Different strategies to overcome multidrug resistance in cancer

Research review

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Abstract

The risk of acquisition of resistance to chemotherapy remains a major hurdle in the management of various types of cancer patients. Several cellular and non-cellular mechanisms are involved in developing both intrinsic and acquired resistance in cancer cells toward chemotherapy. This review covers the various multidrug resistance (MDR) mechanisms observed in cancer cells as well as the various strategies developed to overcome these MDR mechanisms. Extensive studies have been conducted during the last several decades to enhance the efficacy of chemotherapy by suppressing or evading these MDR mechanisms including the use of new anticancer drugs that could escape from the efflux reaction, MDR modulators or chemosensitizers, multifunctional nanocarriers, and RNA interference (RNAi) therapy.

Introduction:

The risk of tumors acquiring resistance to chemotherapy (multidrug resistance) remains a major hurdle to the successful treatment of various types of cancers including blood, breast, ovarian, lung, and lower gastrointestinal tract cancers. Multidrug resistance (MDR) is a phenomenon in which cancer cells exhibit a cross-resistant phenotype against multiple unrelated drugs that are structurally and/or functionally different and may also have different molecular targets.

Methods and Results:

Hypoxia in cancer might lead to multidrug resistance via different cellular pathways such as lost sensitivity to p53-mediated apoptosis, and enhanced P-glycoprotein expression. Till now , the most widely studied MDR mechanisms are those associated with drug efflux mechanisms involving ATP-binding cassette (ABC) membrane transporters .

Conclusions:

Targeted nanocarriers present a powerful and versatile platform to overcome this life threatening disease.

Key words: Cancer, Multidrug resistance, Chemosensitizers, Anticancer agents, Nanocarriers, RNAi therapy