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Gene Section
Mini Review

CDC73 (cell division cycle 73, Paf1/RNA polymerase II complex component, homolog (S. cerevisiae))

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Identity

Hugo: CDC73
Other names: C1orf28; FLJ23316; HPT-JT; HRPT2
Location: 1q31.2
Note: Defects in CDC73 are the cause of hyperparathyroidism-jaw tumor syndrome. Mutations in CDC73 are also a cause of parathyroid carcinoma (see below).

DNA/RNA

Description

17 exons (all coding).

Transcription

CDC73 encodes a 2.7 kb mRNA with a 1596 bp ORF. The transcript has been detected in all tissues tested to date.

Protein

Description

531-amino acid protein (64 kD); termed parafibromin.

Expression

Ubiquitously expressed.

Localisation

Nuclear, bipartite nuclear localization signal.

Function

CDC73 is a tumor suppressor gene encoding a protein called parafibromin. Parafibromin is a member of the human RNA polymerase II-associated complex, Paf1. The human Paf1 complex is composed of parafibromin, LEO1, PAF1, and CTR9. Parafibromin's interaction with this complex is dependent on its C-terminal domain, which is deleted in ca. 80% of clinically relevant mutations.

Homology

Parafibromin shares 54% identity and 67% similarity with the D. melanogaster ortholog and 25% identity and 45% similarity with the C. elegans ortholog. There were no homologies to known protein domains, but moderate identity (32%) and similarity (54%) to the S. cerevisiae ortholog, Cdc73.

Mutations

Germinal

Various types of mutations often leading to inactivation of protein.

Somatic

Various somatic inactivating mutations found in sporadic parathyroid carcinoma.

Implicated in

Hyperparathyroidism-Jaw Tumor Syndrome (HPT-JT)

Disease

HPT-JT is an autosomal dominant, multiple neoplasia syndrome.

Oncogenesis

HPT-JT syndrome is primarily characterized by hyperparathyroidism due to parathyroid tumors.

Thirty percent of individuals with HPT-JT also develop ossifying fibromas, primarily of the mandible and maxilla, which are distinct from the brown tumors associated with severe hyperparathyroidism. Kidney lesions also occur in HPT-JT as bilateral cysts, renal hamartomas or Wilms tumors.

Familial isolated hyperthyroidism

Disease

Familial isolated primary hyperparathyroidism is an autosomal dominant disorder that can represent an early stage of either the multiple endocrine neoplasia type 1 (MEN1) or hyperparathyroidism-jaw tumor (HPT-JT) syndromes; or alternatively caused by a distinct entity involving another locus.

Sporadic parathyroid carcinoma

Disease

These cancers characteristically result in more profound clinical manifestations of hyperparathyroidism than do parathyroid adenomas. Parathyroid carcinomas cause hyperparathyroidism. The hyperparathyroidism is usually severe, with high serum calcium level, severe bone disease, and renal stones.

Prognosis

5-years survival rate is between 50% and 70%.

Oncogenesis

Loss of parafibromin expression strongly predicts parathyroid malignancy

Sporadic renal tumors

Cytogenetics

Loss of heterozygosity (LOH) of HRPT2 was found in clear cell, papillary, chromophobe renal cell carcinomas, oncocytomas, and Wilms tumors. In addition, two novel HRPT2 point mutations were detected in clear cell carcinoma and Wilms tumor.

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