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DOG1 Expression Is in Common Human Tumors: A Tissue Microarray Study on More than 15,000 Tissue Samples

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Abstract : DOG1 (Discovered on GIST1) is a voltage-gated calcium-activated chloride and bicarbonate channel that is highly expressed in interstitial cells of Cajal and in gastrointestinal stromal tumors (GIST) derived from Cajal cells. To systematically determine in what tumor entities and normal tissue types DOG1 may be further expressed, a tissue microarray (TMA) containing 15,965 samples from 121 different tumor types and subtypes as well as 608 samples of 76 different normal tissue types were analyzed by immunohistochemistry. DOG1 immunostaining was found in 67 tumor types, including GIST (95.7%), esophageal squamous cell carcinoma (31.9%), pancreatic ductal adenocarcinoma (33.6%), adenocarcinoma of the Papilla Vateri (20%), squamous cell carcinoma of the vulva (15.8%) and the oral cavity (15.3%), mucinous ovarian cancer (15.3%), esophageal adenocarcinoma (12.5%), endometrioid endometrial cancer (12.1%), neuroendocrine carcinoma of the colon (11.1%) and diffuse gastric adenocarcinoma (11%). Low level-DOG1 immunostaining was seen in 17 additional tumor entities. DOG1 expression was unrelated to histopathological parameters of tumor aggressiveness and/or patient prognosis in cancers of the breast (n=1,002), urinary bladder (975), ovary (469), endometrium (173), stomach (233), and thyroid gland (512). High DOG1 expression was linked to estrogen receptor expression in breast cancer ($p<0.0001$) and the absence of HPV infection in squamous cell carcinomas ($p=0.0008$). In conclusion, our data identify several tumor entities that can show DOG1 expression levels at similar levels as in GIST. Although DOG1 is tightly linked to a diagnosis of GIST in spindle cell tumors, the differential diagnosis is much broader in DOG1 positive epithelioid neoplasms.

Keywords : biomarker, DOG1, immunohistochemistry, tissue microarray
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