A combination of alpha lipoic acid and calcium hydroxycitrate is efficient against mouse cancer models: preliminary results.

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Source

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Abstract

The impact of metabolic dysregulation on tumor development has long been established. We have targeted two enzymes that are altered during carcinogenesis: pyruvate dehydrogenase (PDH), which is down-regulated, and ATP citrate lyase, which is overexpressed in cancer cells. Alpha lipoic acid is a cofactor of PDH, while hydroxycitrate is a known inhibitor of ATP citrate lyase. Our hypothesis is that a combination of these drugs may have antitumoral potential. The efficacy of these molecules was screened in vitro by treatment of different human cancer and murine cell lines. Lipoic acid reduced the cell number by 10-50% depending on concentrations (0.1-10 microM) and cell types. Calcium hydroxycitrate reduced the cell number by 5-60% at different concentrations (10-500 microM). When hydroxycitrate and lipoic acid were used together, there was a major cytotoxic effect: complete cell death was seen following 8 microM lipoic acid and 300 microM hydroxycitrate treatment for 72 h. The combination of alpha lipoic acid and hydroxycitrate was administered to healthy mice, at doses currently utilized for other indications than cancer; no demonstrable toxicity was observed. The combination was used to treat mouse syngenic cancer models: MBT-2 bladder transitional cell carcinoma, B16-F10 melanoma and LL/2 Lewis lung carcinoma. The efficacy of this combination appears similar to conventional chemotherapy (cisplatin or 5-
fluorouracil) as it resulted in significant tumor growth retardation and enhanced survival. This preliminary study suggests that this combination of drugs is efficient against cancer cell proliferation both in vitro and in vivo. A clinical trial is warranted.

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