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Gene Section
Short Communication

ITGA9 (integrin, alpha 9)

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Abstract

Review on ITGA9, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Identity

Other names: ALPHA-RLC, ITGA4L, RLC

HGNC (Hugo): ITGA9

Location: 3p22.2

DNA/RNA

Description

Chromosome 3: 37493606-37865005; forward strand. Segons omim: 3:37493812 - 37861280.

Transcription

Exons: 28; Coding exons: 28; Transcript length: 7889 bps; Translation length: 1035 residues.

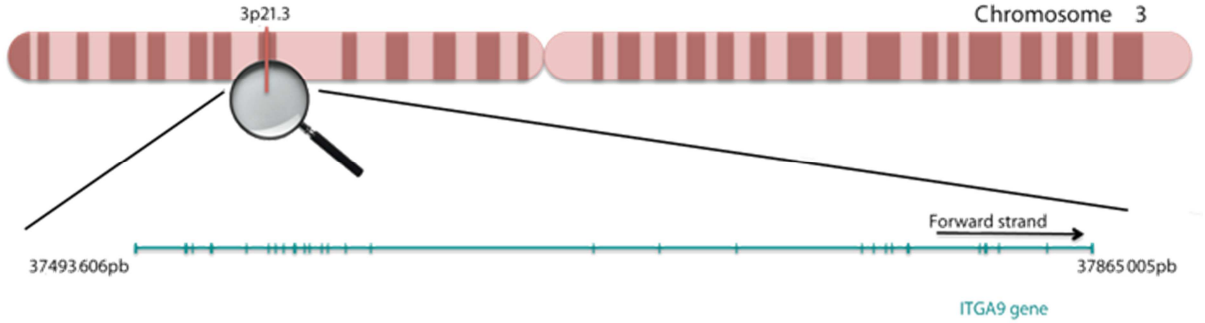
4 splice variants described (7889, 2282, 609 and 428 bp), three of which with protein translation (1035, 632 and 69 aa).

Protein

Note
Alpha9-Integrin.

Description

Alpha-integrins, such as Alpha9-Integrin, are cell surface glycoproteins that contain a large N-terminal extracellular domain with 7 conserved repeats of putative metal-binding domains, a transmembrane segment, and a short C-terminal cytoplasmic tail. ITGA9, like ITGA4, lacks the domain I and the post-translational cleavage that usually occurs in the rest of alpha-integrins. Alpha9-Integrin forms a functional heterodimer with beta1-integrin.



Expression

ITGA9 expression is widely distributed in normal human epithelia and muscle.
For instance, it has been found in airway epithelium, basal layer of squamous epithelium, smooth muscle and skeletal muscle.
Furthermore, its expression has been found in hepatocytes, breast tissue, neutrophils and polymorphonuclear leukocytes.

Localisation

Cell membrane.

Function

Adhesion with extracellular-matrix proteins, cell-cell interactions and signal transduction.
ITGA9 has been shown to bind a plethora of ligands: tenascin, VCAM-1, osteopontin, uPAR, plasmin, angiostatin, several ADAMs (ADAM1, ADAM2, ADAM3, ADAM7, ADAM8, ADAM9, ADAM12, ADAM15, ADAM28 and ADAM33), EMILIN1, fibronectin, VEGF-A, VEGF-C and VEGF-D.
Alpha9 knockout mice died from respiratory failure before day 12 after birth and showed chylothorax, defective lymphatic and venous valve morphogenesis, impaired development of neutrophils, improper re-epithelialisation during cutaneous wound-healing, impaired bone resorption and abnormal osteoclasts.
In cancer, the heterodimer alpha9-beta1 has recently been shown to have an oncogenic role by inducing epithelial-mesenchymal transition and cell migration and metastatic ability in several cancers such as glioma, breast, colon and rhabdomyosarcoma.
However, other authors have reported a tumour suppressor function for ITGA9 in a wide variety of tumours based on deletion or methylation states in varying percentages of patients.
Furthermore, a very small percentage of patients (1%) with point mutations has also been reported.

Homology

Alpha- and beta-integrins are completely distinct, with no detectable homology between them. Sequence identity among alpha-integrins is around 45%.
All alpha-integrins are thought to have evolved from a common ancestor.
Among all alpha-subunits, alpha-9 shows the greatest homology with alpha-4.

Mutations

Malignant melanoma	921 C>T
Squamous cell carcinoma	1048 G>A
Non-small cell lung carcinoma	1129 G>T
Oligodendroglioma	1862 G>T
Squamous cell carcinoma	1967 C>T
Breast ductal carcinoma	2248 C>T
Squamous cell carcinoma	2252 C>T
Pancreatic cancer	2924 G>A
Breast ductal carcinoma	3073 G>T

Implicated in

Small cell lung cancer (SCLC)

Note

Yamakawa et al. (1993) identified a region of homozygous deletions in chromosome 3p21.3 in lung cancer cell lines, where the ITGA9 gene is located.
Furthermore, Hibi et al. (1994) reported an upregulation of the ITGA9 gene in SCLC cell lines and primary tumours, suggesting that an altered expression of the ITGA9 may contribute to the phenotype of this cancer.
An activation of ITGA9 expression has been shown in different human tumours and cancer cells, for

example small cell lung cancer, medulloblastoma, astrocytoma and glioblastoma.
On the other hand, several genetic and epigenetic aberrations (deletions and methylations) of ITGA9 have been described in several types of cancer such as kidney, lung, breast, ovarian, cervical, prostate and colorectal.

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