

Grb10

Identity

Other names

RSS

IRBP

Grb-IR

MEG-1

Hugo

GRB10

Location

7p12-11.2

between two potential genes LOC221982 (in telomeric position) and LOC222987 (in centromeric position).

DNA/RNA

Description at least 16 exons spanning approximately 50 kb

Transcription Four splicing variants are known for human Grb10 gene :

hGrb10 beta alias Grb-IR (accession number U34355)

hGrb10 gamma alias Grb10/IR-SV1 or hGrb-IRbeta/hGrb10

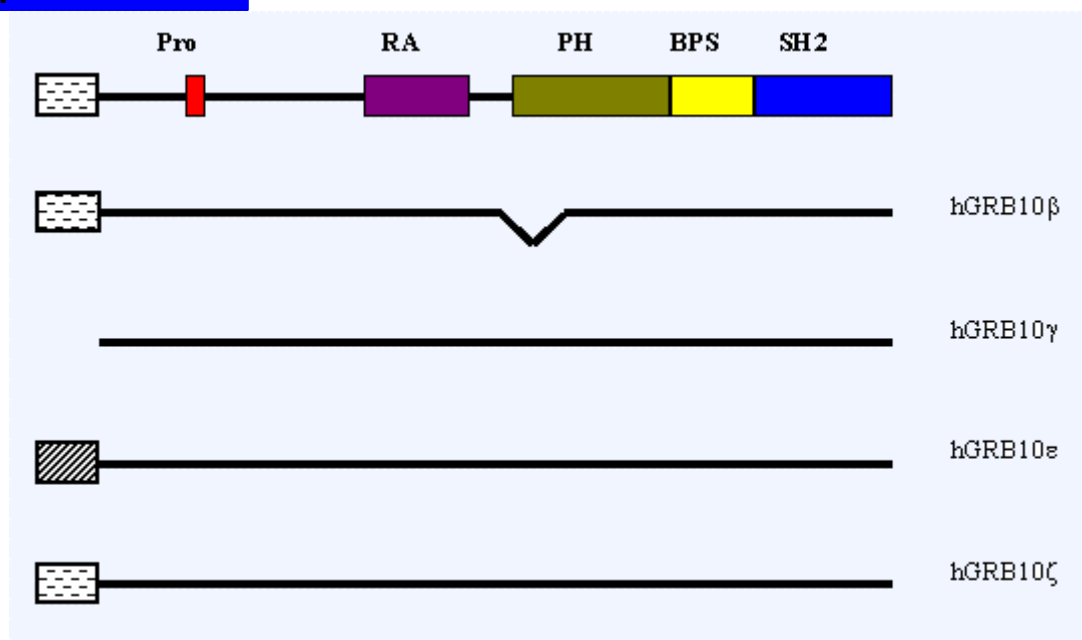
hGrb10 epsilon alias KIAA0207 (accession number D86962)

hGrb10 zeta alias hGrb10 gamma

This nomenclature is a new nomenclature for Grb10 splice variants that was agreed by several researchers

Grb10 gene has a broad expression profile with different size of transcripts depending on the isoforms. Moreover, Grb10 is imprinted in a highly isoform- and tissue-specific manner.

Protein



Description isoform beta: 548 aa, 62 kDa (aa: amino acids)

isoform gamma: 536 aa, 61 kDa

isoform epsilon: 588 aa, 66 kDa

isoform zeta: 594 aa, 67 kDa

The different splice variants share a similar structure with :

a small proline-rich sequence (11 aa) close to the amino-terminus that can interact with SH3 domain of [c-Abl](#) in vitro (domain named Pro on the figure above).

a Ras-associated-like domain (84 aa) homologous to the *C. elegans* MIG-10 protein raising the possibility that Grb10 could directly interact with Ras-like GTP-binding protein (domain named RA on the figure above).

a central Pleckstrin homology domain of 124 aa except for the isoform alpha which contains only 85 aa (domain named PH on the figure above). This domain was proposed to play an important role in targeting Grb10 to the mitochondria.

the BPS (Between PH and SH2) domain is composed of 48 aa and binds to the activated insulin and/or IGF-1 receptors.

an SH2 domain (104 aa) which interacts with phosphotyrosine of several proteins.

PH domain, BPS domain and SH2 domain compose a region of 300 aa termed GM (Grb/Mig). Grb10 is able to dimerize/oligomerize through interaction between the N-terminal domain of one molecule and the GM region of another one

Expression Grb10 protein has been detected in most human cell lines using a highly specific antibody.

Localisation Most of the endogenous Grb10 is peripherally associated with the mitochondria where it interacts with pools of Raf-1. Treatment with serum or IGF-I is able to induce the relocalization of a small proportion of the endogenous Grb10 to the plasma membrane.

