Magnetic nanoparticles for the development of advanced therapies

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Together with regenerative medicine and personalized therapies, nanomedicine represents one of the fields of advanced therapies that are sought to drastically revolutionize heath care and significantly improve quality of life at a global level. Based on nanoscience and nanotechnology, nanomedicine solutions have already entered the field of clinical application by means of drug delivery solutions and contrast agents for medical Imagistics while Nano based carrier and Nano biosensors are in different stages of testing for clinical applications.

The use of Nano-scaled materials, particularly of magnetic Nano-particles (MNP) has evolved as an increasing field of research in life sciences. Both physical and chemical properties of MNPs are relevant for a wide scale of medical application for the diagnostic, prevention and treatment of various diseases.
Iron oxide based MNPs are being explored as agents for cellular magnetic separation magnetic resonance imaging (MRI) or drug delivery. MNPs have been proposed as tracking agents for cell delivery in various cellular therapy scenarios.In the context of multimodal therapies for the treatment of solid malignancies, the use of hyperthermia (HT) as an adjuvant therapy can be traced back to the beginning of the 20th century. During the last decades, different forms of HT have been used in combinatin with radio- or chemotherapy however, local and systemic side effects on healthy tissues are limiting its application. MNP based HT treatment of malignancies has gained significant interest in the recent years as they are able to deliver local targeted HT of improved precision compared to traditional methods.

Proprietary Fe-Cr-Nb-B ferromagnetic nanoparticles display heating properties that recommends them as potent agents for delivery of local hyperthermia for the treatment of solid tumors. Stem cell mediated delivery represent a safe and accurate modality to target remote or metastatic tumor sites. We are currently investigating the interaction of Fe-Cr-Nb-B nanoparticleswith human bone marrow derived stem cells, adipose derived mesenchymal stem cells and human primary osteoblasts. We found that bare and chitosan coated Fe-Cr-Nb-B are internalized by all cell types, can be retained up to 28 days inside the cells without signs of membrane disruption and do not display *in vitro* toxicity. MNPs are uploaded by cells in a time dependent manner with maximum uptake at 7-8 days of cell particle incubation. Particle internalization do not interfere

with proliferative and differentiation potential (osteogenesis and adipogenesis) demonstrating an unaltered cellular phenotype. Further investigation of the potential effect of MNP internalization on cytoskeleton dynamics and in inducing oxidative stress will be required as it is of interest for predicting cell migration and survival after transplantation. Present results are encouraging for the design a stem cell mediated delivery of Fe-Cr-Nb-B magnetic nanoparticles for delivery of local HT or for regenerative purposes.

Key words: nanomedicine; magnetic nanoparticles; regenerative medicine; stem cell therapy; tissue engineering