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Gene Section

Review

TACC1 (transforming, acidic coiled-coil containing protein 1)

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Identity

Other names: Ga55; DKFZp686K18126; KIAA1103

HGNC (Hugo): TACC1

Location: 8p11.23

Note: This gene has three proposed transcription start sites beginning at 38763938 bp, 38733914 bp, 38705165 bp from pter.

DNA/RNA

Description

The gene is composed of 19 exons spanning 124.5 kb.

Transcription

Encodes 11 confirmed splice variants in humans (Line et al., 2002; Lauffart et al., 2006). TACC1A 7735nt, TACC1A* 7521nt, TACC1B 6204nt, TACC1C 6194nt, TACC1D 6193nt, TACC1E 7345nt, TACC1F 7770nt, TACC1G 7904nt (utilizes internal splice site in exon 5), TACC1H 7319nt, TACC1I 7424nt, TACC1S 6528nt. Fully sequenced singleton cDNAs e.g. AK304507 and AK303596 suggest additional variants possible. AK304507 utilizes internal splice site in exon 5. Inclusion of alternate 5' noncoding exons indicated from expressed sequence tags identified in a global search for alternative promoters e.g. DA066351, DA950013 (Kimura et al., 2006).

Note:
- AK304507 and AK303596 sequences may be suspect (see UCSC Genome Bioinformatics Site (http://genome.ucsc.edu) for more details.
- Transcript/isoform nomenclature as per Line et al, 2002 and Lauffart et al., 2006. TACC1F transcript includes exon 1, 2 and 3 (correction to Fig 6 of Lauffart et al., 2006).

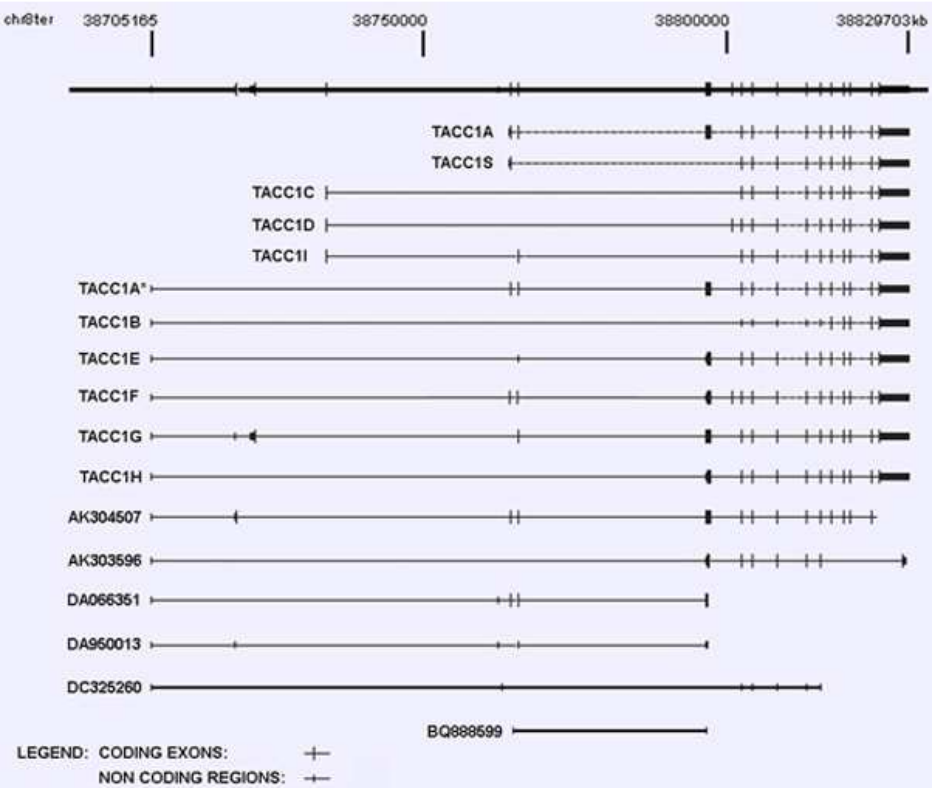
Pseudogene

Partially processed pseudogene:
- 91% identity corresponding to base 596 to 2157 of AF049910.
Location: 10p11.21.
Location base pair: starts at 37851943 and ends at 37873633 from pter (according to hg18-March_2006).
- 87% identity corresponding to base 7381 to 7742 of AF049910.
Location: 8p21.
Location base pair: starts at 84786555 and ends at 84786906 from pter (according to hg18-March_2006).

