ENHANCEMENT OF BLEOMYCIN CYTOTOXIC EFFECT AND REGULATION OF GENE EXPRESSION USING SIMULTANEOUS PLASMID DNA AND BLEOMYCIN ELECTOTRANSFER

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Electrochemotherapy (ETC) is an effective physical technique that enables cytotoxic drugs to have direct access to the cytosol. This budding mode of therapy uses electroporation and anticancer drugs (mainly bleomycin) to trigger cell death in cancerous cells. At this moment, various methods are being explored to increase the impact of ETC, such as gene transfer.

Our preliminary studies have shown that plasmid DNA and bleomycin in the medium allows simultaneous transport of these molecules. In addition, we have shown that the presence of DNA in the medium can increase bleomycin transport and thereby cytotoxicity, whereas the presence of bleomycin may alter the strength and timing of gene expression. These effects can be used to increase the efficiency of ECT (due to more efficient BLM electrotransfer) and to regulate the immune response, by delivering genes, encoding specific cytokines.

In this work, the cytotoxicity effect of the electrotransfer of different concentrations of bleomycin and different size of plasmid DNA by using the same parameters of the electric pulses on Chinese Hamster Ovary cells was determined. Electroporation was performed by using combination of 1 electric pulse of 1400 V/cm pulse strength and 100 μs pulse duration. pMAX GFP (3.5 kb), pEGFP (4.7 kb) and piggyBac (7.1 kb) coding plasmids in concentrations of 200 μg/ml were used.

The obtained results showed that a combination of plasmid DNA, bleomycin, and electroporation increases the cytotoxic effect of the anticancer drug but achieves lower transfection efficiency. Further studies have shown that the cytotoxic effects of anticancer drug (BLM) and transfection efficiency are dependent on plasmid DNA size.

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