Abstract:

In the past decades, nanoparticles have been viewed as a potentially powerful platform for various applications in biomedical sciences. The possible application of nanoparticles varies from drug delivery agents to novel imaging platforms and surely, some application potential still remains hidden. Thus, it is necessary to broadly study their *in vitro* behavior in order to assess the precise theranostic potential as well as to distinguish possible threats to human health. Even though nanoparticles are getting more and more attention in current research, still only a limited amount of information is available, especially regarding interactions of ultra-small (< 5 nm) nanoparticles with biological environment and cells.

The aim of the work presented herein is to provide the reader with information concerning interactions of various ultra-small nanoparticles (silicon-based, gold, nanodiamonds) with biological environment and human cells. Dose- and time-dependent influence of the various nanoparticles on behavior of different human cells (osteoblasts, monocytes, keratinocytes, mesenchymal stem cells) was established under different conditions, stressing out the importance of protein corona (a layer of proteins originating from cultivation medium attached to nanoparticles). Biocompatibility of two different types of silicon-based nanoparticles was tested on different human cells, showing selectivity of one type of the nanoparticles (silicon carbide with different surface terminations) towards immune cells. Furthermore, deeper study of the silicon carbide nanoparticles in respect to their immunomodulatory potential and influence on behavior (e.g. doubling time, differentiation potential) and metabolism of monocytic cells was established. Biocompatibility of gold ultra-small nanoparticles and nanodiamonds was also tested on various human cells. Protein corona forming on these two types of nanoparticles was subsequently analyzed by mass spectrometry, showing that ultra-small nanoparticles are capable of interaction with quite large numbers of proteins. Furthermore, the nanoparticle-cell interactions were observed by various imaging methods, such as holographic microscopy, electron microscopy (TEM, SEM, cryoFIB-SEM SIMS-TOF), flow cytometry or Raman spectroscopic imaging.

This thesis not only presents the importance of basic research on proper characterization of nanoparticle-cell interactions but also suggests possible future directions for further research and possible applications of used nanomaterials in biomedical research.