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Gene Section
Mini Review

ECM1 (Extracellular matrix protein 1)

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Identity

Other names: p85 protein

HGNC (Hugo): ECM1

Location: 1q21.2

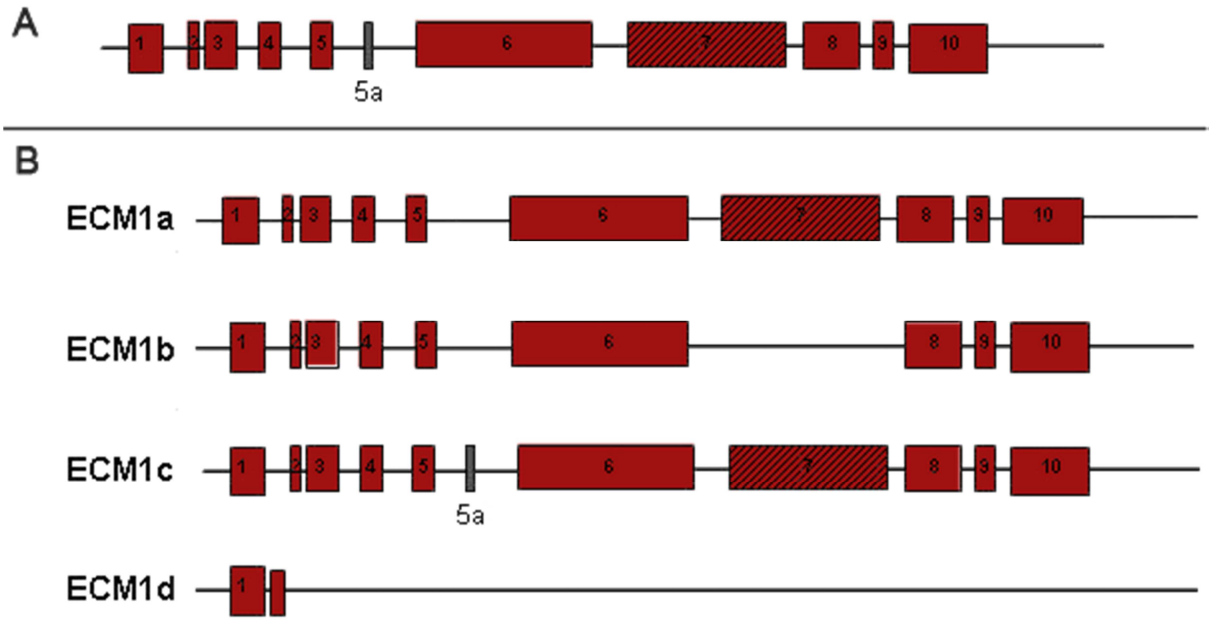
DNA/RNA

Description

The gene was initially described as having 10 exons. Afterwards an alternative spliced exon 5a was detected.

Transcription

Four transcripts are described of which three transcripts have been identified by Northern blot analysis and 1 by PCR.
ECM1a (lacks exon 5a, 1.8 kb);
ECM1b (exon 5a and exon 7 are missing, 1.4 kb);
ECM1c (contains exon 5a, 1.85 kb);
ECM1d (splice variant in which 71 bp of the 3' end of intron 1 are transcribed, resulting in a truncated 57 aa protein, only dedected by PCR, DQ010946).



A. ECM1 DNA. B. ECM1 transcripts.

Protein

Expression

ECM1a is widely expressed in liver, small testines, lung, ovary, prostate, testis, skeletal muscle, pancreas, kidney, placenta, heart, basal keratinocytes, dermal blood vessels, and adnexal epithelia including hair follicles and sweat glands.
ECM1b is dedectable in tonsils and the spinous and granular layers of the epidermis.
ECM1c is expressed in the basal layer of the epidermis.
Important remark: ECM1 antibodies available to detect ECM1 protein are not able to discriminate between ECM1a and ECM1c.
ECM1d: expression pattern is not known yet.

