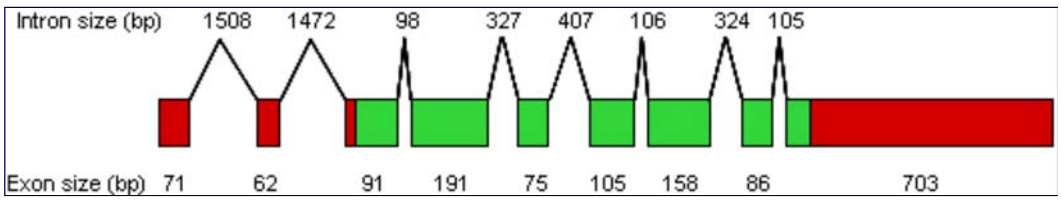
CD151 (CD151 molecule (Raph blood group))

Identity

Other names	**CD151 antigen** **GP27** **MER2** **PETA-3** **PETA3** **PETA3F** **RAPH** **SFA-1** **SFA1** **TSPAN24** **Tspan-24** **Tetraspanin-24**
HGNC (Hugo)	**CD151**
Location	11p15.5
Location_base_pair	Starts at 832952 and ends at 838834 bp from pter (according to hg19-Feb_2009) **[Mapping]**
Local_order	Telomere--PNPLA2--EFCAB4A--CD151--POLR2L--TSPAN4--Centromere.

DNA/RNA

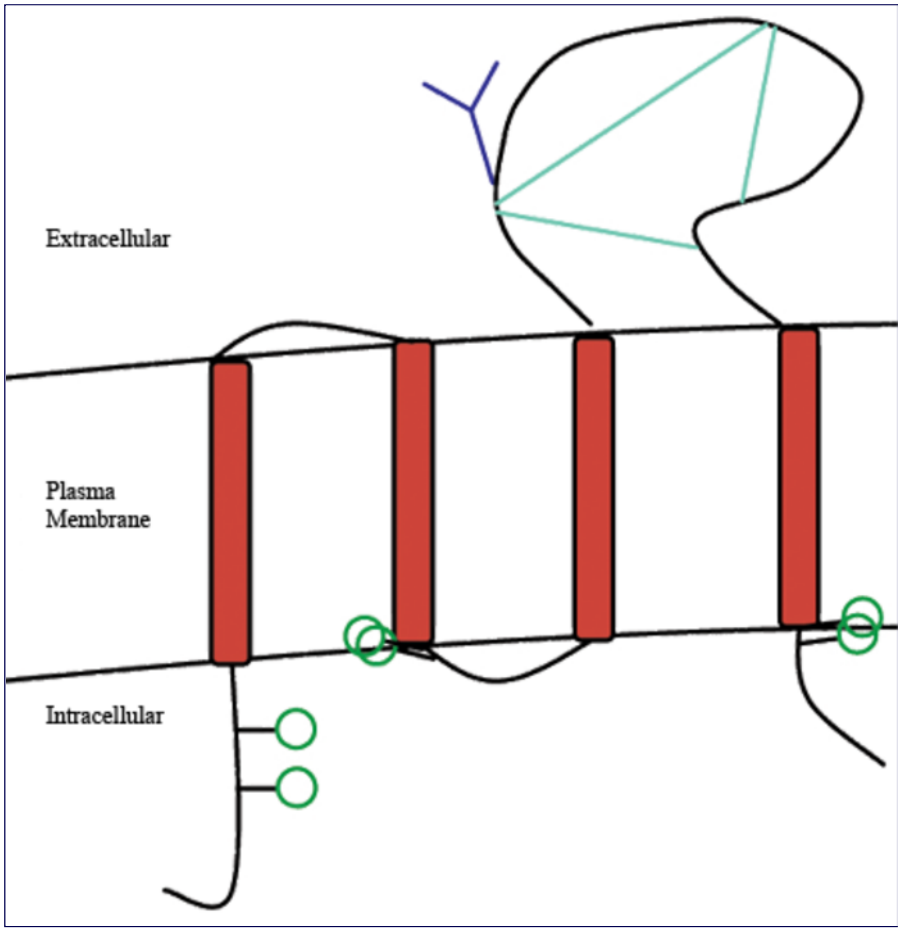
Note	Information sourced from UCSC Genome Database Mar 2006 Assembly (hg18) RefSeq genes and from analysis of mouse gene organisation (Fitter et al., 1998) and human gene structure (Whittock et al., 2001).



