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Aging of periosteal-derived stem cells during expansion: an alternative tool for a customized bone regenerative strategy

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Increased in life expectancy points out the necessity for tailored strategies to restore bone loss due to trauma and/or disease in elderly. Moreover, there is a compelling need for improved cell systems to test scaffolds interfacing with an "aging" tissue. For skeletal tissue regeneration, periosteal-derived stem cells (PDPCs) could represent an easily recruited source of Mesenchymal stromal cells (MSCs) [1,2]. This study investigated the effects of long-term in vitro expansion on the stability and function of PDPCs, since extensive culture expansion is usually performed to obtain clinically relevant cell numbers, but its impact on cell behaviour is still unclear. An integrated approach based on flow cytometry, ultrastructural and quantitative Real time PCR (qRT-PCR) analyses was adopted. Senescent cell data were compared with those of cells isolated from differently aged subjects. Both replicative-senescent PDPCs and cells isolated from old donors were permanently blocked in G1 phase of cell cycle, through a pathway that seemed to involve nitric oxide (NO) production and the expression of tumour suppressor proteins p16 or p53, respectively. Changes in the expression of MSC surface markers were detected in PDPCs during subculturing, whilst it was superimposable in young and aged PDPCs. Cytofluorimetric analysis of the physical parameters (i.e. FSC and SSC) showed a trend toward an increase in cell dimension and internal complexity in both populations analysed. This data was consistent with morphological observation that also evidenced similar alterations in mitochondrial shape. In addition, an intense autophagic activity in early passage PDPCs was observed, whilst in the late passages cells had a robust protein synthesis activity that could be related with "senescence-associated secretory phenotype" (SASP). In conclusion, the morphofunctional similarities detected in replicative-senescent and aged PDPCs suggest that their long-term expansion could be a reproducible and useful tool to mimic in vivo ageing.

References

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Keywords

Periosteal cells, replicative senescence, aging, NO, cytofluorimetric analysis