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Impact of ageing and senescence on endogenous cardiac stem/progenitor cells in the human heart

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The adult myocardium, including human, harbours a rare population of resident multi-potent cardiac stem and progenitor cells (CPCs). CPCs, positive for stem cell markers (i.e. c-kit, Sca-1) and negative for hematopoietic and endothelial lineage (i.e. CD45, CD34 and CD31) and mast cells (i.e. tryptase), exhibit properties of stem cells; being clonogenic, self-renewing and multipotent, both in vitro and in vivo. When tested in an injury model that simulates muscle wear and tear with a small dropout of LV cardiomyocytes (~8%) and in the presence of a patent coronary circulation, CPCs have true intrinsic regenerative capacity. Manipulation of CPCs ex-vivo and in situ has opened new therapeutic avenues for myocardial regeneration. Organ ageing is characterised by a decline in the ability of its tissue-specific stem cells to repair damage and regenerate functional tissue. This decline in regenerative capacity involves both intrinsic molecular changes in the stem cells themselves and/or alterations in the aged environment. Regulation of CPC senescence will impact the efficacy of regenerative therapies, considering the majority of patients in need of it are of advanced age. Authors presentation will focus on the impact of ageing and senescence on human CPCs, and how this influences their myocardial regenerative potential. Author will show that aged-senescent CPCs have a Senescence-Associated Secretory Phenotype (SASP) and how by pharmacologically eliminating senescent cells the regenerative capacity of the aged heart is rejuvenated.

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