Mesenchymal stem cells for bone regeneration – molecular and tissue-engineering strategies

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ABSTRACT

Ex vivo engineering of autologous bone tissue as an alternative to bone grafting is a major clinical need. The fact that mesenchymal stem cells (MSCs) can be easily isolated and culture expanded from, e.g., bone marrow aspirates, and are capable of differentiating into distinct mesenchymal tissues, including bone, makes them an attractive source of osteoprogenitor cells for bone reconstruction. This PhD dissertation is based on three experimental studies evaluating the potential of MSCs for skeletal reconstruction using molecular and tissue-engineering strategies carried out at the Orthopaedic Research Laboratory, Clinical Institute, Department of Orthopaedic Surgery E, Aarhus University Hospital and at the Interdisciplinary Nanoscience Centre (iNANO), University of Aarhus.

The purpose of the first study was to optimize viral and nonviral gene transfer methods for genetic modification of primary porcine MSCs. The second study investigates proliferation, morphology, and osteogenic differentiation of human MSCs stimulated by plain metallic implant surfaces. The aim of the third study was to evaluate the effects of three-dimensional (3-D) dynamic spinner flask culture on the proliferation, distribution, and differentiation of human MSCs.

In conclusion, further improvements of the clinically highly relevant nonviral gene transfer methods are needed. The genetic modification of MSCs by ex vivo adeno associated virus-mediated and retroviral gene delivery is of particular interest for strategies requiring transient and long-term transgene expression, respectively. The combined use of MSCs and tantalum metal can be considered a promising strategy for bone tissue engineering, whereas further studies are needed to fully understand the role of chromium and its alloys in bone implants. Three dimensionally cultured MSCs could be effectively stimulated by dynamic fluid convection during the initial phase of ex vivo bone tissue engineering. To take advantage of MSCs most effectively for their clinical use, the combined use of the strategies proposed in this dissertation could be pursued.