Antisenescence Effects of Stem Cell Therapies

With advancing age ever more cells in your body enter a state of senescence. They stop dividing and emit signals that both degrade surrounding tissue structures and raise the odds of nearby cells also becoming senescent. This is an adaptation of a mechanism involved in embryonic development that lowers the odds of suffering cancer: senescent cells appear in response to cellular damage in a range of circumstances, and the types of damage that provoke cellular senescence either raise the risk of cancerous cells emerging or accompany a rising risk of cancer in normal aging. So cellular senescence is a part of the balance that evolution has come to in humans between declining ability to function on the one hand and fatal cancer on the other.

The research community, however, is going to become very good at dealing with cancer in the decades ahead. Cellular senescence isn't a great partner for a technologically sophisticated humanity, as thedownside in aging very much outweighs whatever good is being done. For my money I think that the first generation of effective treatments that reverse the contribution of cellular senescence to degenerative aging will be blunt efforts that involve the targeted destruction of near-all senescent cells. This targeted destruction in fact goes on all the time in younger years, as one of the jobs of theimmune system is to seek out and remove problem cells. Unfortunately like all biological systems itbecomes damaged and disarrayed in later life, and alongside the damage that provokes a greater incidence of cellular senescence this is one of the reasons why the body accumulates ever more senescent cells as the years pass. We don't need these senescent cells, they can be removed, and we will benefit from their removal. The technologies used will be very similar to those already in trials for the targeted destruction of cancer cells: immune therapies, nanoparticles, engineered viruses, and so forth.

Later forms of treatment may be more sophisticated, however. Why destroy senescent cells if they can be reprogrammed into a non-senescent state? The field of cellular programming is still in its infancy at this point, and even the most impressive results are half happenstance and incompletely understood in the context of the bigger picture. Researchers throw compounds at cells to see what happens, and out of this assemble theories that inform the next set of efforts to throw compounds at cells to see what happens. Cells are enormously complex mechanisms, but from these efforts will eventually emerge a field in which any cell can be instructed to act as we want it to - even while within the body.

Stem cell treatments are leading to a greater knowledge of the mechanisms by which senescent cells might be coerced back into a more useful and functional state. Just as the delivery of stem cells causes regeneration by changing the local tissue environment and releasing signals that convince native cells to get back to work, it seems that this may also beneficially influence the balance of signals that leads to greater or lesser levels of cellular senescence. This possibility is illustrated in the following research using cell cultures. When researchers cultured and stressed their cell lines in the presence of

signals emitted by stem cells, there was measurably less cellular senescence than was the case without those signals:

Rat Induced Pluripotent Stem Cells Protect H9C2 Cells from Cellular Senescence via a Paracrine Mechanism

Quote:
Cellular senescence may play an important role in the pathology of heart aging. We aimed to explore whether induced pluripotent stem cells (iPSCs) could inhibit cardiac cellular senescence via aparacrine mechanism.

We collected iPSC culture supernatant as conditioned medium (CM) for the rat cardiomyocyte-derived cell line H9C2. Then we treated H9C2 cells, cultured with or without CM, with hypoxia/reoxygenation to induce cellular senescence and measured senescence-associated β-galactosidase (SA-β-gal) activity,G1 cell proportion and expressionM of the cell cycle regulators p16INK4a, p21Waf1/Cip1 and p53 atmRNA and protein levels in H9C2 cells. In addition, we [measured] concentrations of trophic factors in iPSC-derived CM.

We found that iPSC-derived CM reduced SA-β-gal activity, attenuated G1 cell cycle arrest and reduced the expression of p16INK4a, p21Waf1/Cip1 and p53 in H9C2 cells. Furthermore, the CM contained more trophic factors, e.g. tissue inhibitor of metalloproteinase-1 and vascular endothelial growth factor, than H9C2-derived CM.

[We conclude that] paracrine factors released from iPSCs prevent stress-induced senescence of H9C2 cells by inhibiting p53-p21 and p16-pRb pathways. This is the first report demonstrating that antisenescence effects of stem cell therapy may be a novel therapeutic strategy for age-related cardiovascular disease.