The red bars indicate utr and green bars indicate coding exons. The size of each intron is indicated at the top and each exon below. An alternate transcript may be generated from splicing out exon 2 in the 5'utr as indicated with the blue lines.

Description	5884 bp, 9 exons (7 coding).
Transcription	mRNA 1574bp (length may vary for utr alternate splicing).
Pseudogene	None in humans.

Protein



The red bars indicate transmembrane regions as predicted by TMHMM (Krogh et al., 2001), with the green circles palmitoylation sites (Berditchevski et al., 2002). The blue Y indicates an N-linked glycosylation site (Fitter et al., 1995) and the light blue lines indicate approximate sites of potential di-sulphide bridges (Seigneuret et al., 2001).

Description	Size: 253 aa, 28247 Da with a mature protein size of 32 kDa; pI: pH 7.44. Post-translational modifications include disulphide bridges and an N-linked glycosylation site in the large extracellular loop and 6 palmitoylation sites.
Expression	Widely expressed, particularly on epithelial cells, endothelial cells, Schwann cells, muscle cells, megakaryocytes and platelets. Tissues typically display expression restricted to these cell types with lung, kidney, spleen, tonsil and cardiac muscle all having high levels. Low expression detected on fibroblasts, erythrocytes and leukocytes (Sincock et al., 1997). Highly expressed (mRNA) in: heart, uterus, lung, prostate, liver (adult), spleen, placenta, pancreas. Low/no expression (mRNA) in: foetal liver, brain, testes, ovaries.
Localisation	Plasma membrane, endosomes, endothelial cell junctions and hemidesmosomes in basal epithelial cells (Sincock et al., 1999; Sterk et al., 2000).
Function	CD151 is a major component of tetraspanin enriched microdomains, which are platforms for assembly of membrane signalling complexes (Hemler et al., 2005; Charrin et al., 2009). CD151 functions in signal transduction through forming direct complexes with integrins particularly alpha3beta1, alpha6beta1, alpha6beta4 and alphaIIbbeta3, thereby influencing a variety of cell functions including motility and adhesion which are outlined further below. CD151 also affects matrix metalloproteinase activity, with overexpression of CD151 in human melanoma cells resulting in increased expression of MMP9 (Hong et al., 2006). CD151 has been shown to interact with pro-matrix metalloptroteinase 7 in osteoarthritic cartilage and regulate its activity (Fujita et al., 2006). In endothelial cells

CD151 associates with the matrix metalloproteinase MT1-MMP and regulates its collagenolytic activity (Yañez-Mó et al., 2008).

Homology — Tetraspanin protein family. This protein family has 33 members in humans and is well conserved throughout vertebrates and also present in invertebrates. Key characteristics include the presence of 4 transmembrane domains with both N- and C-terminals in the cytoplasm, conserved cysteine-containing motifs and disulphide bonds in the large extra cellular loop and charged residues in the transmembrane domains.

Mutations

Note — Only 3 mutations have been identified in humans to date, two (G533A and C511T), are predicted not to significantly alter CD151 function and are not associated with disease (Karamatic Crew et al., 2004; Karamatic Crew et al., 2008).

Germinal — Homozygous 1bp insertion, G383, resulting in a frameshift at Lys127 and a truncated protein at codon 140.
Homozygous G533A substitution resulting in an Arg178His mutation.
Homozygous C511T substitution resulting in an Arg171His mutation.

Implicated in

Note — **In vitro studies**
In vitro assays on Cd151-null keratinocytes, showed lack of migration compared to wild-type keratinocytes (Geary et al., 2008). Over-expression and knock-down studies of CD151 in various cell lines generally show that CD151 promotes migration and adhesion, however these finding are influenced by cell type and extracellular matrix components and primarily appear to be modified by the expression of the integrin alpha3beta1 (Berditchevski et al., 2002; Winterwood et al., 2006; Liu et al., 2007; Yang et al., 2008). CD151 is down-regulated by HIF-1alpha in colon cancer cells and is re-expressed upon normal oxygenation. This is proposed to allow detachment from the primary tumour and re-attachment at sites of metastasis (Chien et al., 2008).