Localisation

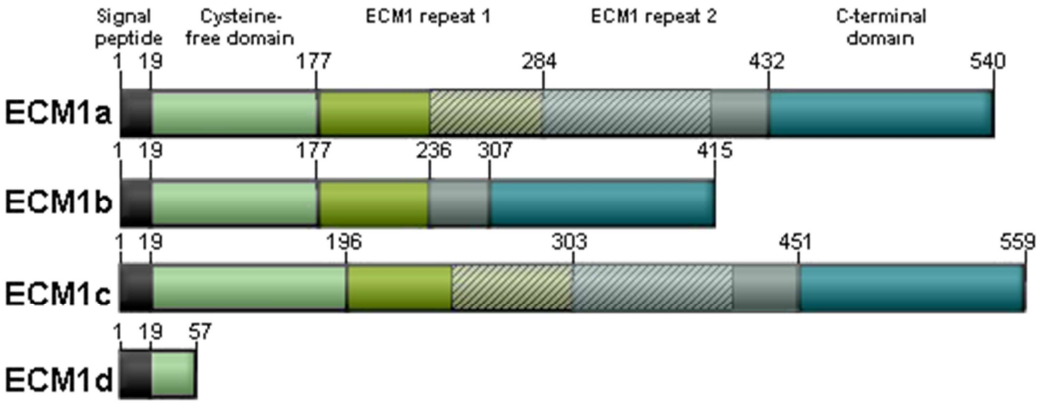
Ultrastructurally, ECM1a/c is a basement membrane protein in human skin and is part of network-like suprastructures containing perlecan, collagen type IV and laminin 332 as constituents.

Function

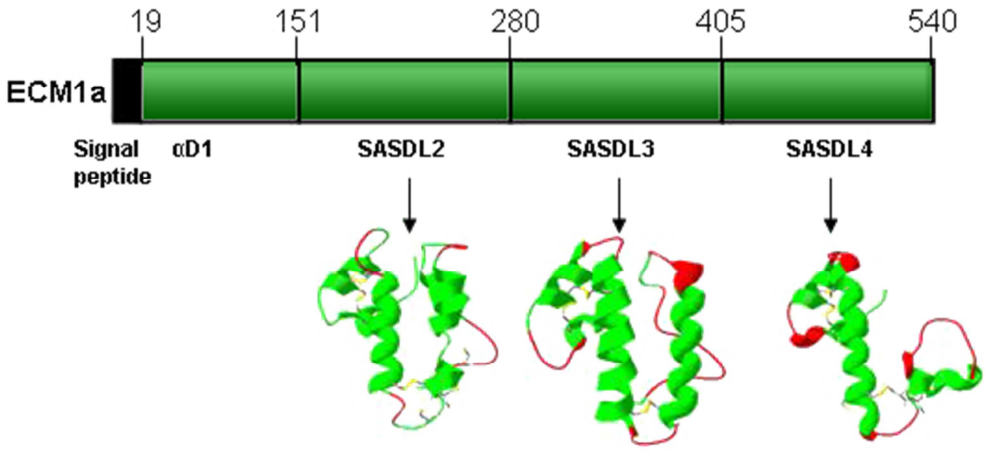
The exact biological function of ECM1 is not elucidated yet, but evidence for its involvement in important biophysiological processes, like skin differentiation, endochondral bone formation and angiogenesis have now emerged. In the broader context of skin biology, ECM1 appears to have many functions and particular a 'biological super-glue' action has been hypothesized.

Homology

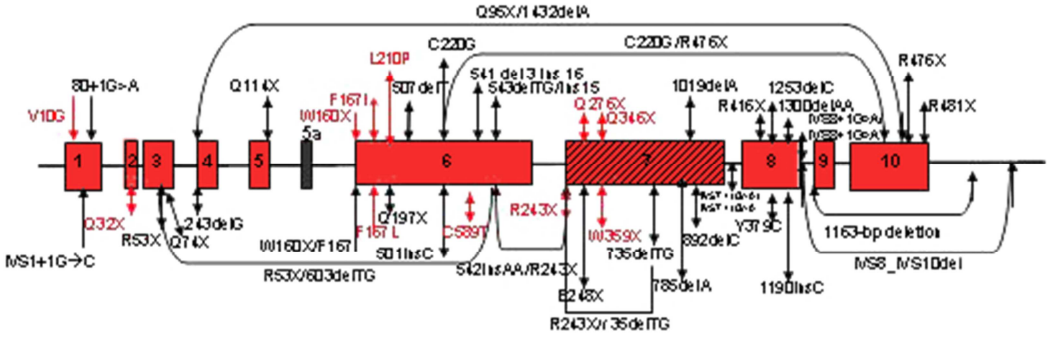
A computationally predicted three-dimensional structure of ECM1a is depicted below. Based on the third serum albumin domain ECM1a protein can be divided into four domains. The first domain containing alpha-helices (alphaD1) and three serum albumin subdomain-like domains (SASDL 2-4), each of three sequences comparable with a complete subdomain of the third serum albumin domain. AlphaD1 exits only of Alpha-helices, whereas SASDL2 and -3 are capable of binding most of the extracellular matrix proteins identified so far (collagen type IV, laminin 332, fibronectin, perlecan, fibulin 1C/D, fibulin-3 and MPP-9).



