Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section
Mini Review

DKK1 (dickkopf homolog 1 (Xenopus laevis))

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Identity

Hugo: DKK1
Other names: Dickkkopf-1; DKK-1; mdkk1; hDkk1; dickkopf (Xenopus laevis) homolog 1; SK
Location: 10q11.2

DNA/RNA

Description

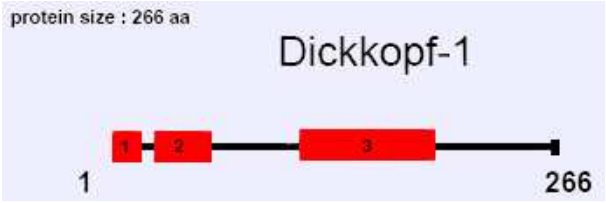
Position: 53744064 - 53747595 ; Strand: (+). DKK1 is present in the contig NT008583 of Genebank; 4 Exon(s) all coding; DNA size 3.07 kb.

Transcription

1 detected transcript; open reading frame: 1494 bp.

hDKK1 contains 3 introns and 4 exons (depictured in red).

Protein



Boxes in red:
1) Signal peptide (1 to 24 aa)
2) Low complexity region (45 to 57 aa)
3) Dickkopf domain (84 to 140 aa)

Description

This gene encodes a protein that is a member of the dickkopf family. HDKK1 encodes for a 266 amino acids (aa) protein. The calculated molecular weight is 28.7 kDa. Isoelectric point: 8.74. It possesses two clusters of ten cysteine residues separated by a linker region.

Expression

Highly expressed in thyroid, small intestine, stomach, liver, placenta, pancreas, uterus, abdominal cavity, bladder and skin. Weaker expression has been detected in colon and spleen. It is involved in embryonic development through its inhibition of the WNT signaling pathway.

Localisation

Extracellular region; secreted protein.

Function

Inhibitor of the Wnt signaling pathway.

Implicated in

Myeloma bone disease

Disease

Patients with multiple myeloma frequently show painful bone lesions and in a recent analysis an increase in Dkk1 in the serum of those patients was noted, whose levels correlated with lesion occurrence. Bone marrow serum containing an elevated level of Dkk1 inhibited the differentiation of osteoblast precursor cells in vitro. Authors propose that Dkk1 produced by myeloma cells blocks osteoblast differentiation, thereby causing the lytic bone lesions. Supporting this idea, treatment of myeloma patients by autologous stem cell transplantation induces a decrease in Dkk1 levels, which is accompanied with elevation of bone formation markers. This raises again interesting therapeutic approaches for interference with the Lrp5/Lrp6-Dkk1 interaction.

Cancer

Disease

Different studies displayed changes of Dkk expression in tumor cell lines or tissues. In colon cancer, DKK-1 is a downstream target gene of beta-catenin, as it is in human ovarian endometrioid adenocarcinomas. DKK-1 is silenced in colon cancer by DNA hypermethylation and this correlates with advanced Dukes' stages of colorectal tumorigenesis. DKK-1 overexpression in colon cancer cells or Hela cells reduces colony formation and tumor growth in xenografts, pointing out to a tumor-suppressor function for DKK-1.

Alzheimer

Disease

DKK-1 has been also related to neurodegenerative disease. DKK-1 has been shown to be induced in degenerating neurons from Alzheimer patients as well as in cultured neurons challenged with beta-amyloid peptide. Hence, DKK-1 may promote apoptosis in Alzheimer neurons by enhancing Gsk3-mediated phosphorylation of the Tau protein in beta-amyloid-treated neurons.

Epilepsia

Disease

Recently, it has been shown that induction of the wnt inhibitor, dickkopf-1, is associated with neurodegeneration related to temporal lobe epilepsy. Strong DKK-1 expression was found in six bioptic samples and in one autoptic sample from patients with mesial temporal lobe epilepsy associated with hippocampal sclerosis. Furthermore, DKK-1 expression was undetectable or very low in autoptic samples from nonepileptic patients or in bioptic samples from patients with complex partial seizures without neuronal loss and/or reactive gliosis in the hippocampus.

References

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