The presence of hCG subunit transcripts and/or protein was demonstrated in cell lines derived from colon cancer, lung cancer, ovarian cancer and leukemia.

hCG stimulated the growth of cancer cells in vitro and in vivo, and anti-hCG antibodies prevented hCG-mediated proliferation in vitro. The hormone may thus provide an important autocrine or paracrine growth-promoting stimulus for cancer cells.

hCG up-modulated the transcription and expression of the key angiogenic factors IL-8 and VEGF in tumor cells and may thus act as a critical component in tumor-associated neo-angiogenesis. Pathway inhibition studies suggested that hCG may act via the MAPK pathway to increase IL-8 secretion in both human and mouse cancer cells, while VEGF secretion in human cancers may occur via the MAPK and PKA pathways and in murine cancers via the PI3K pathway.

hCG up-regulated the key matrix metalloproteases MMP-2 and MMP-9 and promoted the invasion of tumor cells in vitro, actions potently inhibited by anti-hCG antibodies. These studies point to a potential role of the hormone in metastasis.

hCG was demonstrated to act as a chemo-attractant for normal, non-transformed cells, an activity that may have relevance to its tumor-promoting effects. The demonstrated attraction of endothelial cells by hCG may aid in the process of neo-angiogenesis. The specific attractant properties of hCG towards macrophages and T cells (but not B cells) deserves further investigation, given the previously established roles of tumor-associated macrophages and TReg cells in tumor progression.

Up-modulation of the transcription factor FOXP3 was observed when some (but not all) cancer cells were incubated with hCG; up-modulation correlated with the enhanced secretion of the immunosuppressive cytokines TGF-β and IL-10. The inhibitory effect on mixed leucocyte reactions of hCG-incubated cancer cell supernatant was partially attributed to the presence of IL10. Up-regulation of FOXP3 by hCG was also associated with the increased
expression of CTLA4 on the cancer cell surface. Incubation of such cells with mature bone-marrow derived dendritic cells led to the enhanced expression of the tryptophan-catabolising enzyme IDO by the latter, possibly as a consequence of CTLA4-CD80/86 interaction. These results indicate that the presence of hCG can lead to the elaboration of multiple immunosuppressive pathways, ultimately benefiting tumor survival.

Incubation of cancer cells with hCG led to the enhanced secretion of versican, a proteoglycan previously associated with tumorigenesis. Versican sourced from tumors has previously been shown to elicit the secretion of inflammatory cytokines from macrophages. Indeed, supernatants from hCG-treated cancer cells, when incubated with macrophages, induced the heightened secretion of IL-6 and TNF-α, cytokines linked to metastasis. These results further establish mechanisms by which hCG can elicit the collaboration of transformed and non-transformed cells to create conditions conducive for cancer progression.

Passive administration of anti-hCG antibodies reduced the rate of growth of human and mouse tumor cells implanted in nude mice.

The effects of active immunization with βhCG-TT, M.w. or βhCG-TT + M.w. on the growth of LLC-induced tumors in C57BL/6 mice were assessed. Animals receiving either βhCG-TT or M.w. demonstrated significant decreases in tumour volume; co-immunization of βhCG-TT and M.w. provided synergistic benefits in terms of tumor incidence, tumor volumes and animal survival.
Human chorionic gonadotropin induces the activation of several independent tumor-promoting events either directly, or with the cooperation of non-transformed cells.

Vaccination against gonadotropin subunits may be a potential alternate therapy in the management of hormone-dependent cancers.