Oxidative Stress-Induced Proliferation and Death of Skin Stem Cells

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Recent data suggest that ageing is driven by depletion of self-renewing stem cells. According to the widely accepted oxidative stress hypothesis, oxidizing species are produced during aerobic metabolism, consequently causing molecular damage and, over time, cell and tissue dysfunction. However, recent findings, demonstrate that hydrogen peroxide (H_2O_2), controls cell growth and death, functioning as a signaling molecule due to its ability to induce fully reversible protein modifications during events triggered by activated growth-factor receptors. The potencial of H_2O_2 to trigger senescence is thought to be secondary to its ability to induce hyper-proliferation and death, since H_2O_2 itself is a potent inducer of apoptosis. This dual character suggests specificity in its biological activity. We examined the effect of H_2O_2 on the cell cycle and death of skin mesenchymal stem cells (mMES) through qPCR and Flow Cytometry. When exposed to sub-lethal concentrations of H_2O_2, the size of the G2/M population progressively increased by 1.3% 27,8%, 41% and 61,2% at, respectively, 6, 12, 24 and 48h. This analysis was also performed at higher concentrations of the oxidant (1/10 and 1/100 of the DL-50), with a clear decrease (12% to 7.4%) in cell proliferation, shown by the fall on the same population followed by an increase in G0/G1 cells and a greater than 60-fold increase in the mRNA levels of ß-galactosidase, a putative senescence marker. When exposed to higher concentrations (above DL-50) of the pro-oxidant, a 7.2% increase of necrotic cells was observed at 12h, followed by an increase in apoptotic (37.25%) and late-apoptotic/early-necrotic (21.62%) cells at 48h. Therefore, mMES underwent proliferation, senescence or cell death depending on the period of time and intensity of H_2O_2 exposure.

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