Confocal Raman Microscopy for the study of cell uptake of nanoparticles and toxicity

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The development of sufficiently sensitive and fast methods for the detection and localization of NPs within cells is a prerequisite for studying NP - cell interaction. The level and the mechanism of uptake of NPs by cells and their subsequent processing are, for example, major issues concerning the effectivity of nanoparticles as delivery devices. In contrast to toxicity on the molecular level, where toxic compounds directly interfere with the metabolism, toxic effects of NPs may depend on the contact of the surface of the NPs with intracellular components. Nanoparticles may interfere with the complex intracellular machinery by disturbing intracellular organization and transport routes.

The detection and localization of nanoparticles at the cellular level is often not an easy task. NPs have sizes well below the resolution of the optical techniques. Confocal Laser Scanning microscopy (CLSM) can be used to visualize NPs in different cell compartments but requires the labeling of both the NPs as well as particular cell compartments. The labeling of nanoparticles is not always affordable and in many cases would represent an important modification of the nanostructure, which may result in the loss of the designed properties associated with a specific type of nanoparticle. This is particularly critical the smaller the particle is. Transmission Scanning Electron Microscopy (TEM) provides a formidable tool to study the localization of NPs in the cell interior, which neither depends on the labeling of the NPs nor of the cell. Nevertheless, the use of TEM for studying the presence and localization of NPs in cells is time consuming and as a rule requires specific preparation protocols, which may disturb the original pattern of NP distribution.

In this study we have made use of Confocal Raman Microscopy to study the uptake of a wide variety of nanoparticles. The use of Raman Microscopy has the enormous advantage of not requiring nanoparticle labeling.

Confocal Raman Microscopy will be used for the study of the interaction and the internalization of a wide range of nanoparticles. We will specially focus on nanoparticles of poly lactide co glycolic acid , carbon nanotubes and metal oxide nanoparticles. Conclusions on the toxical effects of nanoparticles will be driven from Raman experiments