Age-related differences in osteogenic differentiation of mesenchymal stem cells in vitro

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Introduction:

Mesenchymal stem cells (MSCs) have the capacity to proliferate and differentiate into chondrocytes, osteoblasts and adipocytes. For this reason, MSCs are considered to be of great clinical potential in cell based regenerative strategies for the skeletal system. Questions arise to what extent MSCs are subject to age related changes and whether MSCs based strategies should be limited to patients of selected age groups. The aim of this study was to elucidate the effect of age on MSC-frequency, cell proliferation and differentiation capacity in vitro.

Materials and Methods:

Fifteen donors from 7-85 years were involved in this study. The age range was covered by three groups of 5 donors each. Group 1 ranged from 7-12 years, group 2 from 20-55 years and group 3 included 5 donors from 60-85 years. Mononuclear cells from bone marrow were isolated and CFU-F number was determined. Subcultures were prepared to assess single cell cloning efficiency and proliferation rate. Chondrogenic differentiation was assessed by glycosaminoglycan (GAG) quantification and histologic/immunohistologic evaluation of Alcian blue and Collagen Type II. For osteogenesis, cells were evaluated for membrane bound alkaline phosphatase (ALP) and Alizarin Red S. For adipogenesis, lipid accumulation was quantified by Oil Red O staining.

Results:

No correlation was found between CFU-F frequency or proliferation rate of MSCs and donor age. A negative correlation of single cell cloning efficiency with age was, however, observed (r²= -0.604; p<0.01). While no correlation was obvious between adipogenic differentiation capacity of MSCs and age, activity of bone related ALP (r²=0.413; p<0.05) and calcium deposition (r²=0.721; p<0.001) showed a positive correlation with age. Furthermore we observed significant correlations between ALP activity and calcium deposition (r²=0.6; p<0.01) and between proliferation rate and lipid accumulation (r²=-0.422; p<0.05).

Discussion and Conclusions:

MSC proliferative potential and differentiation capacity to adipogenic lineage did not change with age. Osteogenic capacity correlated
positively with increasing donor age, which sheds a promising light on the potential application of cell based bone remodelling strategies also in patients of older age. It seems promising to further study MSC populations from donors of older age to gain a better understanding about the molecular mechanisms regulating age-related changes in connective tissue biology and their possible consequences for regenerative medicine.