

## **Free hCG $\beta$ modulates epithelial tumour cell growth by inhibition of apoptosis**

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Ectopic production of free beta human chorionic gonadotrophin (hCG $\beta$ ) by epithelial cancers is well described. hCG $\beta$ secreting tumours are more aggressive, radioresistant and have a greater propensity to metastasize. We proposed that the ectopic production of hCG $\beta$  was contributing in an autocrine fashion to the radioresistance and metastatic potential of such secreting tumours. Though we demonstrated that the addition of hCG $\beta$ to the culture media of bladder, cervical and endometrial carcinoma cell lines brought about an increase in cell populations this was not accompanied by a significant increase in the rate of replication. Since a cell population size is a balance of mitosis and mortality, we proposed that hCG $\beta$ was inhibiting apoptosis. We demonstrated that following incubation with recombinant hCG $\beta$ , bladder carcinoma cells refrain from undergoing apoptosis. Quantitation of apoptotic bodies was carried out by immunoassay and corrected to cell number as determined by MTT assay. In each cell line, addition of hCG $\beta$ reduced the number of apoptotic bodies dose-dependently, indicating a diminished apoptotic rate. Furthermore, TGF $\beta$ 1-induced apoptosis could be dose dependently inhibited by co-incubation with hCG $\beta$ . We propose, therefore, that such a decline in apoptosis may account for the cell population increase reported. It may also explain the radioresistance and aggressive nature of hCG $\beta$ -secreting tumours and the poor prognosis associated therein. Immunohistochemical studies of bladder tumour section indicated a correlation between hCG $\beta$  detection and BCL-2 expression by the tumour. However, detailed *in vitro* studies revealed that the addition of exogenous hCG $\beta$  to bladder cancer cell lines did not upregulate BCL-2 protein expression. Further IHC studies on cervical squamous carcinomas demonstrated that hCG $\beta$  expression correlated inversely with the extent of apoptosis within the section.

*In vitro* and *in vivo* observation strongly suggests that hCG $\beta$  expression by epithelial cancers inhibits apoptosis and contributes to the aggressive phenotypes. This highlights hCG $\beta$  importance as a therapeutic target.