Oncogenesis — Increased CD151 expression may lead to enhanced tumour progression and metastatic capacity based on enhanced motility, migration and adhesion of CD151 expressing cells. Antibodies to CD151 blocked in vivo metastasis in model systems (Testa et al., 1999; Zijlstra et al., 2008). Xenograft breast cancer models involving silencing of CD151 showed a delay in tumour formation (Yang et al., 2008). CD151 expression is increased in metastasis compared to primary tumour site in colon cancer (Chien et al. 2008).

Entity — Prostate cancer

Note — Immunohistochemical detection of CD151 in a prostate cancer tissue specimens had greater prognostic value than Gleason grading (Ang et al., 2004).

Prognosis — High CD151 expression was indicative of poor outcome.

Oncogenesis — High CD151 expression indicated poor survival outcome, suggesting a role for CD151 in enhancing tumourigenesis or resistance to treatment. Also refer to 'In vitro studies'.

Entity — Gingival squamous cell carcinoma

Note — Real-time PCR analysis of CD151 gene expression compared to GAPDH was analysed (Hirano et al., 2009). Assessment of protein expression by immunohistochemistry correlated with gene expression however no statistical analyses were performed on protein expression.

Prognosis — High CD151 expression was indicative of poor outcome.

Oncogenesis	High CD151 expression indicated poor survival outcome, suggesting a role for CD151 in enhancing tumourigenesis or resistance to treatment. Also refer to 'In vitro studies'.

Entity	Colon cancer
Note	Real-time PCR analysis of CD151 gene expression compared to beta-actin was analysed (Hashida et al., 2003). Assessment of protein expression by immunohistochemistry correlated with gene expression however no statistical analyses were performed on protein expression.
Prognosis	High CD151 expression was indicative of poor outcome.
Oncogenesis	High CD151 expression indicated poor survival outcome, suggesting a role for CD151 in enhancing tumourigenesis or resistance to treatment. Also refer to 'In vitro studies'.

Entity	Hepatocellular carcinoma
Note	Real-time PCR analysis of CD151 gene expression compared to GAPDH was analysed. Assessment of protein expression by immunohistochemistry and immunoblotting generally correlated with gene expression. CD151 expression was increased in hepatocellular carcinomas compared to normal liver tissues (Ke et al., 2009). Immunohistochemical analysis of tissue microarrays identified a positive correlation between CD151 expression and aggressive histopathological factors such as vascular invasion and poor tumour differentiation. CD151 expression was also indicative of poor outcome (Ke et al., 2009).
Prognosis	High CD151 expression was indicative of poor outcome.
Oncogenesis	High CD151 expression indicated poor survival outcome, suggesting a role for CD151 in enhancing tumourigenesis or resistance to treatment. Also refer to 'In vitro studies'.

Entity	Non-small cell lung carcinoma
Note	Real-time PCR analysis of CD151 gene expression compared to beta-actin was analysed (Tokuhara et al., 2001). Assessment of protein expression by immunohistochemistry correlated with gene expression however no statistical analyses were performed on protein expression.
Prognosis	High CD151 expression was indicative of poor outcome.
Oncogenesis	High CD151 expression indicated poor survival outcome, suggesting a role for CD151 in enhancing tumourigenesis or resistance to treatment. Also refer to 'In vitro studies'.

Entity	Breast cancer
Note	Immunohistochemical analysis of CD151 expression in a cohort of invasive ductal carcinoma identified a significantly higher risk of death from breast cancer in CD151 positive tumours compared to CD151 negative tumours. CD151 expression was also positively associated with the involvement of regional lymph nodes. No associations between CD151 expression and other clinical factors including estrogen receptor status were found (Sadej et al.,2009). Immunohistochemical analysis of CD151 in breast tissue Microarrays identified positive correlations between CD151 expression and high tumour grade as well as negativity for the estrogen receptor. No other associations were identified between CD151 expression and clinical factors (Yang et al., 2008). Associations between CD151 expression and outcome were not able to be made due to unavailability of data.
Prognosis	High CD151 expression was indicative of poor outcome.
Oncogenesis	High CD151 expression indicated poor survival outcome, suggesting a role for CD151 in enhancing tumourigenesis or resistance to treatment. Also refer to 'In vitro studies'.

