

CT antigens, gametogenic recapitulation and tumorigenesis

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The processes of germ cell development and tumor development share important similarities. As much as 100 years ago, the similarity of the biological features of trophoblasts and cancer cells prompted John Beard to propose a trophoblastic theory of cancer in which cancers were seen as arising from germ cells that fail to complete their embryonic migration to the gonads (1). Evidence for an association between germ cell development and cancer has steadily emerged over the years. For example, a facet of a variety of human cancers that has attracted considerable attention is their frequent production of chorionic gonadotropin (HCG) and other trophoblastic hormones (2). These hormones are now used as a prognostic indicator for a number of epithelial tumors (3). A most important and more recent step has been the finding of a growing number of proteins that appear to be present only in germ cells, trophoblasts and tumors - the cancer/testis (CT) antigens (4). In addition to their importance as cancer vaccines, the identification of CT-antigens has led to the theory that aberrant expression of germ line genes in cancer reflects the activation of the silenced gametogenic program in somatic cells and that this programmatic acquisition is one of the driving forces of tumorigenesis (5, 6). Insights into the function of a number of the most frequently expressed CT antigens are now beginning to emerge. These data are consistent with the concept that genetic alterations in cancer can result in the reactivation of normally silent germ line expression programs potentially capable of conferring some of the central characteristics of malignancy on the tumor. Such a causal role in establishing and maintaining tumorigenicity enhances the potential importance of CT antigens as therapeutic targets.

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