cancers

MDPI

Article

Metformin as an Adjuvant to Photodynamic Therapy in Resistant Basal Cell Carcinoma Cells

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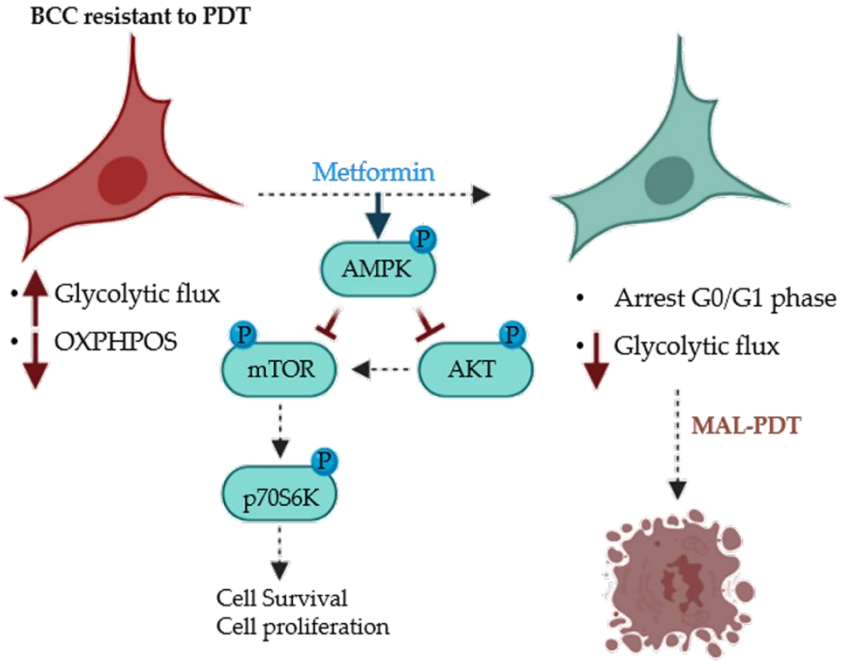
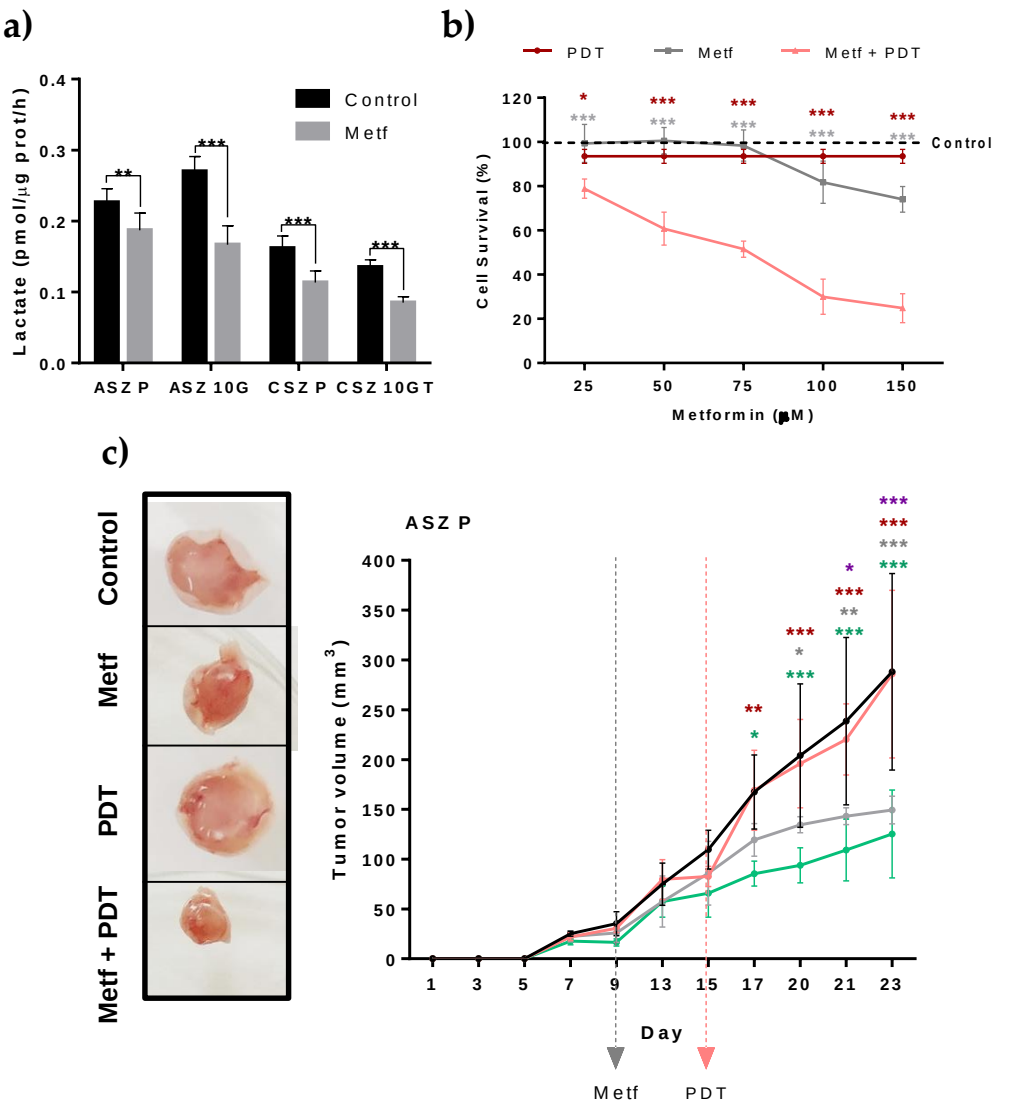
Abstract: Photodynamic Therapy (PDT) with methyl-aminolevulinate (MAL-PDT) is being used for the treatment of Basal Cell Carcinoma (BCC), although resistant cells may appear. Normal differentiated cells depend primarily on mitochondrial oxidative phosphorylation (OXPHOS) to generate energy, but cancer cells switch this metabolism to aerobic glycolysis (Warburg effect), influencing the response to therapies. We have analyzed the expression of metabolic markers (β-F1-ATPase/GAPDH (glyceraldehyde-3-phosphate dehydrogenase) ratio, pyruvate kinase M2 (PKM2), oxygen consume ratio, and lactate extracellular production) in the resistance to PDT of mouse BCC cell lines (named ASZ and CSZ, heterozygous for *ptch1*). We have also evaluated the ability of metformin (Metf), an antidiabetic type II compound that acts through inhibition of the AMP-activated protein kinase (AMPK)/mammalian target of rapamycin (mTOR) pathway to sensitize resistant cells to PDT. The results obtained indicated that resistant cells showed an aerobic glycolysis metabolism. The treatment with Metf induced arrest in the G0/G1 phase and a reduction in the lactate extracellular production in all cell lines. The addition of Metf to MAL-PDT improved the cytotoxic effect on parental and resistant cells, which was not dependent on the PS protoporphyrin IX (PpIX) production. After Metf + MAL-PDT treatment, activation of pAMPK was detected, suppressing the mTOR pathway in most of the cells. Enhanced PDT-response with Metf was also observed in ASZ tumors. In conclusion, Metf increased the response to MAL-PDT in murine BCC cells resistant to PDT with aerobic glycolysis.





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