Schematic representation of ECM1 and its four splice variants: ECM1 protein is divided in a signal sequence (19 aa) (black box) and four different domains based on the presence or absence of cysteines: an N-terminal cysteine-free domain (white box), two tandem repeats (green and gray box), and a C-terminal region (blue box). ECM1c differs from ECM1a containing 19 aa encoded by exon 5a, ECM1b results from an alternative trancript caused by splicing out exon 7(shaded black). ECM1d encodes a truncated protein composed of 57 aa containing exon 1, exon 2 and a part of exon 3.



Computationally predicted three-dimensional structure of ECM1a.



Mutation in ECM1. The homozygous mutations in LiP patients are indicated with double arrows. Missense or nonsense mutations are indicated in red and frameshift mutations in black.

Mutations

Note

Mutations were described in lipoid proteinosis (LiP; OMIN#247100), also known as hyalinosis cutis et mucosae or Urbach-Wiethe disease. This is a rare, autosomal recessive disorder characterized by generalized thickening of skin, mucosae, and certain viscera. Histologically, there is widespread deposition of hyaline (glycoprotein) material and disruption/reduplication of basement membrane. Classic features include beaded eyelid papules and laryngeal infiltration leading to hoarseness. More than 40 distinct missenses, nonsenses, splice sites, small and large deletions and insertions have been reported. Approximately 50% of the mutations cluster to exon 6 and 7 of the gene.

Implicated in

Lipoid proteinosis

Disease

Lipoid proteinosis, also known as hyalinosis cutis et mucosae or Urbach-Wiethe disease.

Lipoid proteinosis is a rare autosomal recessive genodermatosis characterized by the deposition of an amorphous hyaline material in the skin, mucosa, and viscera. Papular infiltration of the margin of the lids producing 'itchy eyes', and infiltration in the tongue and its frenulum, in the larynx leading to hoarseness, and in the skin (e.g., elbows and axilla) are characteristic.

Lichen sclerosus et atrophicus

Disease

Lichen sclerosus (LS) is a chronic inflammatory skin disorder of unknown aethiology that results in white plaques with epidermal atrophy. It has both genital and extragenital presentations. HLA-subtype susceptibility and high rates of other autoimmune disorders suggest that autoantibodies to specific mucocutaneous antigens may be involved in the aetiology of lichen sclerosus. The similarities with lipoid proteinosis, which results from mutations in the ECM1 gene, suggested that this protein may be an autoantigen in lichen sclerosus. Indeed, circulating auto-antibodies to ECM1 were found in the sera of 67% of lichen sclerosus patients.

In conclusion lipoid proteinosis and lichen sclerosus are immunogenetic counterparts targeting ECM1.

Ulcerative colitis

Note

A nonsynonymous SNP (rs11205387) has been associated with ulcerative colitis. ECM1 variation was not associated with Crohn's disease.

Cancer

Note

A survey of ECM1 expression in different tumors indicated that ECM1, although not tumor specific, is significantly elevated in many malignant epithelial tumors that gave rise to metastases. Together with the observation that human recombinant ECM1 stimulates proliferation of cultured endothelial cells and promotes blood vessel formation in the chorioallantoic membrane of chicken embryos suggest that ECM1 is a possible trigger for angiogenesis, tumor progression and malignancies.

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