Aging and replicative senescence of human mesenchymal stromal cells is accompanied by increased loss of RS-cell-subpopulation

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The role of adult mesenchymal stromal cells (MSC) in tissue maintenance and regeneration has received significant attention of late. MSCs in culture undergo senescence after a certain number of cell doublings whereby the cells enlarge and finally reach terminal growth arrest. In this study we have analyzed the behavior of subpopulation of rapidly self-renewing cells (RS-) cells. 22 samples of MSCs were isolated from bone marrow of donors between 22-87 years old. In general, RS-cell fraction was significant lower after 10 days cultivation in samples obtained of donors >50 years (end passage 2: 13,74±4,45% to 22,51±6,21%; p<0.01). With the increase of passage number RS-cell fraction decreased, independent of age of donors. In samples of younger donors (<50 years), the approval of RS-cells was slighter (passage 5: 7,45±3,45% to 16,38±6,29%). The seven samples of donors under 50 years old could always been cultivated until passage 10 (100 days), while MSCs from older donors stopped proliferation before. Interestingly, after RS-cell fraction was dropped down under about 6,65%, the terminal growth arrest was reached reproducibly in all samples, indicating a essential effect of RS-cells on proliferation behavior of the whole population. In flow cytometry approaches only 0,9±0,15% of RS-cells were positive for senescence indicating staining with β-Galactosidase, while the rest of population offered passage-dependent larger numbers of positive cells. Although telomere length varied particularly in donors, an telomere-dependent correlation to the decline of RS-cell subpopulation could not be statistically verified. Thus, the study demonstrated that in vivo and in vitro aging is accompanied by a loss of RS-subpopulation until its dropped under a certain niveau, which is characterized by terminal growth arrest.