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Gene Section
Mini Review

LMO2 (LIM domain only 2 (rhombotin-like 1))

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Identity

Hugo: LMO2
Other names: RBTN2 (rhombotin-2); RHOM2; RBTNL1 (rhombotin-like-1); TTG2 (T-cell translocation gene 2); LMO2 (LIM domain only 2)
Location: 11p13
Local order: telomere LMO1 - NUP98 (11p15) - CD59 - FSHB - LMO2 - PAX6 - PDHX (11p13) centromere.

DNA/RNA

Description

LMO2 belongs to a multigene family, extremely well conserved during evolution, encoding proteins containing two cystein-rich regions referred to as LIM domains: LMO1 (11p15), LMO2 (11p13), LMO3 (12p); 6 exons.

Transcription

3 transcripts: LMO2-a and LMO2-b encode the same 158-amino-acid protein; LMO2-c encodes a 151-amino-acid protein.

Protein

Description

Small cystein rich protein with two tandemly arranged Zinc binding LIM domain motifs: named Lom2; 158 amino acids; 18 kDa; 48 % amino-acid identity with LMO1 protein.
LMO2 contains two transcription activating domains (one in N-term, in a prolin-rich 19 amino acid region, one in C-term) and two LIM domains as transcription repressing domains, selectively inhibiting the N-term activation domain (no effect on the C-term domain).

Expression

Early expressed during development, in all tissues (roughly consistent level in central nervous system, low level in thymus).
Strongly expressed in the precursors of mixed erythrocyte/macrophage/mast, erythrocyte, megakaryocyte, neutrophil and macrophage colonies, undetectable in the mature progeny.
Expressed in early B-cells, in leukemias of both the myeloid and lymphoid lineages.
Nuclear marker in normal germinal center B-cells. Also expressed in endothelial cells. High expression in the brain; expressed in the hippocampus during development.

Localisation

Nuclear.

Function

Hematopoiesis: LMO2 directly interacts with the basic-loop-helix protein TAL1/SCL and the GATA DNA protein GATA1. They form a transcriptional complex: LMO2 has no direct evidence in DNA binding capacity but could act as a bridging molecule bringing together different DNA binding factors (TAL1, LDB1, E12/E47, GATA1) that are essential for hematopoiesis (e.g. in the erythroid complex). This interaction is critical for the regulation of red blood cell development in early stages of hematopoiesis. TAL1 interacts specifically with the LIM domains of LMO2, which in turn binds LDB1. Because LMO2 can also bind to GATA2, a complex LMO2-GATA2 might occur at earlier stages of hematopoiesis when Gata1 is not

expressed. Lmo2 has a central role in adult hematopoietic pathway regulation, on bone marrow pluripotential precursor stem cell mainly. LMO2 and TAL1 are able to partially suppress myeloid differentiation. LMO2 also interacts with retinoblastoma-binding protein 2 and elf-2 (ets transcription factor).
LMO2-c expression is regulated by GATA1 and PU.1; LMO2-c acts as an antagonist of LMO2-a/b, therefore blocking the transactivation of LMO2-a/b.
In the brain, hBEX2, LMO2, NSCL2 and LDB1 could form a similar complex.

Implicated in

t(11;14)(p13;q11)/T-cell leukaemia ⟶ LMO2/ TCRD-A

Disease

Childhood T-cell ALL ; found in 5-10% of T-cell ALL.

Cytogenetics

A variant translocation t(7;11)(q35;p13) has been described.

Abnormal Protein

It was previously believed that LMO2 is activated after chromosomal translocation by association either the T-cell receptor a/T-cell receptor d (14q11) or T-cell receptor b gene (7q35). Chromosome breakpoints occur 25 kb upstream LMO2 gene, in a presumed transcriptional start site, inducing truncation of the promoter/control region and leading to inappropriate Lmo2 level especially in T-cells (abnormal T-cell differentiation). However, it becomes now very likely that removal of a negative regulatory element from the LMO2 locus, rather than juxtaposition to the TCRD enhancer, is the main determinant for LMO2 activation in the majority of t(11;14)(p13;q11) translocations.

del(11)(p12p13) T-cell leukaemia

Disease

Childhood T-cell ALL; found in about 5% of T-cell ALL.

Cytogenetics

Cryptic deletion that varies in size.

Abnormal Protein

LMO2 is activated through a cryptic intrachromosomal deletion, del(11)(p12p13), in which a negative regulatory element (NRE), situated upstream of the LMO2 gene, is deleted. Removal of this NRE causes activation of the proximal promoter of the LMO2 gene leading to its ectopic expression.

Germinal center B-cell lymphomas

Disease

Diffuse large-B-cell lymphomas, follicular lymphomas, Burkitt lymphomas, less often in other haematological malignancies.

Prognosis

LMO2 expression, together with BCL6, FN1, CCND2, SCYA3, and BCL2 expressions, is a predictor of outcome in diffuse large-B-cell lymphoma.

Prostate cancer

Note: Expression of LMO2 is higher in prostate tumours samples than in the normal epithelium. Moreover, overexpression of LMO2 is significantly associated with advanced tumour stage, as well as with the development of distant metastasis.

Oncogenesis

LMO2 may play an important role in prostate cancer progression, possibly via repression of E-cadherin expression.

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