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**GENE EXPRESSION IN HUMAN NEOPLASIA:
A COMPARISON OF mRNA AND
PROTEIN DISTRIBUTION IN
VARIOUS HUMAN TUMORS**

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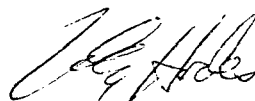
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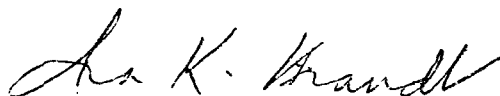
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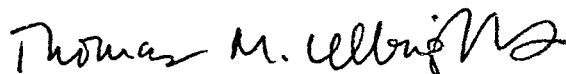
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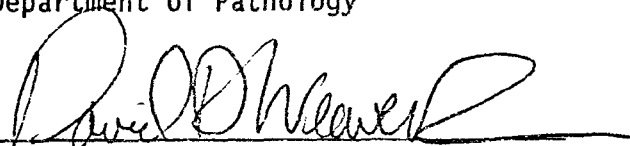
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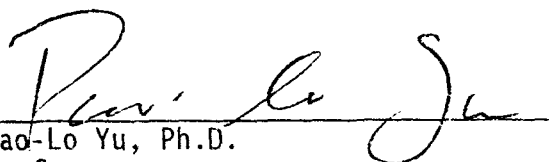
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Abstract

Enzymes are gene products vital to cellular function. Their expression, but probably not the proteins themselves, is often irreversibly altered in cells that have become cancerous. Understanding such alterations is integral to discerning the cause of neoplastic growth.

I have investigated the distribution of four enzymes, alkaline phosphatase, amylase, phosphodiesterase I and ribonuclease in a variety of human neoplasms. Immunohistochemical techniques with specific antibodies were used to compare the distribution of the respective enzymes in normal human tissues and their cancerous counterparts. A number of interesting differences were found. Phosphodiesterase I was abundant in the cytoplasm of malignant epithelia, whereas alkaline phosphatase was often found in subcellular granules. In some tumors, enzyme expression was lost. Salivary gland tumors were notable in this category. These observations provide evidence that the genes controlling the four enzymes are involved in the neoplastic process. The groundwork was therefore established for further molecular studies, and amylase was chosen as a representative.

Amylase is a major component of human parotid gland secretions. I have found that tumors of this gland almost invariably cease to produce amylase protein. In contrast, all tumor cells produce ribonuclease. Molecular biological techniques were used to discern the level of interruption of amylase gene expression in parotid gland tumors.

Southern analysis of DNA from a variety of tumors showed no evidence of major amylase gene rearrangement. This indicates that the structural gene is unaltered in the neoplastic state. In situ hybridization techniques were used to detect cellular amylase mRNA in both normal and neoplastic parotid glands. Amylase mRNA was absent from all parotid tumors examined. This suggests that the interruption in amylase expression occurs at the transcriptional level.

These results are consistent with a bicellular theory of parotid gland tumor origin. I further postulate that ribonuclease and amylase are expressed at opposite ends of a spectrum of parotid acinar cell differentiation. This developmental spectrum is presumably imitated by neoplastic cells. Several models are proposed for control of gene expression, in light of the above hypothesis.

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