Cyclin-Dependent Kinase Inhibitor 2B

**Alternative Names**
- CDKN2B
- Multiple Tumor Suppressor 2
- MTS2
- p15(INK4B)
- TP15
- CDK4B Inhibitor

**OMIM Number**
- 600431

**Gene Map Locus**
- 9p21

**Description**
CDKN2B is known to be a tumor suppressor gene, and is a potential effector of the TGF-beta induced cell cycle arrest. The gene codes for a protein, p15, which is an inhibitor of cyclin dependent kinases, and thus, acts as a negative regulator of cell proliferation. p15 interacts strongly with cyclin-dependent kinases CDK4 and CDK6, and inhibits their ability to interact with cyclins D, thereby blocking the Cyclin/CDK complex from phosphorylating the retinoblastoma protein (RB1). This induces cell cycle arrest at the G1 checkpoint, and prevents transition of the cell cycle into the S phase. Mutations in the gene cause the protein to lose their capacity to block the Cyclin D/CDK activation, resulting in uncontrolled cell proliferations, and development of malignancies. Apart from mutations, hypermethylation of the gene has also been shown to cause inactivation in some cancers. Moreover, mutations in the gene have been shown to cause retinoblastoma, T-cell acute leukemia, meningiomas, neoplasms, and other primary tumors.

**Molecular Genetics**
The CDKN2B gene, is highly homologous to CDKN2A, and like the latter, is located on chromosome 9p21. The gene encompasses 6.4 kb of DNA. The translated product, p15 is 138 amino acids long, with a molecular weight of 14.7 KDa.

**Epidemiology in the Arab World**

**Egypt**
Eissa et al. (2000) examined 168 tumor tissue, 20 schistosomal tissue, and 50 normal tissue samples for the status of the p15 genes using the polymerase chain reaction and by sequencing the DNA fragments produced during PCR. In addition, the expression of the p15 protein was examined by Western blot analysis. Deletion of the p15 gene was observed in 36 bladder tumors. The expression of p15 protein was undetectable in 38 bladder tumors by Western blot analysis.

Mekawy et al. (2002) studied the incidence of p15/INK4B gene deletions in 30 patients with T-cell acute lymphoblastic leukemia (T-ALL). Clinical examination of the patients was followed by laboratory investigation, involving complete hemogram, bone marrow aspiration and examination, flow cytometric studies for B and T cell precursor markers, and PCR using primers specific for the p15 gene. The results showed 23.3% of the patients to have deletions of the p15 gene indicating that loss of tumor suppression involves inactivation of either or both p15 and p16 genes on 9p21 in T-ALL. Follow-up of the patients showed a complete remission (CR) rate of 63.6% in patients with no deletions, in comparison to 100% CR in patients with deletions of p15 gene.

Eissa et al. (2004) evaluated p15 gene deletion in bladder carcinoma among Egyptian patients, in relation to different clinicopathological features of the tumors and presence or absence of bilharziasis. Tissue specimens were obtained from 132 patients with bladder carcinoma and 50 normal tissue samples from the same patients served as control. P15 gene deletions were
examined by polymerase chain reaction (PCR). In all normal samples, p15 gene was detected. P15 gene was deleted in 30.2% (32/106) of bladder tumors. The deletion of p16 and p15 genes was associated with poor differentiation grade and presence of bilharziasis.

References


Contributors

Pratibha Nair: 12.6.2006