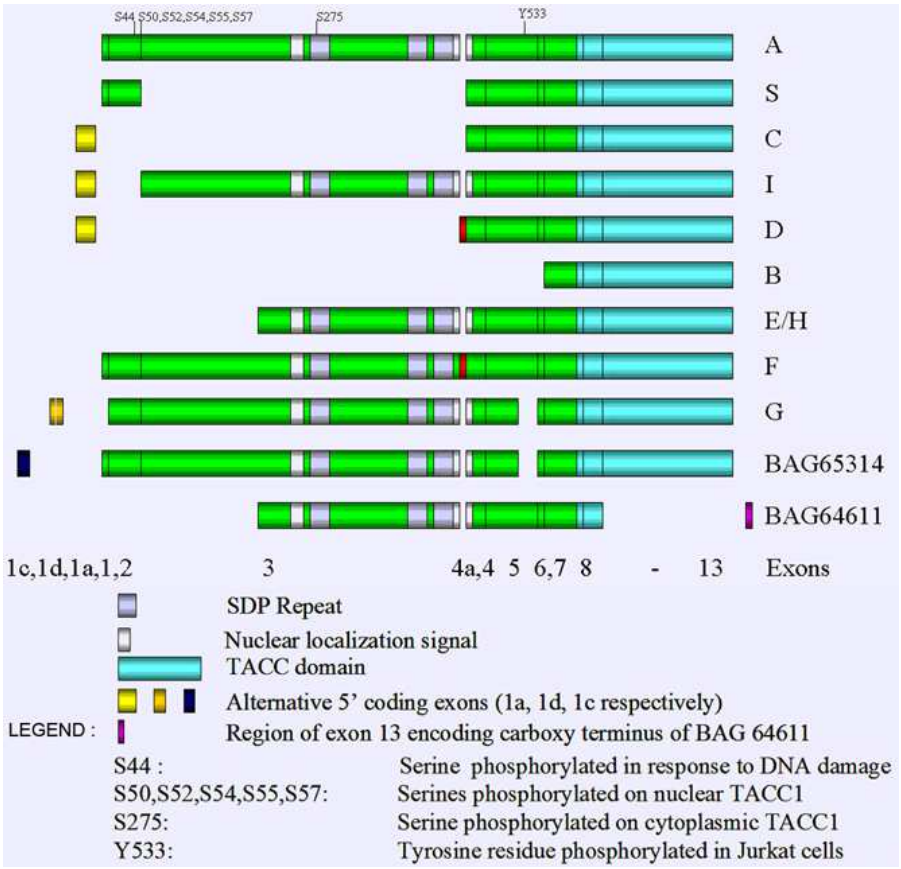
Protein

Note

11 confirmed splice variants generate 9 different protein isoforms. Two additional isoforms suggested by AK304507 and AK303596.
Inclusion of alternative promoters and 5' non coding exons produce one of these known protein isofroms



Transcripts depicted above encompass most transcripts evident in ACEVIEW and USGC genome browsers. Most other ACEVIEW "transcripts" appear to be subsets of those shown or unspliced.



Protein Isoforms

e.g. transcripts defined by DA950013, or BQ888599 would produce TACC1E/H, transcripts defined by DA066351 would produce TACC1A/A* and transcripts defined by DC325260 would produce TACC1B.

Description

TACC1A/TACC1A*, 805 amino acids, 87.8 kDa, TACC1B 243 amino acids 19.4 kDa, TACC1C 367 amino acids 40.9 kDa, TACC1D 379 amino acids 42.3 kDa, TACC1E/H 610 amino acids 67.1 kDa, TACC1F 817 amino acids 89 kDa, TACC1G 731 amino acids 79.9 kDa, TACC1I 777 amino acids 84 kDa, TACC1S 395 amino acids 44 kDa, BAG65314 792 amino acids 86.2 kDa, BAG64611 476 amino acids 51.5 kDa.

Expression

Wide expression in fetus and adult. Detailed analysis reported during mouse development by Lauffart et al., 2006.

Localisation

TACC1 is located in the nucleus and/or cytosol, depending on isoform and cell type (Lauffart et al., 2006). Exon 3 contains a predicted nuclear localisation signal. Most immunohistochemical analyses in sectioned tissues have used antibodies that recognize an epitope located in Exon 3. Thus, studies at the protein level have concentrated on exon 3 containing isoforms A, A*, E, F, G, H and I, but fail to differentiate between them. TACC1A weakly interacts with the centrosome during mitosis (Gergely et al., 2000). Overexpression can result in accumulation in cytoplasm in some cells resulting in oligmerisation in punctate structures (Gergely et al., 2000).