Entity	Pancreatic cancer
Note	Immunohistochemical analysis of pancreatic cancer cell lines and pancreatic tumours identified high CD151 expression associated with tumours/cell lines compared to normal tissue. Tumour stroma also expressed CD151 (Geiserich et al., 2005).
Oncogenesis	Refer to 'In vitro studies'.

Entity	Neovascularisation/Pathologic Angiogenesis
Note	Determined from in vivo studies in Cd151-null mice and in vitro studies of Cd151-null mouse lung endothelial cells (Takeda et al., 2007). Analysis of a rat myocardial ischaemia model also showed that viral delivery of CD151 can promote neovascularisation (Zheng and Liu, 2006).
Disease	Cancer, ischaemia
Oncogenesis	Lack of Cd151 expression resulted in impaired tumour angiogenesis, suggesting that Cd151 may be involved in promoting tumour angiogenesis.

Entity	Nephropathy
Note	CD151 is expressed normally in the kidney particularly in the glomerular basement membrane (Sincock et al., 1997).
Disease	Nephropathy in humans (Karamatic Crew et al., 2004). Cd151-null mice develop progressive renal failure on the FVB/N strain but not the C57BL/6 strain (Sachs et al., 2006; Baleato et al., 2008).
Prognosis	Loss of CD151 activity leads to chronic renal failure.
Cytogenetics	Homozygous frameshift mutation causing a premature stop codon (codon 140) due to the insertion of 1bp in exon 5 of CD151 (G383).
Hybrid/Mutated Gene	Resultant protein lacks the integrin binding domain and causes null expression of the CD151/MER2 antigen (Karamatic Crew et al., 2004).

Entity	Pretibial epidermolysis bullosa
Note	The Nephropathy described above is attributed to the same mutation in CD151 and occurs in conjunction with pretibial epidermolysis bullosa and deafness (Karamatic Crew et al., 2004). Wound repair in wild-type mice is associated with an up-regulation of Cd151 in the migrating epidermis at the wound edge (Cowin et al. 2006).
Disease	Pretibial epidermolysis bullosa in humans. Defective wound repair in Cd151-null mice (Cowin et al. 2006; Geary et al 2008).
Cytogenetics	Homozygous frameshift mutation causing a premature stop codon (codon 140) due to the insertion of 1bp in exon 5 of CD151 (G383).
Hybrid/Mutated Gene	Resultant protein lacks the integrin binding domain and causes null expression of the CD151/MER2 antigen.

Entity	Deafness
Note	This loss of function of CD151 is attributed to the same mutation in CD151 as that described above for nephropathy and pretibial epidermolysis bullosa, with all 3 disorders occurring in the same patients (Karamatic Crew et al., 2004).
Prognosis	Progressive deafness occurring by early adulthood.
Cytogenetics	Homozygous frameshift mutation causing a premature stop codon (codon 140) due to the insertion of 1bp in exon 5 of CD151 (G383).
Hybrid/Mutated Gene	Resultant protein lacks the integrin binding domain and causes null expression of the CD151/MER2 antigen.

Entity	Hemostasis
Note	As assessed in Cd151-null mice, loss of Cd151 caused increased bleeding time and decreased clotting ability, suggesting endothelial and/or platelet cell functional defects. Cd151-null mice did not show any overt physiological differences unless challenged (Wright et al., 2004). Further in vitro analysis of Cd151-null platelets showed impaired functions relating to aggregation, spreading and clot retraction (Lau et al., 2004).

