Anti-TDP-43 Antibody (Clone DB9)

Alternative Names: TAR DNA-binding protein 43, TDP-43, transactive response DNA binding protein 43 kDa

Catalogue Number: AX17-10010-100ug

Size: 100 µg

Background Information

TAR DNA-binding protein 43 (TDP-43) is an RNA binding protein (RBP) that has been shown to bind both DNA and RNA and have multiple functions in transcriptional repression, pre-mRNA splicing and translational regulation. It belongs to the hnRNP protein family and is highly expressed in the pancreas, placenta, lung, genital tract and spleen[1]. Characterisation of transcriptome-wide binding sites revealed that thousands of RNAs are bound by TDP-43 in neurons. Mutations in TDP-43 have been associated with amyotrophic lateral sclerosis, frontotemporal dementia, Parkinson's disease and Alzheimer's disease.

TDP-43 is predominantly located in the nucleus under normal physiological conditions. However, hyperphosphorylated, fragmented and ubiquitinated forms of TDP-43 have been identified as core components of cytosolic inclusions in sporadic ALS and frontotemporal lobar degeneration (FTLD) [2,3,4,5,6,7,8].

TDP-43 contains a nuclear localising signal (NLS) as well as a nuclear export signal (NES)[8], which enables the shuttling of TDP-43 between the nucleus and the cytosol. Under normal conditions, TDP-43 interacts with mRNAs on which ribosomes are located separately, forming polysomes. Various stresses can induce clustering of ribosomes into a 'stalled' state, resulting in the formation of stress granules (SG) containing TIA-1, G3BP, ataxin-2 and eIF4G1/2.

In the stalled state, transcription is inhibited in a homeostatic response. However, sustained stress and TDP-43 misfolding creates aberrant SGs and pathogenic TDP-43 aggregates [9]. Misfolding and cytosolic mislocalisation also lead directly to a loss of normal TDP-43 function, and the resultant disruption of protein and RNA homeostasis is considered another likely pathogenic mechanism in addition to the toxicity of inclusions in ALS[9].

Product Information

Antibody Type:	Monoclonal	**Host:**	Mouse
Isotype:	IgG1 kappa	**Species Reactivity:**	Human
Immunogen:	A His-tagged recombinant protein from the C-termnal of human TDP-43 (aa 208-414)		
Format:	100 µg in 100 µl PBS containing 0.02% sodium azide.		
Storage Conditions:	6 months: 4˚C. Long-term storage: -20˚C. Avoid multiple freeze and thaw cycles.		
Applications:	ELISA I IHC I WB I ICC I IF ELISA, IHC 1:200, WB 1:1000, ICC 1:200 I IF 1:200		

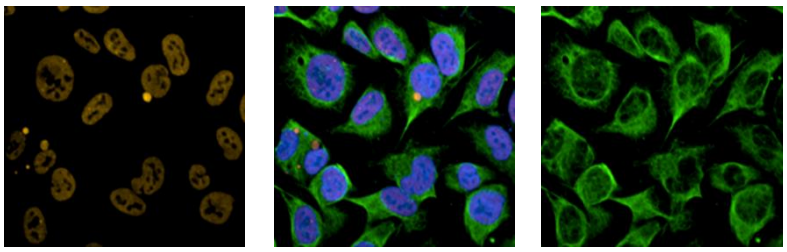
Additional Information

Subcellular location:	Nucleus	MW:	43kDa (Intended as a general guide and does not allow for all isoforms and species variations).
Gene ID	23435	Uniprot ID:	Q13148

References

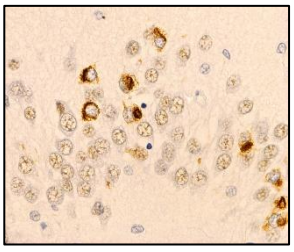
1. Strong MJ, Volkening K, Hammond R, et al. (2007). TDP43 is a human low molecular weight neurofilament (hNFL) mRNA-binding protein. Molecular and Cellular Neuroscience. 35 (2): 320–7.
2. Kwong LK, Neumann M, Sampathu DM, et al. (2007). TDP-43 proteinopathy: The neuropathology underlying major forms of sporadic and familial frontotemporal lobar degeneration and motor neuron disease. Acta Neuropathologica. 114 (1): 63–70.
3. Arai, T. et al. TDP-43 is a component of ubiquitin-positive tau-negative inclusions in frontotemporal lobar degeneration and amyotrophic lateral sclerosis. Biochem. Biophys. Res. Commun. 351, 602–611 (2006). CAS
4. Neumann M, Sampathu DM, Kwong LK, Truax AC, et al. (2006). Ubiquitinated TDP-43 in Frontotemporal Lobar Degeneration and Amyotrophic Lateral Sclerosis. Science. 314 (5796): 130–3.
5. Tan, C. F. et al. TDP-43 immunoreactivity in neuronal inclusions in familial amyotrophic lateral sclerosis with or without SOD1 gene mutation. Acta Neuropathol. 113, 535–542 (2007).
6. Igaz, L. M. et al. Enrichment of C-terminal fragments in TAR DNA-binding protein-43 cytoplasmic inclusions in brain but not in spinal cord of frontotemporal lobar degeneration and amyotrophic lateral sclerosis. Am. J. Pathol. 173, 182–194 (2008).
7. Tremblay C, St-Amour I, Schneider J, et al. (2011). Accumulation of transactive response DNA binding protein 43 in mild cognitive impairment and Alzheimer disease. J Neuropathol Exp Neurol. 70 (9): 788–98.
8. Winton, M. J. et al. Disturbance of nuclear and cytoplasmic TAR DNA-binding protein (TDP-43) induces disease-like redistribution, sequestration, and aggregate formation. J. Biol. Chem. 283, 13302–13309 (2008).
9. Yoshitaka Tamaki et al. Elimination of TDP-43 inclusions linked to amyotrophic lateral sclerosis by a misfolding-specific intrabody with dual proteolytic signals. Scientific Reports: volume 8, Article number: 6030 (2018)

Images



ALS patient line showing proteinopathy.
TDP43: Cat No: AX17-10010
Lot AX17-1808-0002
Technique: ICC
Secondary Ab: Alexa 488
Primary Ab dilution: 1:200

Images courtesy of Dr Laura Ferraiuolo and Mr Marco Destro at the University of Sheffield



The antibody was used at a dilution of 1:200.
TDP43: Cat No: AX17-10010
Technique: IHC
Detection method: Vectastain Elite ABC HRP (peroxidase) Mouse IgG kit, using DAB as substrate and counterstained with hematoxylin.

Image courtesy of Yvonne Davidson, Manchester Brain Bank