. The right panel shows that ToF-SIMS images can be reconstructed into 3D space to give molecular distributions of gold and reducing agent in three different culture environments resulting in three different nanostructures (spheres, irregular particles and nanoribbons)

New publications:

Leibrock, L., S. Wagener, A. V. Singh, P. Laux and A. Luch (2019). "Nanoparticle induced barrier function assessment at liquid-liquid and air-liquid interface in novel human lung epithelia cell lines." Toxicology Research 8(6): 1016-1027.

Singh, A. V., H. Jungnickel, L. Leibrock, J. Tentschert, P. Reichardt, A. Katz, P. Laux and A. Luch (2020). "ToF-SIMS 3D imaging unveils important insights on the cellular microenvironment during biomineralization of gold nanostructures." Sci Rep 10(1): 261.

Tentschert, J., P. Laux, H. Jungnickel, J. Brunner, I. Estrela-Lopis, C. Merker, J. Meijer, H. Ernst, L. Ma-Hock, J. Keller, R. Landsiedel and A. Luch (2020). "Organ burden of inhaled nanoceria in a 2-year low-dose exposure study: dump or depot?" Nanotoxicology 14(4): 554-576.

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