Metabolism and mitochondria alterations in melanoma cells induced by Octpep-1

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Octpep-1, a venom-derived tachykinin-peptide from the *Octopus kaurna*, impairs melanoma cellular viability in human melanoma BRAF$^{(V600E)}$-mutated cells, while is innocuous in healthy fibroblasts. Due to the selectivity of this peptide towards melanoma of BRAF mutations, we explored its mechanism of action in tumor cells. We performed a metabolic characterization of cells treated with Octpep-1 using Seahorse Flux technology and microscopy. Specifically, we investigated its effect in glycolysis and OXPHOS as well as changes in mitochondria and mitochondrial dynamics. In addition, we studied the possible effects that these changes may induce in the behavior of melanoma cells and the possible involvement of senescence in the antiproliferative capacity of Octpep-1 by MitoTracker™ Red staining and senescence markers, respectively. Our results showed that Octpep-1 increases oxygen consumption rates, and overall, mitochondrial respiration, without changes in glycolysis in melanoma cells. Hyperactivity of mitochondrial metabolism relates to higher levels of reactive oxygen species without leading to cell apoptosis. Remarkably, dynamic analysis of mitochondria indicated that Octpep-1 does not change the number of mitochondria in cells, but promotes their aggregation in clusters, altering mitochondrial dynamics. These changes could be related to the migratory and proliferative capacities of melanoma cells. Altogether, our results suggest that the antiproliferative profile of Octpep-1 in melanoma BRAF$^{(V600E)}$-mutated cells may be due to alterations in cellular metabolism. These changes are accompanied by alterations in mitochondrial dynamics in melanoma cells.