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Titel des Beitrags: ISL1 expression is not restricted to pancreatic well-differentiated neuroendocrine neoplasms, but is also commonly found in well and poorly differentiated neuroendocrine neoplasms of extrapancreatic origin.

Abstract: The human insulin gene enhancer-binding protein islet-1 (ISL1) is a transcription factor involved in the differentiation of the neuroendocrine pancreatic cells. Recent studies identified ISL1 as a marker for pancreatic well-differentiated neuroendocrine neoplasms. However, little is known about ISL1 expression in pancreatic poorly differentiated and in extrapancreatic well and poorly differentiated neuroendocrine neoplasms. We studied the immunohistochemical expression of ISL1 in 124 neuroendocrine neoplasms. Among pancreatic neuroendocrine neoplasms, 12/13 with poor differentiation were negative, whereas 5/7 with good differentiation but a Ki67>20% were positive. In extrapancreatic neuroendocrine neoplasms, strong positivity was found in Merkel cell carcinomas (25/25), pulmonary small cell neuroendocrine carcinomas (21/23), medullary thyroid carcinomas (9/9), paragangliomas/pheochromocytomas (6/6), adrenal neuroblastomas (8/8) and head and neck neuroendocrine carcinomas (4/5), whereas no or only weak staining was recorded in pulmonary carcinoids (3/15), olfactory neuroblastomas (1/4) and basaloid head and neck squamous cell carcinomas (0/15). ISL1 stained the
neuroendocrine carcinoma component of 5/8 composite carcinomas and also normal neuroendocrine cells in the thyroid, adrenal medulla, stomach and colorectum. Poorly differentiated neuroendocrine neoplasms, regardless of their ISL1 expression, were usually TP53 positive. Our results show the almost ubiquitous expression of ISL1 in extrapancreatic poorly differentiated neuroendocrine neoplasms and neuroblastic malignancies and its common loss in pancreatic poorly differentiated neuroendocrine neoplasms. These findings modify the role of ISL1 as a marker for pancreatic neuroendocrine neoplasms and suggest that ISL1 has a broader involvement in differentiation and growth of neuroendocrine neoplasms than has so far been assumed.

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