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Gene Section
Mini Review

MRC1 (mannose receptor, C type 1)

Silvia Rasi, Alessio Bruscaggin, Gianluca Gaidano

Division of Hematology, Department of Clinical and Experimental Medicine & Center of Biotechnologies for Applied Medical Research, Amedeo Avogadro University of Eastern Piedmont, Via Solaroli 17, 28100 Novara, Italy (SR, AB, GG)

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Identity

Other names: CD206; CLEC13D; MMR

HGNC (Hugo): MRC1

Location: 10p12.33

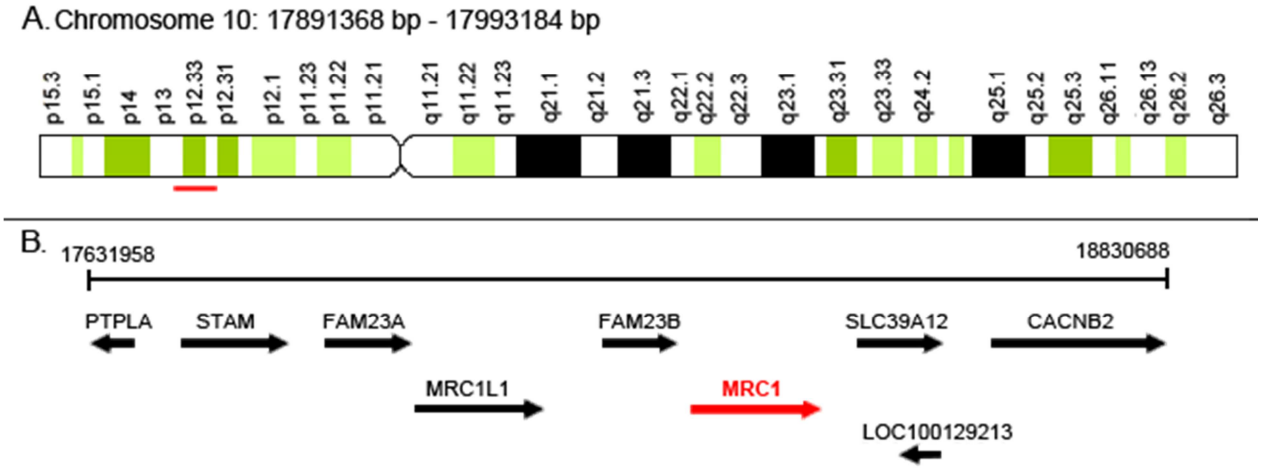
Local order: MRC1 is located on chromosome 10 on the short arm (forward strand), and lies between the FAM23B (family with sequence similarity 23, member B) and SLC39A12 (solute carrier family 39 - zinc transporter, member 12) genes.

The gene loci including MRC1, MRC1L1 (mannose receptor, C type 1-like 1), FAM23B and LOC340893 consists of two nearly identical genomic regions, that probably are a part of a duplicated region.

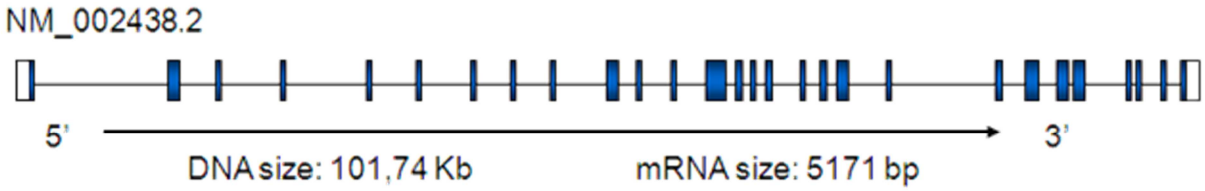
Note

MRC1 belongs to the mannose receptor (MR) family; all members of the MR family share a common extracellular domain structure but distinct ligand-binding properties and cell type expression patterns.

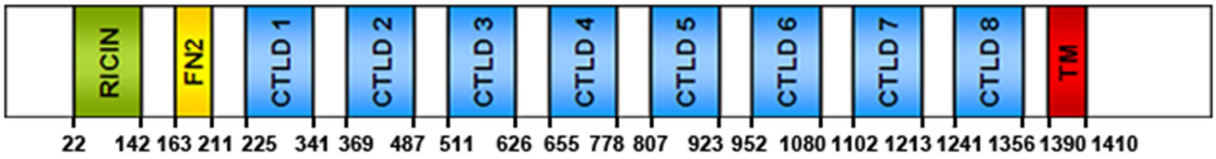
The MR family comprises 4 members in mammals: MRC1, MRC2 (mannose receptor C, type 2), LY75 (lymphocyte antigen 75) and PLA2R1 (phospholipase A2 receptor 1).



A. Chromosomal location of MRC1 gene.
B. Mapping of MRC1 gene and local order on genomic context of the chromosome 10.



Exon-intron structure of MRC1 gene. The blue boxes correspond to protein coding sequences, while the white boxes correspond to non coding regions.



Representation of the MRC1 protein with localization of recognized domains. The ricin b-type lectin domain (RICIN) is shown in green, the fibronectin type-II domain (FN2) in yellow, the C-type lectin-like domains (CTLDs) in blue, while the transmembrane domain (TM) in red (UniProtKB/Swiss-Prot entry P22897).

DNA/RNA

Description

MRC1 is a functional gene of 101.74 kb comprising 30 exons and 29 introns. The 5' part of exon 1 and the 3' part of exon 30 are non coding.

