Delocalized lipophilic cations selectively target the mitochondria of carcinoma cells.


Source

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Abstract

Traditional chemotherapies, aimed at DNA replication in rapidly dividing cells, have achieved only limited success in the treatment of carcinomas due largely to their lack of specificity for cells of tumorigenic origin. It is important, therefore, to investigate treatment strategies aimed at novel cellular targets that are sufficiently different between normal cells and cancer cells so as to provide a basis for selective tumor cell killing. Delocalized lipophilic cations (DLCs) are concentrated by cells and into mitochondria in response to negative inside transmembrane potentials. The higher plasma and/or mitochondrial membrane potentials of carcinoma cells compared to normal epithelial cells account for the selective accumulation of DLCs in carcinoma mitochondria. Since most DLCs are toxic to mitochondria at high concentrations, their selective accumulation in carcinoma mitochondria and consequent mitochondrial toxicity provide a basis for selective carcinoma cell killing. Several of these compounds have already displayed some degree of efficacy as chemotherapeutic agents in vitro and in vivo. The effectiveness of DLCs can also be enhanced by their use in photochemotherapy or combination drug therapy. Discovery of the biochemical differences that account for the higher membrane potentials in carcinoma cells is expected to lead to the design of new DLCs targeted specifically to those differences, resulting in even greater selectivity and efficacy for tumor cell killing.

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