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Olfactory Receptor 51E1 is a Potential Novel Tissue Biomarker for the Diagnosis of Small Intestine Neuroendocrine Tumors

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Background: Small intestine neuroendocrine tumor (SI-NET) patients get late diagnosis. We have previously reported olfactory receptor 51E1 (OR51E1) as a novel SI-NET mRNA marker. We aimed at understanding whether, OR51E1 protein may be developed as a novel diagnostic marker.

Methods: OR51E1 coding sequence was cloned by using total RNA from human NET cells and patient specimens. Laser capture microdissection (LCM) isolated SI-NE tumor and normal cells. OR51E1 mRNA expression was investigated in CNDT2.5, KRJ-1, different cancer and fibroblast cell lines, and normal liver cells and tissue by using QRT-PCR. OR51E1 protein expression was investigated on paraffin-embedded sections from 70 SI-NET patients (43 primary tumors, 28 mesentery metastases and 18 liver metastases) by using conventional immunohistochemistry. Adjacent tumor mucosa and tumor material was investigated by using double immunofluorescence [OR51E1, vesicular-monoamine-transporter-1 (VMAT1)].

Results: OR51E1 coding sequence analysis showed absence of mutation in tumor cells from established NET cell lines and from patient specimens. CNDT2.5 and KRJ-1 cells are OR51E1-negative. OR51E1 expression in LCM SI-NET cells is higher than in the stroma cells. Normal human liver tissue and a panel of normal human hepatic cells do not express OR51E1. Moreover, we detected OR51E1 protein expression both in the primary and in the metastatic tumor cells. Cytoplasmic, perinuclear and membranous OR51E1 expression was detected. Primary tumors (42%), mesentery metastases (25%) and liver metastases (33%) show over 50% OR51E1 positive cells. OR51E1 and VMAT1 co-localize in a minority of EC cells in the adjacent tumor SI-mucosa, whereas they co-localize in the majority of SI-NE tumor cells from patients at different stage of disease.

Conclusion: OR51E1 protein is a novel potential diagnostic SI-NET biomarker. Its role in the pathophysiology in SI-NETs has to be further characterized. Moreover, it may retain a proper specificity to be developed as therapeutic target.