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Variability of Somatostatin Receptor Type 2 Immunohistochemical Staining Patterns Among Gastroenteropancreatic Neuroendocrine Tumors

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BACKGROUND: Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) can be difficult to diagnose with current imaging standards. Somatostatin receptor 2 (SSTR2) can be overexpressed on cellular surfaces, making some patients eligible for SSTR2-based imaging and therapy. However, density of SSTR2 overexpression varies among patients. Determination of which tumors express SSTR2 is critical for deciphering the underlying mechanisms causing some patients to lack SSTR2.

METHODS: We investigated SSTR2 expression among 75 GEP-NET patients at our institution. Tissue microarrays (TMAs) were immunohistochemically stained for SSTR2. Staining was assessed based on published recommendations and scored: 0 = absent, 1 = cytoplasmic only, 2 = membrane reactivity in <50% of tumor cells, 3 = membrane reactivity in > 50% of tumor cells. TMAs were quantified for positive percentage and intensity of SSTR2 staining (membrane versus cytoplasmic) with an automated custom MATLAB code. Chi-square test was used when assumptions were met, otherwise likelihood ratio (LR) was used.

RESULTS: Overall, 71.8% were of pancreatic origin, compared to 28.2% of non-pancreatic origin, including small intestine, ampulla, duodenum, ileum, and stomach. 80.8% of patients were SSTR2 positive and 19.2% were SSTR2 negative. In SSTR2 positive GEP-NETs, staining was scored as 1 for 15.4%, 2 for 7.7%, and 3 for 62.8%. Tissues with high SSTR2 expression were more likely to be of pancreatic origin, where 83.7% of SSTR2 score 3 were of pancreatic origin (df = 1, LR = 9.410, p = 0.024). There was a significant difference between SSTR2 staining

of primary versus metastatic tumors ($df = 1$, $LR = 18.039$, $p < 0.001$). 58.3% of patients with SSTR2 score 1 were metastatic, compared to only 22.4% of those with score 3.

CONCLUSION: Our study found an association between high SSTR2 expression and GEP-NETs of pancreatic origin. Tumors with a lower SSTR2 expression were likely to be metastatic than primary tumors.

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