

Super-paramagnetic nanoparticles for enhancement of bone growth and differentiation

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Background and Introduction:

The development of super-paramagnetic nanoparticles opens new possibilities for directed growth factor delivery to enhance healing of bone defects. Proteins or plasmids (pDNA) can be coupled to super-paramagnetic nanoparticles (SPION), be directed to intra- or extracellular targets and then be released by magnetic force e.g. an intermittent magnetic field.

Rationale:

Since SPION have been developed recently there are only a few data about the influence of nanoparticles on cellular proliferation and differentiation. As a first step to use nanoparticles for biomedical purposes we examined the biocompatibility of plain coated SPION and its effect on osteogenic differentiation in vitro.

Methods:

Osteogenic precursor cells (MC3T3) and mesenchymal stem cells (C3H10T1/2) were cultured in presence or absence of amnio-polyvinylalcohol- (aPVA) and carboxy-polyvinylalcohol- (cPVA) coated SPION for 1h, 4h, 3d, 7d, 14d or 21d. The samples were stimulated in a static or intermittent magnetic field (1Hz, 1 or 4 h/d). The intracellular iron content, the cellular proliferation and the activity of bone specific alkaline phosphatase were measured and Cy-3 labelled SPION were detected by confocal laser scanning microscopy. The staining of the

actin skeleton, focal adhesions (vinculin/paxillin) and calcified matrix was performed.

Results:

It was shown that the coating of SPION with aPVA enables and with cPVA inhibits the intracellular uptake of the SPION by changing of the particle load. In presence of aPVA-coated SPION (intermittent magnetic field, 4h) a weaker expression of the actin skeleton was observed. Beside this, no morphological changes were found. In presence of a static magnetic or intermittent (1Hz, 4h) field the particles seemed not to have any effect on cellular proliferation and differentiation. If frequency was increased to 2 Hz and applied for a longer daily time (8 h) aPVA-coated particles increased cell proliferation while alkaline phosphatase activity per μg DNA was decreased.

Discussion and Conclusion:

SPION have been shown to deliver proteins or pDNA to cellular targets. In absence of magnetic fields particles seem not to change the cellular properties of MC3T3 and C3H10T1/2 cells. In presence of an intermittent magnetic field SPION might change proliferation and differentiation properties depending on the surface coating and the used frequency. In future delivery- and release-mechanisms of SPION-coupled proteins or pDNA have to be examined to develop SPION-based applications for the clinical use.