



## Rejuvenating the Regenerative Capacity of the Aged Heart

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### Abstract

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 stem cell senescence will impact the efficacy of regenerative therapies, especially if the majority of patients in need of it are of advanced age as occurs with heart disease and failure.

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, PDGFR $\alpha$ ) 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 (Smith et al. 2014, Nat Protoc; Vicinanza et al. 2017, Cell Death & Diff). 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 (Ellison et al. 2013, Cell). Manipulation of CPCs ex-vivo and in situ has opened new therapeutic avenues for myocardial repair and regeneration.

My talk will focus on the impact of ageing and senescence on human CPCs, and how this influences their myocardial regenerative potential (Lewis-McDougall et al. 2019, Aging Cell). I will show how by pharmacologically eliminating senescent cells using senolytic drugs, the regenerative capacity of the aged heart can be rejuvenated.

### Biography

Georgina Ellison-Hughes completed her PhD from Liverpool JM University, UK and postdoctoral studies at New York Medical College, and Mount Sinai School of Medicine, NYC, USA. She is Professor of Regenerative Muscle Physiology and Marie Curie Fellow at King's College London, UK. Her research has been at the forefront of adult-derived cardiac stem/progenitor cells and has made a seminal contribution in the paradigm shifting work to establish the adult heart as a self-renewing organ with regenerative potential. She has published more than 60 peer-reviewed papers in reputed journals (Total Impact Factor = 430; Citations = 3320; H-index =32 (Scopus)) and is an editorial board member of Scientific Reports, BMC Molecular and Cell Biology, PharmAdvances and Stem Cells International.

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