PLAG1

Zinc finger protein PLAG1 is a protein that in humans is encoded by the PLAG1 gene.

Pleomorphic adenoma gene 1 encodes a zinc finger protein with 2 putative nuclear localization signals. PLAG1, which is developmentally regulated, has been shown to be consistently rearranged in pleomorphic adenomas of the salivary glands. PLAG1 is activated by the reciprocal chromosomal translocations involving 8q12 in a subset of salivary gland pleomorphic adenomas.

PLAG1 has been shown to interact with Karyopherin alpha 2.

PLAG1 (pleomorphic adenoma gene 1) is frequently activated in pleomorphic adenoma (PA). Carcinoma ex pleomorphic adenoma (CXPA) arises in PA, and PLAG1 expression is believed to be maintained from PA to CXPA, as it can contribute to the carcinogenesis process. To evaluate if PLAG1 is a good marker of malignant transformation from PA to CXPA as well as to evaluate if PLAG1 expression is associated with progression and histopathologic subtype of CXPA. Forty PAs, 21 residual PAs (without malignant transformation), and 40 CXPAs were analyzed by immunohistochemistry with PLAG1 antibody. The proportion of positive neoplastic cells was assessed according to a 2-tiered scale: >10% to 50%, and >50% positive cells. The CXPA group was classified according to histopathologic subtype and invasiveness degree. Thirty-seven PAs (92.5%), 15 residual PAs (71%), and 14 CXPAs (35%) were positive for PLAG1. In relation to the CXPA group, among the intracapsular cases, myoepithelial carcinoma and epithelial-myoepithelial carcinoma showed the highest level of PLAG1 expression. PLAG1 expression is lost when PA undergoes malignant transformation, possibly due to other pathway activation and different clone cells. In addition, PLAG1 expression seems to be present mainly in low-grade carcinomas and in cases with early phase of invasion, due to its regulation of oncogene-induced cell senescence. In CXPA, PLAG1 expression was most associated with myoepithelial differentiation. This way, loss of PLAG1 expression can be considered a hallmark of CXPA carcinogenesis, mainly when there is only epithelial differentiation [1)].

Although pituitary neuroendocrine tumor is a malignant tumor, it can present as invasive growth in some cases. MicroRNA (miR)-26a has been found to be abnormally highly expressed in pituitary neuroendocrine tumor, indicating possible involvement in pathogenesis. As a known target gene of miR-26a, PLAG1 has abnormally low expression in pituitary neuroendocrine tumor. The correlation between miR-26a or PLAG1 expressional abnormality and occurrence of pituitary neuroendocrine tumor is still unknown, as is its association with invasiveness of pituitary neuroendocrine tumor.

pituitary neuroendocrine tumor tissues, including both invasive and non-invasive subtypes, were collected from the Neurosurgery Department Yantaishan Hospital, Yantai, Shandong, China, in parallel with normal pituitary tissues from postmortem autopsy. qRT-PCR was used to detect mRNA expression of miR-26a and PLAG1, while Western blotting was used to test PLAG1 protein expression. The correlation between miR-26a and PLAG1, and with pathological features, were analyzed. ROC analysis revealed the utility of miR-26a and PLAG1 in differential diagnosis of invasive/non-invasive pituitary tumors and in analyzing their effects on patient prognosis.

MiR-26a was remarkably upregulated in pituitary tumors, while PLAG1 was downregulated, especially in invasive pituitary tumors. miR-26a and PLAG1 had higher diagnostic values for differentiating

between invasive and non-invasive pituitary tumors (AUC=0.889 and 0.818, respectively). Those patients with miR-26 overexpression and PLAG1 downregulation had unfavorable prognosis. miR-26 and PLAG1 are independent factors affecting patient diagnosis.

MiR-26a can facilitate occurrence of pituitary tumor and invasiveness, probably via inhibiting PLAG1 expression [2].

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2)
Yu C, Li J, Sun F, Cui J, Fang H, Sui G. Expression and Clinical Significance of miR-26a and Pleomorphic Adenoma Gene 1 (PLAG1) in Invasive pituitary neuroendocrine tumor. Med Sci Monit. 2016 Dec 24;22:5101-5108. PubMed PMID: 28012286.