SORBS2 (sorbin and SH3 domain containing 2)

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Identity

Other names: ARGBP2 (Arg/Abl-interacting protein 2); FLJ93447; KIAA0777; PRO0618
HGNC (Hugo): SORBS2
Location: 4q35.1

DNA/RNA

Transcription
Various transcripts.

Protein

Description
The N-term region of the protein contains a sorbin homology (SoHo) domain. Sorbin, a 153 amino acid peptide, was isolated from porcine intestine (Vagne-Descroix et al., 1991). As a matter of fact, human sorbin is spliced from an alternative transcript from the SORBS2/ArgBP2 gene locus (Hand and Eiden, 2005). The sorbin homology domain is a motif for the targeting of proteins to lipid rafts (Kimura et al., 2001); 3 proteins present the SoHo domain: SORBS2/ArgBP2, SORBS1 (also called c-Cbl-associated protein (CAP), or ponsin) (10q24), and SORBS3 (vinexin) (8p21). The C-term region of the three SORBS genes contains 3 SH3 domains. The three genes share the same structural organization and present overlapping functions.

Expression
Widely expressed; very abundant in heart.

Localisation
Cytoplasm and nucleus (like its partner ABL1).

Function
Adaptor protein.
Signaling proteins like ABL1 and ABL2 (ARG) (1q25) associate with and phosphorylate SORBS2 (Wang et al., 1997).
SORBS2 negatively regulates ABL1 and ABL2 by recruiting CBL (11q23.3) in a complex with ABL1, facilitating phosphorylation of CBL by ABL1 and promoting CBL-directed ubiquitination and degradation of ABL1 and SORBS2 in the proteasome (Soubeyran et al., 2003).
Role in AKT/PAK1 cell survival pathway: ArgBP2gamma (another SORBS2 splice) interacts with AKT and PAK1. Expression of ArgBP2gamma induces PAK1 activity and overrides apoptosis induced by ectopic expression of BAD or DNA damage (Yuan et al., 2005).
Cytoskeletal proteins: SORBS2 also binds VCL (vinculin) (10q22) a protein which plays an important role in cell adhesion and migration, and MLLT4 (also called AF6 or afadin) (6q27), another component of cell membranes at specialized sites of cell-cell contact (Kawabe et al., 1999).
SORBS2 has been found to localize at the Z-disks of cardiac myofibrils, indicating that ArgBP2 has a specialized function associated with the contractile apparatus of cardiac muscle (Wang et al., 1997).
SORBS2 binds alpha actinin, an actin crosslinking protein and a major component of the Z-disks, and PALLD (palladin) (4q32), a protein associated with the alpha actinin network.
SORBS2 co-localize with ABL1 in actin stress fibers (bundles of actin filaments which appear/disappear upon stimuli) (Wang et al., 1997).
nArgBP2, a spliced form of SORB2 with a zinc finger motif in the central part of the protein, is found in the...
post-synaptic densities and binds DLGAP1 (SAPAP, 19p13) (Kawabe et al., 1999).
SORB2 also interacts with SPTAN1 (alpha 2-spectrin) (9q34), another component of the membrane-associated cytoskeleton, DN1M (9q34) and DNM2 (19p13) (dynamins) (GTPases implicated in the regulation of actin dynamics and abundantly found in the brain), WASF2 (1p36), and SYNJ2 (synaptojanin 2) (6q25), the last two undergo ubiquitination and ABL1-dependent tyrosine phosphorylation (Cestra et al., 2005).

ABL1 plays an important role in axonogenesis; ABL1-dependent tyrosine phosphorylation (Cestra et al., 2008).

Proliferation or sensitivity to apoptosis (Taieb et al., 2005).

Migration) rather than to the regulation of cell adhesion and migration (inhibition of cell migration) instead of cell adhesion and migration (inhibition of cell migration) rather than to the regulation of cell proliferation or sensitivity to apoptosis (Taieb et al., 2008).

SORB2 binds WASF1 (also called WAVE1) (6q21) and PTPN12, a protein tyrosine phosphatase, prevents SORB2 phosphorylation by ABL1. Phosphorylation of WASF1 induced by the overexpression of ABL1 was enhanced in the presence of SORB2, and overexpression of PTPN12 abolished the ABL1-mediated phosphorylation of WASF1 (Taieb et al., 2008).

SORB2 inhibits adhesion and migration of pancreatic cells (Taieb et al., 2008).

Lipid rafts: SORB2 links via its SH3 domains with proline-rich motifs of CBL and that of PTK2B (PYK2) (8p21) in a complex that is recruited to lipid rafts (via its SoHo domain) following growth factor stimulation, partially co-localizing with actin, which appears to be critical for cytoskeletal rearrangements in growing neurites (Haglund et al., 2004).

**Homology**
SORBS1 and SORB3.

**Implicated in**

\[ t(4;11)(q35;q23) \] in acute myeloid leukemia \( \rightarrow \) SORB2 - MLL

Hybrid/Mutated gene
5’ MLL - 3’ SORB2

Pancreas cancer

Oncogenesis
SORBS2 is repressed during pancreas carcinogenesis and during progression of the disease. The antitumoral potential of SORB2 appears to be linked to the control of cell adhesion and migration (inhibition of cell migration) rather than to the regulation of cell proliferation or sensitivity to apoptosis (Taieb et al., 2008).

### References


This article should be referenced as such: