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Isolation and Characterization of Small Bowel Neuroendocrine Tumor Cell Line

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BACKGROUND: According to SEER Program, the age-adjusted annual incidence of neuroendocrine tumors arising from jejunum and ileum is 0.67 per 100,000. A significant barrier to research in small bowel neuroendocrine disease is the lack of a well characterized cell line that will grow in tissue culture and as a mouse xenograft.

METHODS: A tumor was resected from the proximal ileum from the small bowel of a female patient after an Informed Consent to Participate in Research was obtained under the guidance of the Institutional Review Board at the University of Iowa. The tumor tissue was minced with a scalpel, mechanically disrupted using pipetting and placed in Ham's F12 media containing 5% FBS, 10 mM HEPES, 1 µg/ml hydrocortisone, 5 µg/ml insulin and the antimetabolites penicillin, streptomycin and amphotericin. The cells were grown attached in tissue culture treated flasks at 4% oxygen 37°C. After multiple passages cells were injected into nude female mice.

RESULTS: Cells grew well in culture. After 5 passages cells were processed for immunohistochemistry. The cells stained negative for chromogranin A but positive for synaptophysin. Unlike the original tumor, cells grown in culture were negative for SSTR2 by Western blot and serotonin by ELISA. Tumors grew when either 5 or 10 million cells were injected into nude mice. An excised tumor was negative for chromogranin A, CDX2, CXCR4, and highly positive for keratin AE1/AE3, synaptophysin and SSTR2A by immunohistochemistry antibody staining.

CONCLUSION: We have successfully grown and characterized a small bowel neuroendocrine tumor cell line in both tissue culture and as a xenograft mouse tumor. These cells represent a good model for future research in small bowel neuroendocrine disease.