External links

	Nomenclature
HGNC (Hugo)	CD151 1630
Entrez_Gene (NCBI)	CD151 977 CD151 molecule (Raph blood group)
	Cards
Atlas	**CD151ID967ch11p15**
GeneCards (Weizmann)	CD151
Ensembl (Hinxton)	ENSG00000177697 [Gene_View] chr11:832952-838834 [Contig_View] CD151 [Vega]
AceView (NCBI)	CD151
Genatlas (Paris)	CD151
euGene (Indiana)	977
SOURCE (Stanford)	NM_001039490 NM_004357 NM_139029 NM_139030
	Genomic and cartography
GoldenPath (UCSC)	CD151 - 11p15.5 chr11:832952-838834 + 11p15.5 [Description] (hg19-Feb_2009)
Ensembl	CD151 - 11p15.5 [CytoView]
Mapping of homologs : NCBI	CD151 [Mapview]
OMIM	179620 602243 609057
	Gene and transcription
Genbank (Entrez)	AK130369 AK223186 AK293073 AL161965 AU099249
RefSeq transcript (SRS)	NM_001039490 NM_004357 NM_139029 NM_139030
RefSeq transcript (Entrez)	NM_001039490 NM_004357 NM_139029 NM_139030
RefSeq genomic (SRS)	AC_000054 AC_000143 NC_000011 NG_007478 NT_009237 NW_001838016 NW_924962
RefSeq genomic (Entrez)	AC_000054 AC_000143 NC_000011 NG_007478 NT_009237 NW_001838016 NW_924962
Consensus coding sequences : CCDS (NCBI)	CD151
Cluster EST : Unigene	Hs.654379 [SRS] Hs.654379 [NCBI]
Alternative Splicing : Fast-db (Paris)	444
Gene Expression	CD151 [NCBI-GEO] CD151 [EBI - ARRAY_EXPRESS]

	Protein : pattern, domain, 3D structure
UniProt/SwissProt	P48509 (SRS) P48509 (Expasy) P48509 (Uniprot)
With graphics : InterPro	P48509
Splice isoforms : VarSplice FASTA	P48509(VarSplice FASTA)
Domaine pattern : Prosite (SRS)	TM4_1 (PS00421)
Domaine pattern : Prosite (Expaxy)	TM4_1 (PS00421)
Domains : Interpro (SRS)	Tetraspanin Tetraspanin_CS Tetraspanin_EC2 Tetraspanin_sub
Domains : Interpro (EBI)	Tetraspanin Tetraspanin_CS Tetraspanin_EC2 Tetraspanin_sub
Related proteins : CluSTr	P48509
Domain families : Pfam (SRS)	Tetraspannin (PF00335)
Domain families : Pfam (Sanger)	Tetraspannin (PF00335)
Domain families : Pfam (NCBI)	pfam00335
Blocks (Seattle)	P48509
PDB (SRS)	
PDB (PDBSum)	
PDB (IMB)	
PDB (RSDB)	
Human Protein Atlas	ENSG00000177697
HPRD	03763
	Protein Interaction databases
DIP (DOE-UCLA)	P48509
IntAct (EBI)	P48509
FunCoup	ENSG00000177697
REACTOME	CD151
	Polymorphism : SNP, mutations, diseases
SNP Single Nucleotide Polymorphism (NCBI)	CD151
SNP (GeneSNP Utah)	CD151
SNP : HGBase	CD151
Genetic variants : HAPMAP	CD151
Somatic Mutations in Cancer : COSMIC	CD151
CONAN: Copy Number Analysis	CD151

Mutations and Diseases : HGMD	CD151		
OMIM	179620	602243	609057
GENETests	179620	602243	609057
Disease Genetic Association	CD151		
Genomic Variants	CD151		
	General knowledge		
Homologs : HomoloGene	CD151		
Homology/Alignments : Family Browser (UCSC)	CD151		
Phylogenetic Trees/Animal Genes : TreeFam	CD151		
Chemical/Protein Interactions : CTD	977		
Ontology : AmiGO	protein binding membrane fraction cytosol plasma membrane integral to plasma membrane cell adhesion hemidesmosome assembly		
Ontology : EGO-EBI	protein binding membrane fraction cytosol plasma membrane integral to plasma membrane cell adhesion hemidesmosome assembly		
Pathways : BIOCARTA			
Pathways : KEGG			
	Other databases		
	Probes		
Probes : Imagenes	CD151 Related clones (RZPD - Berlin)		
	Litterature		
PubMed	**63 Pubmed reference(s) in Entrez**		
PubGene	CD151		

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Contributor(s)

Written 07-2009 Judith Weidenhofer, Leonie K Ashman
Medical Biochemistry, School of Biomedical Sciences and Pharmacy, University of Newcastle, NSW, Australia

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For comments and suggestions or contributions, please contact us

jlhuret@AtlasGeneticsOncology.org.