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Diagnostic Utility of SATB2 in Determining the Site of Origin of Well-Differentiated Neuroendocrine Tumors

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BACKGROUND: Determining the site of origin of a metastatic, well-differentiated neuroendocrine tumor (NET) can be challenging and has important prognostic and therapeutic implications. An immunohistochemical (IHC) panel consisting of TTF1, CDX2, PAX6, and Islet1 can be helpful. However, there can be significant IHC overlap among different primary sites. Herein we sought to determine the utility of Special AT-rich sequence binding protein-2 (SATB2) in determining the primary site.

METHODS: Paraffin tissue microarrays consisting of 95 WDNets (26 lung, 22 small bowel, 6 appendix, 4 stomach, 4 duodenum, 7 rectum, and 26 pancreas) were stained for SATB2, Islet1, PAX6, TTF1, and CDX2. The results were recorded as no staining, weak, moderate, and strong staining.

RESULTS: Except for one, all rectal and appendiceal NETs were moderately to strongly positive for SATB2. In comparison, all pancreatic and lung NETs were negative for SATB2. Almost half of small bowel NETs were positive for SATB2, but none of them were moderately to strongly positive. In comparison, 90% of the small bowel NETs were moderately to strongly positive for CDX2. ISL1 and PAX6 were positive in 18 of 24 (75%) and 15 of 21 (71%) pancreatic NETs, respectively. However, either Islet1 or PAX6 was also positive in 3 of 4 (75%) duodenal, 6 of 6 rectal, and 1 of 5 (20%) appendiceal NETs. The results of SATB2 and CDX2 stains are compared in Table 1.

CONCLUSION: SATB2 stain is useful in separating pancreatic from rectal NET, as rectal NETs are positive for SATB2 and pancreatic NETs are negative for SATB2. Strong and diffuse staining for SATB2 is suggestive of appendiceal and colorectal primary. CDX2 is a better marker than SATB2 for small intestinal primary. SATB2 may therefore complement the panel of TTF1, CDX2, PAX6, and Islet1 in determining the site of origin of a NET.

Table 1. Comparison of SATB2 and CDX2 in Primary WDNets.

Anatomic Location	Number of cases	Total Number of SATB2 Positive Cases (%)	Total Number of CDX2 Positive Cases (%)
Stomach	4	0 (0)	1 (25)
Duodenum	4	0 (0)	3 (75)
Small bowel	22	10/21 (48)	21 (95)
Appendix	6	6 (100)	5/5 (100)
Rectum	7	7 (100)	4/6 (67)
Pancreas	26	0/25 (0)	6/25 (24)
Lung	26	1 (4)	0 (0)

Abbreviation used: NA: Not applicable.