Transcription

Length of the transcript is 5171 bp.
Coding sequence: CDS 104-4474.
mRNA is mainly expressed in thyroid, spleen and blood.

Protein

Description

Protein length of the unprocessed precursor: 1456 amino acids.
Molecular weight of the unprocessed precursor: 166 kDa.
The protein encoded by the MRC1 gene is classified as a type I transmembrane receptor since the protein COOH terminus is located on the cytoplasmic side of the membrane.
MRC1 is a membrane receptor containing:
- a ricin b-type lectin domain (RICIN), that is a cystein-rich (CysR) domain located at the extreme N-terminus and that can bind specific sulphated glycoproteins,
- a fibronectin type-II domain (FN2), that is the most conserved of the extracellular domains of the MR family and can bind several forms of collagen,
- 8 C-type lectin-like domains (CTLDs), that are Ca(2+)-dependent structural motifs. The fourth of these domains, CTLD4, is the only functional domain. In cooperation with CTLD5, CTLD4 is central to ligand binding by the receptor,
- a single transmembrane domain (TM),
- a short cytosolic domain that contains motifs capable of recognizing components of the endocytic pathway.

The first 3 exons of MRC1 gene encode the signal sequence, the RICIN domain and the FN2 domain, while exon 30 encodes the TM anchor and the cytoplasmic tail. The other 26 exons encode the 8 CTLD domains and intervening spacer elements.
Probably the MRC1 receptor acts with an alternation between bent and extended conformations that might serve as a "conformational switch" to regulate ligand binding and receptor activity.
MRC1 interacts with CHEK2 (CHK2 checkpoint homolog - S. pombe) protein.

Expression

MRC1 is commonly expressed on macrophages and endothelial cells.

Localisation

Plasma membrane.

Function

- MRC1 mediates the endocytosis of glyproteins by macrophages binding both sulfated and non-sulfated polysaccharide chains.
- MRC1 acts as a phagocytic receptor binding a range of pathogens, such as bacteria, viruses and fungi, through high-mannose structures that are in their surface.
- MRC1 is required for rapid clearance of a subset of mannose-bearing serum glycoproteins that are normally elevated during inflammation.
- MRC1 binds and internalises collagen and gelatin in a carbohydrate-independent mechanism.
- MRC1 can function as an antigen-acquisition system in a subset of dendritic cells.
- MRC1 is implicated in the regulation of macrophage migration during different stages of pathogenesis.
- MRC1 has an important role in binding and transmission of HIV-1 by macrophages.

Homology

Ortholog to murine Mrc1, rat Mrc1, cow LOC787578, chimpanzee MLR1L1, canine LOC487114.
Paralog to MRC1L1, CD302, PLA2R1, MRC2.

Mutations

Note
No mutations have been reported for MRC1 gene.

Implicated in

Pediatric acute lymphoblastic leukemia (ALL)

Disease
ALL is a form of leukemia characterized by excess of lymphoblastic cells that is most common in childhood. The rate of cure in children is of nearly 80%, while only 30/40% of adults with ALL are cured.
It is a heterogeneous disease consisting of a number of genetically distinct leukemia subtypes that differ in the response to chemotherapy. These include B-lineage leukemias that contain t(9;22)[BCR-ABL], t(1;19)[E2A-PBX1], t(12;21)[TEL-AML1], rearrangements in the MLL gene on chromosome 11q23, or a hyperdiploid karyotype, and T-lineage leukemias (T-ALL).

Prognosis
ALL is a heterogeneous disease and patients are assigned to specific risk groups. In fact, ALL prognosis differs among individuals and depends on several factors: sex, age and white blood cell count at diagnosis, leukemia spread to the central nervous system, morphological, immunological, and genetic subtypes, patient's response to initial treatment.
Various genetic alterations are correlated with prognosis in ALL. In particular ALLs with the presence of t(12;21)[TEL-AML1] and hyperdiploid karyotype have favorable prognosis, while ALLs with t(9;22)[BCR-ABL], t(1;19)[E2A-PBX1] or rearrangements in MLL (11q23) have a poor prognosis.

Oncogenesis
In cases having ALL with MLL rearrangements, expression of MRC1 is lower than in normal cells, suggesting a putative involvement of MRC1 in MLL-mediated growth of leukemic cells.

Acute monocytic leukemia (M5-AML)

Note
In acute monocytic leukemia, a trimannose conjugate (TMC), with a high affinity for mannose-specific lectins, binds to MRC1 and this concatenation may play an important role in the activation of monocytic leukemia cells. TMC may be a good candidate to target MRC1 in leukemia cells.

Disease
Acute monocytic leukemia is a type of acute myeloid leukemias (AML), characterized by a dominance of monocytes in the bone marrow.

Cancer

Note
MRC1 on lymphatic endothelial cells is involved in leukocyte trafficking and contributes to the metastatic behavior of cancer cells. Moreover, expression of the MRC1 gene is up-regulated in vascular endothelial cells during early development indicating that this gene is a potential regulator of vasculature formation.
Blocking of MRC1 may provide a new approach to controlling inflammation and cancer metastasis by targeting the lymphatic vasculature.

Kaposi's sarcoma (KS)

Note
KS cells express MRC1, since MRC1 is detected in more than 95% of KS cells in all of the major clinical forms of the disease. It is likely that KS lesions derive from tissue accumulation and local proliferation of a subset of macrophages with endotelial features.

Disease
KS is a multicentric proliferative disease, involving cutaneous and visceral tissues. The etiology is unknown and the pathogenesis is unclear. KS lesions derive from local proliferation of spindleshaped cells (KS cells), that represent the histological hallmark of this disease.

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