A dual role of autophagy in the anticancer therapy

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In the development of cancer, autophagy demonstrates a dual role. It can both inhibit disease progression as well as protect cells and stimulate tumour growth. Many studies indicate that the main mechanism of cytotoxic action of cytostatic is induction of apoptosis process. However, the initiation of this process is often inhibited by triggering the process of autophagy - in this way the damaged organelles can be removed and the cell death induction inhibited. Based on these opposing properties of autophagy, attempts to inhibit or activate the process can be effective strategies in the fight against cancer. In the present study, it has been analysed whether the process of apoptosis will be induced by inhibiting autophagy in breast cancer cells MCF-7 and MCF-7/Dox using doxorubicin and its two nanoforms (N-DOX/ N-DOX-gh625) . In order to determine the intensity of the autophagy process, a staining technique with monodansylcadaverine was used, whereas in order to analyse pro-apoptotic properties of the analysed compounds, the activity of caspase 3 was measured. The research showed that the drugs in question simultaneously trigger apoptosis and autophagy in cells. NH4Cl was used in the study and it was shown that this compound can inhibit autophagy. Ammonium chloride, which is a weak alkali can accumulate inside lysosomes, increase pH and inactivate hydrolyses. Ammonium chloride inhibited autophagy in MCF-7 and MCF-7/Dox cells. Interestingly, the process of autophagy was most effective after 48 hours of post-incubation culture, both in cells treated with doxorubicin and its two nanoforms, despite the use of antioxidants (NAC, Tiron, Trolox) in the cell were generated damage. This shows that the damage caused by doxorubicin and its two nanoforms was removed from the cell. By removing the damaged cellular organelles, which can be a source of free radicals, autophagy prevented the signals necessary to start the apoptosis process.

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