Immunhistologie

Anti-p16 INK4a

Clone JC2: CE/IVD-classified antibody for detection of p16 INK4a

The p16 INK4a protein, also known as *Cyclin Dependent Kinase Inhibitor* 2A, was discovered in the early 1990s and has since been studied extensively for its ability to affect cell cycle progression at the transition from G1 to S phase [1]. The 16 kDa protein was described as a specific inhibitor of cyclin-dependent kinase 4 (***Cyclin Dependent Kinase*** 4, CDK4) - the suffix INK4 stands for *Inhibitor of Cyclin Dependent Kinase* 4. Cyclin-dependent kinases 4 and 6 (CDK4 and CDK6) regulate the cell cycle at the end of G1 phase. During G1 phase, cyclin D levels in the cell increase, cyclin D binds to CDK4 and CDK6 and the resulting cyclin/CDK protein complexes phosphorylate the retinoblastoma protein (Rb). Phosphorylation inactivates the Rb protein and bound and thus inactive transcription factors of the E2F family are released and mediate the expression of a variety of proteins essential for cell cycle progression and DNA synthesis, such as cyclin E, cyclin A, and thymidine kinase [1,2]. p16 INK4a binds to CDK4 and/or CDK6 and inhibits the catalytic activity of the cyclin/CDK complexes. Rb remains inactive, binds and inhibits E2F, preventing the transition of cells into the S phase of the cell cycle and progression of cell proliferation. Numerous other functions have been described for p16 INK4a over time. For example, it mediates MDM2-dependent degradation of p53, suppresses the kinase activity of c-Jun N-terminal kinases (JNK), is involved in the regulation of AKT/Survivin signaling, and represses transcription of numerous genes, such as *RB, TP53, VEGF (vascular endothelial growth factor), MMP-2 (matrix metalloproteinase 2)* or *NF-κB* [3]. It is therefore not surprising that p16 INK4a plays a critical role in key processes such as cell cycle, senescence and apoptosis.

p16 INK4a is encoded by the *CDKN2A* gene. *CDKN2A* is one of the most studied tumor suppressor genes. Mutations, DNA methylation, and homozygous or heterozygous gene loss can affect *CDKN2A* gene expression. Post-translational modifications modulate functionality and activity of the protein. A reduction in activity to complete inactivation of the tumor suppressor p16 INK4a involved in the regulation of G1 phase represents a frequent and early event in the pathogenesis of solid tumors [4,5]. However, while in these tumors the p16 INK4a protein is partly absent, or the expression level can be very diverse, in HPV-induced carcinomas there is an overexpression in the tumor cells [6]. The previously described complex of Rb and the transcription factor E2F, among others, also inhibits the transcription of the *CDKN2A* gene and thus the expression of p16 INK4a.

When the viral oncoprotein E7 is expressed as a result of HPV infection, it binds and inactivates the Rb protein. E2F transcription factors are released, p16 INK4a is expressed and accumulates in the cell, and yet the cell continues unhindered through the cell cycle [5,7].

p16 INK4a detection at cervical intraepithelial neoplasia CIN3 (Mouse anti-p16 INK4a clone JC2, MSK123-05, 1:50; EDTA pH 9.0; ZytoChem Plus (HRP) Polymer Kit, POLHRP-100; DAB High Contrast, DABPLUS-5000)

Produktinformation

Description	Status	Form	Dilution	Amount	Art-No.
p16 INK4a Clone: JC2 Host: Maus	CE/IVD	Ready-to-use	-	6 ml	MSG123
		Concentrate	1:50 - 1:100	0.5 ml	MSK123-05

The antibody, which is CE/IVD classified, is used for the localization of the p16 INK4a protein in tissue sections of formalin-fixed and paraffin-embedded tissue.
The antibody has been intensively tested in Zytomed Systems' own as well as in independent pathology laboratories using different manual and automated methods and protocols.

Literatur

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