

## **Immunodepletion of hCG $\beta$ reduces cancer cell growth in vitro**

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The free  $\beta$ -subunit of human chorionic gonadotrophin (hCG $\beta$ ) is well established as an ectopic product of epithelial tumors. Originally explained as an epi-phenomenon, hCG $\beta$  production by many types of carcinoma is increasingly regarded as a significant tumor event. Studies in bladder cancer have shown that hCG $\beta$  production, while not diagnostic, is a very good indicator for poor prognosis through correlations with resistance to radiotherapy and rapid metastasis. These clinical findings led to *in vitro* studies that have shown a direct response to hCG $\beta$  by bladder carcinoma cell lines. This response is linked by inhibition of apoptosis to an increase in cell population. More recently, studies on hCG $\beta$  as a marker for poor prognosis in other epithelial cancers now suggest that this phenomenon may not be restricted to bladder carcinoma. Thus, ectopic hCG $\beta$  represents an ideal target for immunodepletive therapy. Antisera were generated from mice vaccinated with modified forms and antigenic sequences of hCG $\beta$ . These antigens comprised full-length hCG $\beta$  carboxy terminal peptide (CTP37) and a truncated region comprising 24 of the amino acids of the CTP (CTP24). The effect of the resultant murine antisera on bladder carcinoma cell growth in vitro was investigated. When CTP37 antisera were incubated with hCG $\beta$ -producing cell lines, significant reductions in cell number (up to 43%) were observed. In the bladder cancer cell line T24, which does not produce hCG $\beta$ , CTP37 antisera had no effect on cell number. CTP24 antiserum, like control sera from mice immunized with wild-type CPMV, had no effects on the in vitro growth of any cell lines. This implies that full-length CTP37, but not CTP24, is involved in the oncogenic inhibition of apoptosis by hCG $\beta$ . A further series of antisera raised against hCG $\beta$  constructs, for which the CTP had been constrained, were subsequently tested. Using the same in vitro model, this series was also found to have similar growth inhibitory effects.

HCG $\beta$ -CTP vaccines are available as well-tested anti-fertility vaccines in the Third World. They have now been tested on cancer patients. These studies are the only in vitro evidence that such a vaccine would have beneficial antitumor effects via immunodepletive mechanisms. We propose that vaccines such as this could be used as an adjuvant therapy in the treatment of hCG $\beta$ -producing epithelial cancers.