Function

TACC1 has been proposed to function in microtubule dynamics in interphase, mitosis and cytokinesis based upon interactions with Aurora A kinase and Aurora B kinase and CKAP5 (ch-TOG/XMAP215) by interactions with the TACC domain (see Pessat and Vernos 2008 for Review). TACC1A may function in RNA splicing, decapping and/or degradation through interactions with SmG (SNRPG) and LSm-7 (LSM7) via amino acids 1-53 (Conte et al., 2002). Increased expression of TACC1A in mammary gland activates ras-MAPK and PI-3K pathways (Cully et al., 2005). The former may be due in part on TACC1A-mediated retention of pERK in the cytoplasm (Lauffart et al., 2007b). Nuclear localized TACC1 is phosphorylated on S50,S52,S54,S55,S57, cytoplasmic TACC1 is phosphorylated on S275, while Y533 is phosphorylated in Jurkat cells (Rush et al., 2005, Olsen et al., 2006). Amino acids 152-258 binds to TDRD7, but function of this interaction is unknown (Conte et al., 2003). TACC1A is a possible indirect activator of CREB via FHL family of proteins (Lauffart et al., 2007b). Uncharacterized roles in transcriptional regulation have been proposed based on TACC1 binding to GAS41 (YEATS4) via amino acid 206-427, hGCN5L2 (KAT2A), FHL coactivator/corepressor proteins and retinoid X-receptor beta via the TACC domain (Gangisetty, 2004; Lauffart et al., 2002; 2007b; 2008; Vettaikkorumakankauv et al., 2008). TACC1A can interact with BARD1 in vitro, and is phosphorylated on serine residue 44 in response to DNA damage (Matsuoka et al., 2007).
Amino acid residues involved in binding or subject to phosphorylation are quoted for TACC1A, but residues, if present in other isoforms, may also be subject to the same interactions or modifications.

Homology

Founding member of the TACC family, based on the presence of the conserved approximately 200 amino acid carboxy terminal coiled coil domain (TACC domain) (Still et al., 1999; Still et al., 2004).

Mutations

Note

To date, no mutation of TACC1 gene have been described.

Implicated in

Breast cancer

Prognosis

Expression associated with resistance to tamoxifen and fulvestrant and shorter relapse-free survival (Ghayad et al., 2008).

Oncogenesis

TACC1 protein downregulated in breast cancer (Conte et al., 2002). Expression retained in tamoxifen and fulvestrant resistant tumors (Ghayad et al., 2008).

Ovarian Cancer

Prognosis

Retention of expression in Stage III tumors associated with favorable prognosis (Partheen et al., 2006).

Oncogenesis

Total cellular expression or nuclear localization lost in ovarian cancer (Lauffart et al., 2005).

Wilms' Tumor

Prognosis

Expression associated with more favorable prognosis (Li et al., 2005).

Oncogenesis

Expressed at lower levels in anaplastic versus tumors with favorable histology (Li et al., 2005).

Gastric Cancer

Prognosis

Increased expression of TACC1D and TACC1F variants associated with gastric cancer (Line et al., 2002).

Oncogenesis
Change in splicing pattern in gastric cancer (Line et al., 2002).

Prostate Cancer

Prognosis
Increased expression of TACC1 detected in advanced stages (pT3 and/or N1/M1) and associated with androgen-independent prostate carcinoma (Devilard et al., 2006).

Oncogenesis
TACC1 protein expression in prostate cancer noted in cytoplasm (Devilard et al., 2006), compared to nucleus in normal prostate epithelium (Lauffart et al., 2006).

Breakpoints

Note
Potential deletion as a result of translocation event associated with 8p11 myeloproliferative disorder (Etienne et al., 2007).

