Simvastatin-Induced Senescence is Correlated with Increased Levels of ROS in Human Melanoma Cells

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Simvastatin (SIM) induces apoptosis and cell cycle arrest in several types of malignant tumors. However, simvastatin effects on senescence in melanoma cells have not been described yet. The aim of this work was to evaluate the effects of simvastatin on cellular senescence of WM9 metastatic melanoma cells, and elucidate its action mechanism. Cell viability was measured by crystal violet staining upon treatment with SIM at different concentrations (0.05 to 1μmol.L⁻¹) for different time points. We observed 24% reduction in cell viability when WM9 cells were treated with SIM (1μmol.L⁻¹) for 72h. Measurements of ROS with DCF-DA probe showed that simvastatin (1μmol.L⁻¹, 72h) increased cellular ROS content by 51%. Cell cycle analysis by flow cytometry showed an increase in the number of WM9 cells into G1 phase of the cell cycle. In agreement with these results, senescence-associated β-galactosidase staining was evident in WM9 cells treated with SIM. In addition, the mRNA expression levels of cell cycle markers and antioxidant enzymes were evaluated by RT-qPCR. Increased expression of Catalase mRNA levels were observed, possibly due to a feedback mechanism. Together, our results indicate that simvastatin treatment affects the viability and proliferation of human WM9 melanoma cells, inducing the senescent state. These effects could be mediated by increased levels of ROS.

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