POSTER ABSTRACTS

Combined treatment of caffeic acid and DMAPT induces AMPK dependent death in MDA-MB231 cells

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Triple negative breast cancer (TNBC) represents about 10-15% of diagnosed cancers and constitutes a heterogeneous group of neoplasms that are in most cases aggressive and associated with a poor prognosis [1]. It is known in the literature that an accumulation of lipid droplets (LDs) can increase the degree of aggressiveness of triple negative breast cancer cells. In fact these lipids can be mobilitated from the droplets to promote growth and metastasis of cancer cells and protect cells from oxidative stress[2]. The AMPK enzyme, in conditions of energy stress or nutritional deficiency, is responsible for the dispersion and use of LD as an energy source. Studies conducted on triple negative breast cancer cells MDA-MB231 have shown that the combined treatment of caffeic acid (CA), AMPK activator, and the fumarate salt of DMAPT (DMAPT), a sesquiterpene lactone capable of inducing cell death in MDA-MB231[3,4], induce a reduction in cell viability in a synergistic way. Staining with Oil-red O showed that the combined treatment, compared to the effect of single compounds, causes a decrease in the number of LD. The results obtained also demonstrate that the CA/DMAPT treatment determines an increase in both the active phosphorylated form of AMPK and its target acetyl-CoA carboxylase (ACC), in the inactive phosphorylated form. The addition of Dorsomorphin, an AMPK inhibitor, counteracts the effects observed on cell viability and on the drop in LD induced by the combined treatment. It was also observed that the CA/DMAPT treatment determines the increase and production of Bax oligomers and the fall of antiapototic factors BclxL and Bcl2. Further analyses are needed to understand the mechanism that leads to the synergistic action between CA and DMAPT but certainly a main role is given by AMPK, which determine lipotoxicity in MDA-MB231, due to the dismantling of lipid droplets.

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