PPM1D

Protein phosphatase 1D is an enzyme that in humans is encoded by the PPM1D gene.

The protein encoded by this gene is a member of the PP2C family of Serine threonine protein phosphatases. PP2C family members are known to be negative regulators of cell stress response pathways. The expression of this gene is induced in a p53-dependent manner in response to various environmental stresses. While being induced by tumor suppressor protein TP53/p53, this phosphatase negatively regulates the activity of p38 MAP kinase (MAPK/p38) through which it reduces the phosphorylation of p53, and in turn suppresses p53-mediated transcription and apoptosis. This phosphatase thus mediates a feedback regulation of p38-p53 signaling that contributes to growth inhibition and the suppression of stress induced apoptosis. This gene is located in a chromosomal region known to be amplified in breast cancer. The amplification of this gene has been detected in both breast cancer cell line and primary breast tumors, which suggests a role of this gene in cancer development [1].

The aim of a study was to clarify the expression and gene copy number levels of protein phosphatase 1D magnesium-dependent, delta isoform (PPM1D), which is thought to be a regulator of the p53 protein in meningiomas of all three different WHO grades. Genomic DNA and mRNA were extracted from frozen tissues of meningiomas (WHO grade I, 20 cases; grade II, 17 cases; grade III, 20 cases). For analysis of the mRNA expression and gene dosage level of PPM1D, semiquantitative duplex RT-PCR, real-time RT-PCR, and semiquantitative duplex PCR were performed. We also analyzed several genes which locate near PPM1D in the genomic locus 17q22-24 using semiquantitative duplex RT-PCR. We found that the mean mRNA expression of PPM1D is higher in WHO grade II and III meningiomas than in grade I tumors. This finding is accompanied by moderate gene dosage increases for PPM1D in meningiomas of higher grades. Other genes located in the vicinity of PPM1D also showed mRNA overexpression in single meningioma cases. For these genes, however, no significant expression differences between meningioma grades could be observed. Thus, PPM1D in the chromosomal location 17q22-24 might be the most relevant candidate gene with respect to a potential functional implication in meningioma progression [2].

1)
Hsu JI, Dayaram T, Tovy A, De Braekeleer E, Jeong M, Wang F, Zhang J, Heffernan TP, Gera S, Kovacs JJ, Marszalek JR, Bristow C, Yan Y, Garcia-Manero G, Kantarjian H, Vassiliou G, Futreal PA, Donehower LA, Takahashi K, Goodell MA. PPM1D Mutations Drive Clonal Hematopoiesis in Response to Cytotoxic Chemotherapy. Cell Stem Cell. 2018 Nov 1;23(5):700-713.e6. doi: 10.1016/j.stem.2018.10.004. PubMed PMID: 30388424.

2)
Fukami S, Riemenschneider MJ, Kohno M, Steiger HJ. Expression and gene doses changes of the p53-regulator PPM1D in meningiomas: a role in meningioma progression? Brain Tumor Pathol. 2016 Jul;33(3):191-9. doi: 10.1007/s10014-016-0252-x. Epub 2016 Mar 4. PubMed PMID: 26942600.