Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

WRAP53 (WD repeat containing, antisense to TP53)

Marianne Farnebo

Karolinska Institutet, Cancer Center Karolinska (CCK) R8 :04, 17176 Stockholm, Sweden (MF)

Published in Atlas Database: November 2010

Online updated version : http://AtlasGeneticsOncology.org/Genes/WRAP53ID50705ch17p13.html
DOI: 10.4267/2042/45986

Identity

Other names: FLJ10385; TCAB1; WDR79

HGNC (Hugo): WRAP53

Location: 17p13.1

DNA/RNA

Description

The WRAP53 gene encompasses 16 kb of DNA; 13 exons (three non-coding alternative start exons: exon 1alpha, 1beta and 1gamma. Exon 1alpha directly overlaps the first exon of TP53 in an antisense fashion by up to 227 base pairs (bp), depending on transcription start site (TSS) usage. Exon 1gamma of WRAP53 is located in the first intron of TP53 overlapping the previously identified transcript Hp53int1 in an antisense fashion.

Transcription

At least 17 splice variants. 1.9 kb mRNA; 1647 bp open reading frame.

Regulatory antisense RNA

Expression: widely expressed at low levels.
Localisation: cytoplasm and nucleus.
Function: regulates p53 mRNA levels by interacting with the 5'UTR of p53 mRNA.
Homology: conserved in mouse.
Diseases implication currently not analysed.

Pseudogene

Not known.

Protein

Description

548 amino acids; 75 kDa protein; contains from N-term to C-term, a proline-rich region (aa 8-57), a WD40 domain, 5 repeats (160-441), and a glycin-rich region (533-545).

Expression

Widely expressed, overexpressed in cancer.

Localisation

Cytoplasm and nucleus (enriched in Cajal bodies).

Function

Essential for Cajal body formation and maintenance. Targets the SMN complex, scaRNAs and telomerase enzyme (via TERC) to Cajal bodies. Inhibition of WRAP53 triggers mitochondrial-dependent apoptosis specifically in cancer cells.

Homology

Highly-conserved in mammals, the WD40 domain is conserved from human to fly.

Mutations

Note

Single nucleotide polymorphisms (SNPs) in women with breast cancer (see below).

Germinal

Not reported.

Somatic

Not reported.

Implicated in

Breast and ovarian cancer

Note

Single nucleotide polymorphisms (SNPs) in WRAP53 were found to be overrepresented in women with breast cancer, in particular estrogen receptor negative breast cancer. The same SNPs were also associated with aggressive ovarian cancer. The SNPs are located in the coding region of WRAP53 and results in the amino acid change R68G.

Spinal muscular atrophy (SMA)

Note

WRAP53 targets the SMN complex to Cajal Bodies. WRAP53 and SMN association is disrupted in SMA patients suggesting a role of WRAP53 in SMA pathogenesis.

Disease

Spinal muscular atrophy (SMA) is a common neurodegenerative disorder caused by reduced levels of SMN due to mutations or deletions of the SMN1 gene. SMA is the leading genetic cause of infant mortality worldwide, affecting approximately 1 in 6000 infants.

References

Garcia-Closas M, Kristensen V, Langerød A, Qi Y, Yeager M, Burdett L, Welch R, Lissowska J, Peplonska B, Brinton L, Gerhard DS, Gram IT, Perou CM, Børresen-Dale AL, Chanock S. Common genetic variation in TP53 and its flanking genes, WDR79 and ATP1B2, and susceptibility to breast cancer. Int J Cancer. 2007 Dec 1;121(11):2532-8

Mahmoudi S, Henriksson S, Corcoran M, Méndez-Vidal C, Wiman KG, Farnebo M. Wrap53, a natural p53 antisense transcript required for p53 induction upon DNA damage. Mol Cell. 2009 Feb 27;33(4):462-71

Schildkraut JM, Goode EL, Clyde MA, Iversen ES, Moorman PG, Berchuck A, Marks JR, Lissowska J, Brinton L, Peplonska B, Cunningham JM, Vierkant RA, Rider DN, Chenevix-Trench G, Webb PM, Beesley J, Chen X, Phelan C, Sutphen R, Sellers TA, Pearce L, Wu AH, Van Den Berg D, Conti D, Elund CK, Anderson R, Goodman MT, Lurie G, Carney ME, Thompson PJ, Gayther SA, Ramus SJ, Jacobs I, Krüger Kjaer S, Hogdall E, Blaakaer J, Hogdall C, Easton DF, Song H, Pharoah PD, Whittemore AS, McGuire V, Quaye L, Anton-Culver H, Ziogas A, Terry KL, Cramer DW, Hankinson SE, Tworoger SS, Calingaert B, Chanock S, Sherman M, Garcia-Closas M. Single nucleotide polymorphisms in the TP53 region and susceptibility to invasive epithelial ovarian cancer. Cancer Res. 2009 Mar 15;69(6):2349-57

Tycowski KT, Shu MD, Kukoyi A, Steitz JA. A conserved WD40 protein binds the Cajal body localization signal of scaRNP particles. Mol Cell. 2009 Apr 10;34(1):47-57

Venteicher AS, Abreu EB, Meng Z, McCann KE, Terns RM, Veenstra TD, Terns MP, Artandi SE. A human telomerase holoenzyme protein required for Cajal body localization and telomere synthesis. Science. 2009 Jan 30;323(5914):644-8

Mahmoudi S, Henriksson S, Weibrecht I, Smith S, Söderberg O, Strömblad S, Wiman KG, Farnebo M. WRAP53 is essential for Cajal body formation and for targeting the survival of motor neuron complex to Cajal bodies. PLoS Biol. 2010 Nov 2;8(11):e1000521

Mahmoudi S, Henriksson S, Farnebo L, Roberg K, Farnebo M.. WRAP53 promotes cancer cell survival and is a potential target for cancer therapy. Cell Death Dis. 2011;2:e114;doi:10.1038/cddis.2010.90.

This article should be referenced as such:

Farnebo M. WRAP53 (WD repeat containing, antisense to TP53). Atlas Genet Cytogenet Oncol Haematol. 2011; 15(7):596-597.