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DEPENDENCE OF THE DEATH OF RAS-EXPRESSING TUMOR CELLS ON MITOCHONDRIA AFTER TREATMENT WITH ANTITUMOR AGENTS

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Ras-expressing tumor cells are considered to be therapy-resistant, because of their ability to restore viability upon treatment with antitumor agents by activating cytoprotective processes. Search for effective therapy targets generated interest towards mitochondria, because Ras-mutated tumor cells obtain ATP predominantly from oxidative phosphorylation in mitochondria, not from glycolysis, as many other types of tumor cells do. In present work, the abilities of X-ray irradiation and mitochondria permeability inhibitor ABT199/venetoclax to induce death of Ras-mutated tumor cells. Cells demonstrate different response during the 72 hours of treatment. At the early terms (2–24 hours) after damage autophagy is induced that eliminates damaged mitochondria and decreases cell death, but later, after 72 h, senescence, linked with suppression of proliferation, is detected. Suppression of autophagy and senescence decreases viability of irradiated cells, pointing on the key role of these processes in maintenance of cellular viability. So, suppression of these processes might allow to increase the effectiveness of elimination of Ras-mutated tumor cells upon treatment with damaging agents.

Keywords: autophagy, mitochondria, ionizing irradiation, senescence, ABT199