SIMVASTATIN MODULATE THE AUTOPHAGIC PROCESS IN A MELANOMA MODEL

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Melanoma is a type of cancer that can be triggered by environmental factors, genetic predisposition and phenotypic factors. It is a tumor with low incidence, but aggressive and has resistance to conventional treatments. Some cellular processes, such as autophagy, are related to tumor growth and therapeutic resistance, which supports autophagy as a therapeutic target in the treatment and prevention of different types of tumors, including melanoma. Previous studies in our groups shows that simvastatin, drug from the statin class, is able to induce cell proliferation arrest, reduce cell viability and induce apoptosis and senescence phenotypes in human metastatic melanoma cells. The objective of this study is evaluate the effect of simvastatin on cell viability and autophagy process in human WM9 metastatic melanoma cells. Cell viability was assessed by MTT method, crystal violet staining and Neutral Red incorporation assays. Cells were treated with different concentrations of simvastatin (0.25 µmol/L, 1µmol/L e 5µmol/L) for 72 hours. It was observed reduction of cell viability in a concentration-dependent manner for all the methods analysed. Specifically, it was showed a reduction of about 56% at a concentration of 1µmol/L and 77% at 5µmol/L. In addition, it was calculated the autophagy arbitrary units (AAU), and the results indicated an induction of autophagic cell death concomitant with an increased concentrations of simvastatin. The evaluation of autophagy was performed by the technique of Western Blotting. It was observed that the proteins levels of LC3 I/II and Beclin-1, the essential markers of autophagic process, were altered after simvastatin treatment. Levels of LC3 I/II were increased after treatment of 0.25µmol/L and 1µmol/L simvastatin, but the Beclin-1 protein was inhibited in 5µmol/L simvastatin. These results highlight the need for understanding of dynamic regulation of autophagy in human melanoma cells treated with simvastatin, in the search for more effective therapy for melanoma.

Key-words: melanoma; autophagy; simvastatin.