

Does hCG play a role in cancer cell biology?

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Ectopic expression of hCG β is a recognized phenomenon in 20-40% of patients with common carcinomas arising from mucosal epithelia such as bladder, cervix, lung and naso-pharynx. Recent studies have indicated that hCG β may act as an autocrine growth factor inhibiting apoptosis. Furthermore, antibodies targeted against hCG β increase tumour cell apoptosis and in this respect, hCG β meets the criteria of a clinically useful biomarker fulfilling the Her2 paradigm.

However, the role that hCG might play in the oncogenic process in breast cancer is not as clear cut. The detection of ectopically expressed hCG(β) by breast tumors has been employed as a biomarker of malignancy, and hCG has been proposed as a ligand vehicle for toxic drugs (with the aim of targeting the LH/hCG receptor which is reported to be expressed by malignant breast tissue). Conversely, there is substantial work to suggest that hCG is a protective agent against the development of breast cancer. This has lead some to advocate hCG administration to non-pregnant women as a cancer preventative measure.

This apparent paradox could be resolved if the free beta subunit of hCG produced by tumours acts as an autocrine anti-apoptotic growth factor, whilst, in pregnancy, intact heterodimeric hCG is part of a developmental signal that initiates breast ductal tissue differentiation and hence reduces the population density of stem-like cells which are susceptible to carcinogenic factors and oncogenic change.

The structural glycovariants or even dimeric partners of these distinct hormonal/cytokine molecular entities may confer further specific interactions contributing to oncogenesis. In addition, molecular studies are now suggesting distinct expression profiles of ectopic *CG β* gene expression as apposed to eutopic expression by the placenta of the genes/pseudogenes of the so called *LH/CG β* gene cluster.

These molecular revelations are lending support to current developments in immunotherapeutic interventions, principally adjuvant vaccine therapies based upon the free β -subunit of hCG, which should provide prolonged, innate counteraction to the growth factor effects of hCG β in malignant tumours that express it,. Although not an independent therapy, such adjuvant immunotherapy should improve hCG β positive cancers responsiveness to cytotoxic drugs and radiotherapy.