To be noted

Note
The gene name TACC1, for Transforming Acidic Coiled coil containing was derived based on the initial finding that this gene could transform murine fibroblasts and is found in a chromosomal region amplified in breast cancer (Still et al., 1999). Studies in transgenic mice have demonstrated that constitutive overexpression of the TACC1A variant in the mammary gland predisposes to the development of breast cancer (Cully et al., 2005). This may be mediated by the aberrant activation of the ras-MAPK and PI-3K pathways. The former may be due in part to TACC1A mediated retention of pERK in the cytoplasm (Lauffart et al., 2007b). However, other studies have suggested that TACC1 protein is lost or mislocalised in breast cancer (Conte et al., 2002) and ovarian cancer (Lauffart et al., 2005).
The molecular function of this protein is still unclear. The protein is implicated in centrosomal dynamics during mitosis through confirmed interactions with ch-TOG/XMAP215 and Aurora kinase family members (Peset and Vernos, 2008 for review). TACC1 is also implicated in cytokinesis (Delaval et al., 2004). siRNA knockdown results in multipolar spindles but fails to impede the cell cycle (Gergely et al., 2003). TACC1A is involved in intracellular signaling pathways as a substrate (Rush et al., 2005; Olsen et al., 2006), and can interfere with ras-MAPK and PI-3K pathways (Cully et al., 2005; Lauffart et al., 2007b). TACC1A is highly phosphorylated cells (S50,S52,S54,S55,S57,S275, Y533 of TACC1A) (Rush et al., 2005; Olsen et al., 2006), in part accounting for aberrant migration of protein in SDS-polyacrylamide gel electrophoresis (Lauffart et al., 2002). TACC1A is phosphorylated in response to DNA damage on S44 (Matsuoka et al., 2007). Role in DNA damage response is unknown, although TACC3 has been shown to have some protective affects against adriamycin mediated DNA damage in ovarian cancer cells (Lauffart et al., 2007a). Alternative functions have been ascribed in transcription through interaction with FHL proteins (Lauffart et al., 2007b), YEATS4 (GAS41) and the (SWI/SNF) chromatin remodeling complex (Lauffart et al., 2002), KAT2A (hGCN5L2) (Gangisetty et al., 2004), retinoid-X receptor (Vettaikkorumakankauv et al., 2008) and RNA processing through SmG and LSm-7 (Conte et al., 2002).

References

Still IH, Hamilton M, Vince P, Wolfman A, Cowell JK. Cloning of TACC1, an embryonically expressed, potentially transforming coiled coil containing gene, from the 8p11 breast cancer amplicon. Oncogene. 1999 Jul 8;18(27):4032-8

Gergely F, Karlsson C, Still I, Cowell J, Kilmartin J, Raff JW. The TACC domain identifies a family of centrosomal proteins that can interact with microtubules. Proc Natl Acad Sci U S A. 2000 Dec 19;97(26):14352-7

Conte N, Charafe-Jauffret E, Delaval B, Adélaïde J, Ginestier C, Geneix J, Isnardon D, Jacquemier J, Birnbaum D. Carcinogenesis and translational controls: TACC1 is down-regulated in human cancers and associates with mRNA regulators. Oncogene. 2002 Aug 15;21(36):5619-30

Lauffart B, Howell SJ, Tasch JE, Cowell JK, Still IH. Interaction of the transforming acidic coiled-coil 1 (TACC1) protein with ch-TOG and GAS41/NuBI1 suggests multiple TACC1-containing protein complexes in human cells. Biochem J. 2002 Apr 1;363(Pt 1):195-200

Line A, Slucka Z, Stengrevics A, Li G, Rees RC. Altered splicing pattern of TACC1 mRNA in gastric cancer. Cancer Genet Cytogenet. 2002 Nov;139(1):78-83

Conte N, Delaval B, Ginestier C, Ferrand A, Isnardon D, Larroque C, Prigent C, Séraphin B, Jacquemier J, Birnbaum D. TACC1-chTOG-Aurora A protein complex in breast cancer. Oncogene. 2003 Nov 6;22(50):8102-16

Gergely F, Draviam VM, Raff JW. The ch-TOG/XMAP215 protein is essential for spindle pole organization in human somatic cells. Genes Dev. 2003 Feb 1;17(3):336-41

Delaval B, Ferrand A, Conte N, Larroque C, Hernandez-Verdun D, Prigent C, Birnbaum D. Aurora B -TACC1 protein complex in cytokinesis. Oncogene. 2004 Jun 3;23(26):4516-22

Gangisetty O, Lauffart B, Sondarva GV, Chelsea DM, Still IH. The transforming acidic coiled coil proteins interact with nuclear histone acetyltransferases. Oncogene. 2004 Apr 1;23(14):2559-63

Still IH, Vettaikkorumakankauv AK, DiMatteo A, Liang P. Structure-function evolution of the transforming acidic coiled coil genes revealed by analysis of phylogenetically diverse organisms. BMC Evol Biol. 2004 Jun 18;4:16

Cully M, Shiu J, Piekorz RP, Muller WJ, Done SJ, Mak TW. Transforming acidic coiled coil 1 promotes transformation and mammary tumorigenesis. Cancer Res. 2005 Nov 15;65(22):10363-70

