Enhanced efficacy of gemcitabine by indole-3-carbinol in pancreatic cell lines: the role of human equilibrative nucleoside transporter 1.

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Source

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Abstract

Pancreatic cancer patients treated with gemcitabine (2',2'-difluorodeoxycytidine) can eventually develop resistance. Recently, published data from our laboratory demonstrated enhanced efficacy of gemcitabine with the dietary agent, indole-3-carbinol (I3C). The current study examined the possible mechanism for this I3C-enhanced efficacy. Several pancreatic cell lines (BxPC-3, Mia Paca-2, PL-45, AsPC-1 and PANC-1) were examined for modulation of human equilibrative nucleoside transporter 1 (hENT1) expression, the major transporter for gemcitabine, by I3C alone and combined with gemcitabine. I3C significantly (p<0.01) up-regulated hENT1 expression in several cell lines. Gemcitabine alone showed no effect on hENT1 expression. However, combining gemcitabine with I3C further increased hENT1 expression. Cell viability assays revealed no effect of I3C on normal cells, hTERT-HPNE. hENT1-specific inhibitor, nitrobenzylthioinosine, significantly abrogated I3C-induced gemcitabine cytotoxicity, further demonstrating its specificity. This study demonstrates that up-regulation of hENT1 expression may be a novel mechanism involved in the additive effect of I3C and gemcitabine.

PMID:

21965724