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Effect of spermine synthase on the sensitivity of cells anti-tumour agents

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The role of spermine in the sensitivity of cells to various estaclished and experimental anti-tumour agents was examined, using paired cell lines that possess or lack spermine synthase. All spermine- synthase-deficient cells had no detectable spermine, and elevated spermidine, content. Spermine content did not alter the cell growth rare. There was little or no difference in sensitivity of immortalized mouse embryonic fibroblasts to doxorubicin, etoposide, cisplatin, H202 and only a slight increase in sensitivity to vinblastine and nocodazole. However, the absence of spermine clearly increased the sensitivity to BCNU, suggesting that depletion of spermine may be a useful way to increase the anti-neoplastic effects of anti-tumour agents that form chloroethy-mediated interstrand DNA cross-links. The effects of spermine on the response to polyamine analogues (which have been proposed to be useful anti-neoplastic agents) were complex, and depended on the compound examined and on the cells tested. Sensitivity to CHENSpm was substantially preater in immortalized fibroblasts that lack apermine. In contrast, BE-3-4-3 and BE-3-3-3 were more active against cells that contained spermine. The presence of spermine correlated with a greater induction of SSAT by BE-3-3-3, which is consistent with suggestions that this induction is important for the response to this drug. These findings support the concepts that different polamine analogues have different sites of action and that CHENSpm has a different site of action from BE-3-3-3.
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