

VAV1 (vav 1 oncogene)

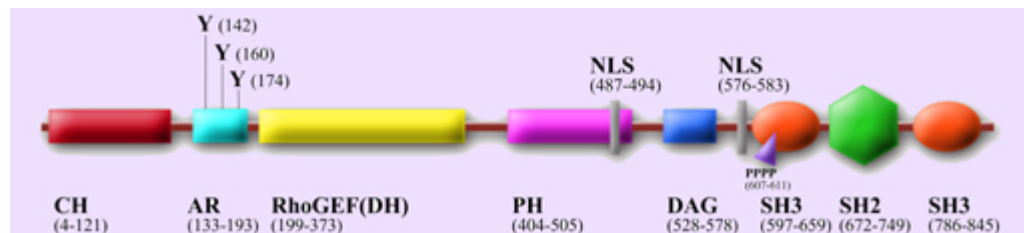
Identity

Other names **VAV**
 Hugo **VAV1**
 Location 19p13.2

DNA/RNA

Transcription 2535 mRNA complete codons

Protein



Note Vav1 was discovered when DNA from five esophageal carcinomas were tested for their transforming activity. This newly identified gene represented the sixth oncogene detected in Dr. Barbacid's laboratory and it was thus designated Vav1, after the sixth letter of the Hebrew alphabet. Vav1 was activated as an oncogene in vitro by replacement of 67 amino-acid residues of its amino-terminus (CH region) with 19 amino-acids residues of pSV2neo sequences, co-transfected as a selectable marker. Wild-type Vav1 produces minimal transformation of NIH3T3 murine fibroblasts only when the protein is grossly over-expressed. Removal of its amino terminus sequences (65 residues), thus mimicking its original mode of activation, is sufficient to induce Vav1 transformation.

Description Vav1 encodes a highly unique protein that contains numerous modular motifs known to play a role in tyrosine-mediated signal transduction cascades, such as a dbl homology (DH) region, which exhibits a guanine nucleotide exchange factor (GEF) activity towards the Rho family GTPases; a pleckstrin homology (PH) domain which interacts with polyphosphoinositides; a Src Homology 2 (SH2) and two Src Homology 3 (SH3) domains that mediate protein-protein interactions; a proline- rich motif that enables binding to SH3 -containing proteins, an acidic-rich (Ac) region and a 'calponin-homology' (CH) region, which functions as an actin-binding domain in other proteins and two nuclear localization signals(NLS). In fact, Vav1 is the only known Rho GEF that combines in the same protein the DH/PH motifs and the structural

hallmark of signal transducer proteins, the SH2 and SH3 domains.

Expression	Vav1 is specifically expressed in the hematopoietic system.
Function	The Vav1 protein (95 kDa) is rapidly tyrosine-phosphorylated following stimulation of various receptors on hematopoietic cells (TCR, BCR , IgE, etc). Vav1 can then function in various signaling cascades. First, as a tyrosine-phosphorylated protein, Vav1 operates as a guanine nucleotide exchange factor (GEF) for Rac1, Rac2 and RhoG. It is the only known GEF protein whose activity is regulated by tyrosine phosphorylation. As a regulator of activation of the Rho/Rac GTPases, Vav1 participates in several processes that require cytoskeletal reorganization, such as the formation of the immunological synapse (IS), phagocytosis, platelet aggregation and spreading. Vav1 can also function in GEF-independent pathways through its association with other proteins such as ZAP-70, SLP-76, Ly-GDI (an inhibitor of Rho/RacGTPases), Grb2 and cytoskeletal proteins such as Zyxin. Vav1 plays a critical role in stimulation of NFAT (Nuclear Factor of Activated T cells), culminating in the production of numerous vital cytokines. Vav1 also leads to the induction of an intracellular calcium flux by regulating the activation of phospholipase C γ 1 (PLC γ 1) via phosphoinositide 3-kinase (PI3K) dependent and -independent pathways. The activity of Vav1 also leads to the activation of NF-κB and the extracellular signal regulated kinase (ERK) mitogen-activated protein kinase (MAPK) signaling cascade. There is compelling evidence from studies of gene-targeted mice to indicate that Vav1 participates in the development and function of many types of immune cell such as the positive- and negative-selection events that are imposed on double-positive thymocytes
Homology	Vav1 is one of a larger family of proteins that include Vav2 and Vav3 which unlike Vav1 are also ubiquitously expressed and the Vav homologues in <i>Drosophila Melanogaster</i> and in the nematode, <i>C. elegans</i> . These proteins are similar in their structure to Vav1, thus also functioning as signal transducer proteins.

Mutations

Somatic	Although, no mutants of Vav1 have been reported thus far in "real" human tumors, it was recently found that Vav1 is expressed in the majority of 42 specimens of human neuroblastoma, suggesting a possible involvement of this protein in the neoplastic process in a subset of neuroblastomas. Furthermore, it was recently found to be involved in a large number of Pancreatic tumors.
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Implicated in

Disease	Neuroblastoma
Disease	Pancreatic tumors

External links

Nomenclature

[Hugo](#) [VAV1](#)
[GDB](#) [VAV1](#)
[Entrez_Gene](#) [VAV1_7409](#) vav 1 oncogene

Cards

[Atlas](#) [VAV1ID195ch19p13](#)

[GeneCards](#) [VAV1](#)

[Ensembl](#) [VAV1](#)

[CancerGene](#) [VAV1](#)

[Genatlas](#) [VAV1](#)

[GeneLynx](#) [VAV1](#)

[eGenome](#) [VAV1](#)

[euGene](#) [7409](#)

Genomic and cartography

[GoldenPath](#) [VAV1](#) - [19p13.2](#) [chr19:6723722-6808371](#) + [19p13.3](#) (hg17-May_2004)

[Ensembl](#) [VAV1](#) - 19p13.3 [[CytoView](#)]

[NCBI](#) [Genes Cyto](#) [Gene Seq](#) [[Map View - NCBI](#)]

[OMIM](#) [Disease map \[OMIM\]](#)

[HomoloGene](#) [VAV1](#)

Gene and transcription

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[Genbank](#) [AF030203](#) [SRS] [AF030203](#) [ENTREZ]

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[Genbank](#) [AF030205](#) [SRS] [AF030205](#) [ENTREZ]

[RefSeq](#) [NM_005428](#) [SRS] [NM_005428](#) [ENTREZ]

[RefSeq](#) [NT_086894](#) [SRS] [NT_086894](#) [ENTREZ]

[AceView](#) [VAV1](#) AceView - NCBI

[TRASER](#) [VAV1](#) Traser - Stanford

[Unigene](#) [Hs.116237](#) [SRS] [Hs.116237](#) [NCBI] [HS116237](#) [spliceNest]

Protein : pattern, domain, 3D structure

[SwissProt](#) [P15498](#) [SRS] [P15498](#) [EXPASY] [P15498](#) [INTERPRO]

[Prosit](#) [PS50021 CH](#) [SRS] [PS50021 CH](#) [Expasy]

[Prosit](#) [PS00479 DAG PE BIND DOM 1](#) [SRS] [PS00479 DAG PE BIND DOM 1](#) [Expasy]

[Prosit](#) [PS50081 DAG PE BIND DOM 2](#) [SRS] [PS50081 DAG PE BIND DOM 2](#) [Expasy]

[Prosit](#) [PS00741 DH 1](#) [SRS] [PS00741 DH 1](#) [Expasy]

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[Interpro](#) [IPR001715 Calponin-like](#) [SRS] [IPR001715 Calponin-like](#) [EBI]
[Interpro](#) [IPR003247 CH_type](#) [SRS] [IPR003247 CH_type](#) [EBI]
[Interpro](#) [IPR002219 DAG_PE-bind](#) [SRS] [IPR002219 DAG_PE-bind](#) [EBI]
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[Interpro](#) [IPR000980 SH2](#) [SRS] [IPR000980 SH2](#) [EBI]
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[Interpro](#) [IPR003096 SM22_calponin](#) [SRS] [IPR003096 SM22_calponin](#) [EBI]
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[Pfam](#) [PF00307 CH](#) [SRS] [PF00307 CH](#) [Sanger] [pfam00307](#) [NCBI-CDD]
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[Smart](#) [SM00109 C1](#) [EMBL]
[Smart](#) [SM00033 CH](#) [EMBL]
[Smart](#) [SM00233 PH](#) [EMBL]
[Smart](#) [SM00325 RhoGEF](#) [EMBL]
[Smart](#) [SM00252 SH2](#) [EMBL]
[Smart](#) [SM00326 SH3](#) [EMBL]
[Prodom](#) [PD000093 SH2](#) [INRA-Toulouse]
[Prodom](#) [P15498 VAV_HUMAN](#) [Domain structure] [P15498 VAV_HUMAN](#) [sequences sharing at least 1 domain]
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[Blocks](#) [P15498](#)
Polymorphism : SNP, mutations, diseases
[OMIM](#) [164875](#) [[map](#)]
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General knowledge

[Family](#)

[VAV1](#) [UCSC Family Browser]

[Browser](#)

[SOURCE](#)

[NM_005428](#)

[SMD](#)

[Hs.116237](#)

[SAGE](#)

[Hs.116237](#)

[Amigo](#)

[function|diacylglycerol binding](#)

[Amigo](#)

[function|guanyl-nucleotide exchange factor activity](#)

[Amigo](#)

[process|intracellular signaling cascade](#)

[Amigo](#)

[component|nucleus](#)

[Amigo](#)

[function|transcription factor activity](#)

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Other databases

Probes

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