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Gene Section
Mini Review

RUNX2 (runt-related transcription factor 2)

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Identity

Hugo: RUNX2
Other names: PEBP2-ALPHA-A; OSF2; AML3; CBFA1
Location: 6p21

DNA/RNA

Description

124,63 kb, 8 Exon at least.

Transcription

The transcription of the RUNX2 gene is regulated by two different promoters. The larger P1 transcript gives rise to a protein starting with the amino acid sequence MASNS (Runx2-type II or OSF2/CBFA1a, 521 amino acids), whereas the P2 gives rise to a protein starting with MRIPV (Runx2-type I or isoform c, 507 amino acids). Transcript variants of this protein have been reported as well due to alternative splicing.

Protein

Description

Runx2 is a transcription factor belonging to Runx family. This family is characterized by a highly conserved region of 128 amino acids, termed the Runt domain. The Runt domain is responsible for DNA binding and heterodimerization with CBFB (PEBP2b), which increases its DNA-binding affinity and also stabilizes RUNX proteins against proteolytic degradation. The C-terminal portion is rich in proline, serine and threonine (PST region) and contains functional domains acting to regulate transcription.

Expression

Runx2 expression is largely restricted to osteoblasts and mesenchymal condensations forming bones, cartilages and teeth.

Localisation

Nuclear.

Function

Runx2 is an osteoblast-specific transcription factor that plays a central role in osteoblast differentiation, chondrocyte maturation, bone formation and remodeling. Moreover, it is a key target of mechanical signals that affect bone biology.

Homology

RUNX family.

Mutations

Note: Heterozygous mutations (frameshift, nonsense, missense, splicing mutations) of the Runx2 gene have been identified in patients with Cleidocranial dysplasia (CCD).

Implicated in

Cleidocranial Dysplasia (CCD)

Disease

CCD is a dominantly inherited autosomal skeletal disorder that is characterized by open sutures and delayed closure of sutures, hypoplastic or aplastic clavicles, short stature, large fontanelles, dental anomalies and delayed skeletal development.

Prognosis

CCD does not affect life expectancy and most diagnosed persons enjoy good overall health. There is no specific treatment for CCD and the dental problems are the most significant complications.

Lymphomas

Disease

Runx2 and MYC collaborate in lymphoma development by suppressing apoptotic and growth arrest pathways in vivo.

Multiple myeloma

Disease

Human myeloma cells express the bone regulating gene Runx2 and produce osteopontin that is involved in angiogenesis in multiple myeloma patients.

Metastatic properties of cancer cells

Disease

Runx2 control multiple genes that contribute to the metastatic properties of cancer cells and their activity in the bone microenvironment.

Breast cancer

Disease

Involvement of Runx2 transcription factors in breast cancer cells.

Malignant melanoma

Disease

Coexpression of bone sialoprotein and Runx2, in malignant melanoma.

Prostate cancer

Disease

Prostate cancer expression of runt-domain transcription factor Runx2.

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