Lauffart B, Vaughan MM, Eddy R, Chervinsky D, DiCioccio RA, Black JD, Still IH. Aberrations of TACC1 and TACC3 are associated with ovarian cancer. BMC Womens Health. 2005 May 26;5:8

Li W, Kessler P, Williams BR. Transcript profiling of Wilms tumors reveals connections to kidney morphogenesis and expression patterns associated with anaplasia. Oncogene. 2005 Jan 13;24(3):457-68

Rush J, Moritz A, Lee KA, Guo A, Goss VL, Spek EJ, Zhang H, Zha XM, Polakiewicz RD, Comb MJ. Immunoaffinity profiling of tyrosine phosphorylation in cancer cells. Nat Biotechnol. 2005 Jan;23(1):94-101

Devilard E, Bladou F, Ramuz O, Karsenty G, Dalès JP, Gravis G, Nguyen C, Bertucci F, Xerri L, Birnbaum D. FGFR1 and WT1 are markers of human prostate cancer progression. BMC Cancer. 2006 Nov 30;6:272

Kimura K, Wakamatsu A, Suzuki Y, Ota T, Nishikawa T, Yamashita R, Yamamoto J, Sekine M, Tsuritani K, Wakaguri H, Ishii S, Sugiyama T, Saito K, Isono Y, Irie R, Kushida N, Yoneyama T, Otsuka R, Kanda K, Yokoi T, Kondo H, Wagatsuma M, Murakawa K, Ishida S, Ishibashi T, Takahashi-Fujii A, Tanase T, Nagai K, Kikuchi H, Nakai K, Isogai T, Sugano S. Diversification of transcriptional modulation: large-scale identification and characterization of putative alternative promoters of human genes. Genome Res. 2006 Jan;16(1):55-65

Lauffart B, Dimatteo A, Vaughan MM, Cincotta MA, Black JD, Still IH. Temporal and spatial expression of TACC1 in the mouse and human. Dev Dyn. 2006 Jun;235(6):1638-47

Olsen JV, Blagoev B, Gnad F, Macek B, Kumar C, Mortensen P, Mann M. Global, in vivo, and site-specific phosphorylation dynamics in signaling networks. Cell. 2006 Nov 3;127(3):635-48

Partheen K, Levan K, Osterberg L, Horvath G. Expression analysis of stage III serous ovarian adenocarcinoma distinguishes a sub-group of survivors. Eur J Cancer. 2006 Nov;42(16):2846-54

Etienne A, Gelsi-Boyer V, Carbuccia N, Adélaïde J, Barba G, La Starza R, Murati A, Eclache V, Birg F, Birnbaum D, Mozziconacci MJ, Mecucci C, Chaffanet M. Combined translocation with ZNF198-FGFR1 gene fusion and deletion of potential tumor suppressors in a myeloproliferative disorder. Cancer Genet Cytogenet. 2007 Mar;173(2):154-8

Lauffart B, Gangisetty O, Still IH.. Evolutionary conserved interaction of TACC2/TACC3 with BARD1 and BRCA1:potential implications for DNA damage response in breast and ovarian cancer. Cancer Therapy. 2007a Dec; 5(2): 409-416.

Lauffart B, Sondarva GV, Gangisetty O, Cincotta M, Still IH. Interaction of TACC proteins with the FHL family: implications for ERK signaling. J Cell Commun Signal. 2007 Jun;1(1):5-15

Matsuoka S, Ballif BA, Smogorzewska A, McDonald ER 3rd, Hurov KE, Luo J, Bakalarski CE, Zhao Z, Solimini N, Lerenthal Y, Shiloh Y, Gygi SP, Elledge SJ. ATM and ATR substrate analysis reveals extensive protein networks responsive to DNA damage. Science. 2007 May 25;316(5828):1160-6

Peset I, Vernos I. The TACC proteins: TACC-ling microtubule dynamics and centrosome function. Trends Cell Biol. 2008 Aug;18(8):379-88

Vettaikkorumakankauv AK, Lauffart B, Gangisetty O, Cincotta MA, Hawthorne LA, Cowell JK, Still IH.. The TACC proteins are coregulators of the Retinoid X Receptor beta. Cancer Therapy. 2008 Dec; 6 (2): 805-816.

Ghayad SE, Vendrell JA, Bieche I, Spyratos F, Dumontet C, Treilleux I, Lidereau R, Cohen PA. Identification of TACC1, NOV, and PTTG1 as new candidate genes associated with endocrine therapy resistance in breast cancer. J Mol Endocrinol. 2009 Feb;42(2):87-103

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