Function Grb10 is able to interact with a lot of proteins (Insulin receptor, IGF-1 receptor, ELK receptor, PDGFRB, GHR, EGFR, [RET](#), HGFR, [FGFR](#), RAF-1, MEK1, [JAK2](#), [BCR-AbI](#) TEC kinase, NEDD4, cABL, AKT, [c-KIT](#)). Several studies suggest a role for Grb10 in cell proliferation. However, despite the clear involvement of Grb10 in pathways activated by IR and IGF-R, there is still some controversy about whether its effect is inhibitory or stimulatory. One report showed that stable overexpression of mGRB10 alpha inhibits IGF-1 mediated cell proliferation, whereas another report demonstrated that overexpression of the same mGrb10 alpha increased DNA synthesis upon growth factor stimulation (PDGFBB, IG-1, or insulin). These contradictions might be explained by the use of different cell lines or experimental procedures.

Grb10 seems to have also a role in apoptosis regulation. Grb10 SH2 domain is able to interact with Raf1 and MEK1. Transfection of SH2 domain Grb10 mutants induces apoptosis in HTC-IR and COS-7 cells suggesting that Grb10 may influence the equilibrium between ERK and [JNK](#) pathways and determine the choice between proliferation and programmed cell death. As Grb10 is located at the mitochondrial membrane it may be involved in communication between plasma membrane receptors and apoptosis regulators located on the mitochondrial outer membrane.

Grb10 interacts with Akt and is proposed to be a positive regulator of the Akt pathway downstream of PI3-K. By acting as an adaptator involved in

the relocalization of Akt to the cell membrane, Grb10 may contribute to Akt activation and regulation of different biological processes such as proliferation, apoptosis and growth.

Homology Grb10 is a member of the Grb7 family of adapter molecules which contains three member Grb7, Grb10 and Grb14. Grb10 counterparts are found in mouse, rat, fly and worm.

Implicated in

Disease The mapping of Grb10 gene to 7p made it a candidate gene for Russel-Silver Syndrome (RSS). But recent data suggest that Grb10 is unlikely to be the gene responsible for RSS.

External links

Nomenclature

[Hugo](#) [GRB10](#)
[GDB](#) [GRB10](#)
[Entrez Gene](#) [GRB10 2887](#) growth factor receptor-bound protein 10

Cards

[Atlas](#) [GRB10ID278](#)
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[euGene](#) [2887](#)

Genomic and cartography

[GoldenPath](#) [GRB10](#) - [chr7:50431975-50574259 - 7p12.2](#) (hg17-May_2004)
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Gene and transcription

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Protein : pattern, domain, 3D structure

[SwissProt](#) [Q13322](#) [SRS] [Q13322](#) [EXPASY] [Q13322](#) [INTERPRO]
[Prosite](#) [PS50003 PH DOMAIN](#) [SRS] [PS50003 PH DOMAIN](#) [Expasy]
[Prosite](#) [PS50200 RA](#) [SRS] [PS50200 RA](#) [Expasy]
[Prosite](#) [PS50001 SH2](#) [SRS] [PS50001 SH2](#) [Expasy]
[Interpro](#) [IPR001849 PH](#) [SRS] [IPR001849 PH](#) [EBI]

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[Smart](#) [SM00233 PH](#) [EMBL]
[Smart](#) [SM00314 RA](#) [EMBL]
[Smart](#) [SM00252 SH2](#) [EMBL]
[Prodom](#) [PD000093 SH2](#)[INRA-Toulouse]
[Prodom](#) [Q13322 GRBA HUMAN](#) [Domain structure] [Q13322 GRBA HUMAN](#) [sequences sharing at least 1 domain]
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Polymorphism : SNP, mutations, diseases

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General knowledge

[Family Browser](#) [GRB10](#)[UCSC Family Browser]
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[SOURCE](#) [NM_005311](#)
[SMD](#) [Hs.164060](#)
[SAGE](#) [Hs.164060](#)
[Amigo](#) [function|SH3/SH2 adaptor protein activity](#)
[Amigo](#) [process|cell-cell signaling](#)
[Amigo](#) [component|cytoplasm](#)
[Amigo](#) [process|insulin receptor signaling pathway](#)
[Amigo](#) [process|intracellular signaling cascade](#)
[Amigo](#) [component|plasma membrane](#)
[PubGene](#) [GRB10](#)

Other databases

Other database [The Grb7, Grb10 and Grb14 protein family](#)

Probes

[Probe](#) [GRB10 Related clones \(RZPD - Berlin\)](#)

PubMed

[PubMed](#) [22 Pubmed reference\(s\) in LocusLink](#)

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