



2005 Progress Report Caring for Carcinoid Foundation Research Grant

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“Proteomic analysis of GI neuroendocrine tumors”

The overall goal of this project is to determine whether there are unique protein expression patterns in gastrointestinal (GI) neuroendocrine tumors that can provide novel insights into disease pathogenesis. Through this approach, we hope to identify specific therapeutic targets that have been previously unrecognized. This strategy has never been undertaken in the study of GI neuroendocrine tumors and is a powerful, unbiased way to identify some of the key proteins involved in tumor development.

Our strategy was to examine human tumor samples, in contrast to cultured cell lines. While there is some inherent tissue heterogeneity, this approach is appealing in that the proteins identified are likely to be functionally relevant in actual tumors. We began our analysis with pilot experiments to optimize protein solubilization techniques with samples of normal human pancreas. Gel electrophoretic studies revealed a clean separation of total protein. The gel was then divided into 22 fractions based upon protein size, and proteins from each fraction were analyzed by mass spectrometry. A total of 997 distinct proteins were definitively identified, many of which are known to be present at very low concentrations. Studies are now underway to optimize sub-fraction analysis. In particular, we are interested in the analysis of cell surface glycoproteins as well as phospho-proteins. In this manner, we hope to target key cell surface proteins as well as intracellular signaling molecules. After our protocols have been optimized for these sub-fractions in normal tissues, we will then proceed with our analysis of gastrointestinal carcinoid and pancreatic neuroendocrine tumor tissues stored in our tumor bank. By comparing differences in protein expression patterns between normal and tumor tissue, we hope to identify not only individual proteins but also signaling pathways that may play pivotal roles in the development of these poorly understood tumors.