Human adipose-derived stem cells applications for bone tissue engineering-current developments

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Background: Human adipose-derived stem cells (hASCs) have proved their potential to differentiate towards the osteogenic lineage. Current approach for successful bone tissue engineering (BTE) in patients with bone defects involves the use of an appropriate combination of scaffold properties and cells with potential for bone repair, such as hASCs. The inclusion of graphene-oxide (GO) in the scaffold composition was shown to favor proliferation and differentiation of mesenchymal stem cells during in vitro culture.
Aim. The aim of this study was to investigate hASCs osteogenic potential in contact with BTE-designed scaffolds based on natural polymers improved with GO and to evaluate this cell-scaffold system for efficiency in functional bone tissue production.
Materials and methods. 3D cell-scaffold culture was obtained and tested for biocompatibility via standard assays (MTT, LDH, LiveDead and fluorescence microscopy). The optimal cell-scaffold composition was then exposed to osteogenic induction for more than 1 month in *in vitro* conditions. Cell distribution and scaffold structure before and during differentiation were analyzed by scanning electron microscopy (SEM). hASCs adhesion to the material was visualized by confocal microscopy showing the development of cytoskeleton. Histological stainings were performed to monitor the osteogenic differentiation process and mineralization. Osteogenic markers gene and protein expression were analyzed quantitatively via qPCR and confocal microscopy, respectively.
Results: The addition of increasing GO percentages in the composition of the materials resulted in increasing biocompatibility of the system. Optimal cell-scaffold composition was determined in the presence of 3% GO. SEM confirmed that cells populated the pores of the scaffolds and adhered to the GO containing materials better than to control, revealing also the accumulation of mineral calcium deposits in the system. Mineralization during differentiation was also confirmed by histological staining, starting from 14 days. Typical osteogenic markers runt-related transcription factor 2 (RUNX2) and osterix (OSX) were found to be upregulated starting with 7 days post induction. Extracellular matrix (ECM) marker osteopontin (OPN) displayed an increasing profile of gene and protein expression.
Conclusion: The results suggest that hASCs were able to adhere and differentiate towards mature osteocytes, when cultured in a 3D scaffold and under the positive influence of appropriate osteogenic inducers and 3% GO. The presence of typical osteogenic markers in the secreted ECM prove the functionality of the differentiated cells, thus suggesting the possibility of further using this cell-scaffold system for BTE clinical applications.
Perspectives. Further improvement and optimization of cell-scaffold systems is required to address patient needs. One possibility would be the addition of autologous platelet-rich plasma (PRP) at the implantation site.
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