



Anti- TDP43 Antibody - Clone DB9

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

Catalogue Number: AX17-10010

Size: 100ug

Background Information

TAR DNA-binding protein 43 (TDP-43) 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. TDP-43 regulates alternate splicing of the CFTR gene. The resulting aberrant splicing is associated with pathological features typical of cystic fibrosis.

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.

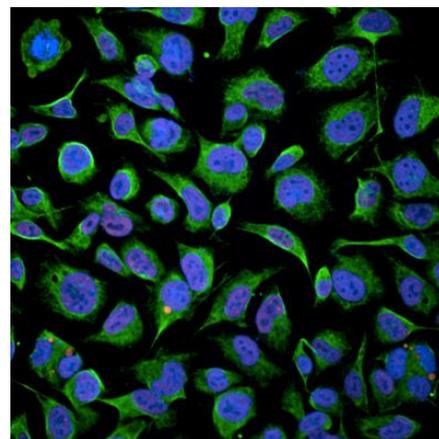
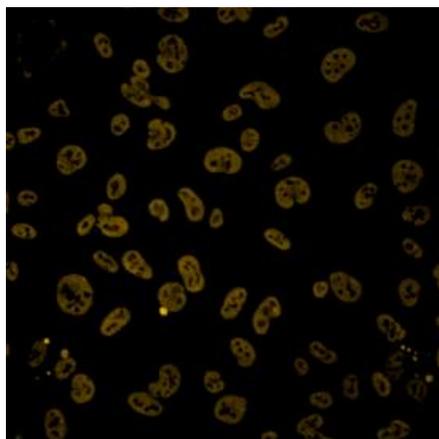
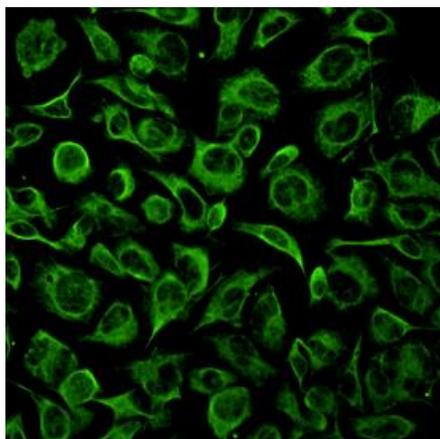
In the stalled state, transcription is inhibited as a homeostatic response. However, sustained stress and ensuing TDP-43 misfolding creates aberrant SGs and pathogenic TDP-43 aggregates [9]. Moreover, membrane-less organelles in the cytosol formed by the liquid-liquid phase separation of RNPs4 and RNA13 are implicated in TDP-43 proteinopathy. 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 mechanism14 in addition to the toxicity of inclusions [9]. Mutations in TDP-43 have been associated with amyotrophic lateral sclerosis, frontotemporal dementia, Parkinson's disease and Alzheimer's disease.

Product Information

Antibody Type:	Monoclonal	Host:	Mouse
Isotype:	IgG1 kappa		
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.		
Immunogen:	A His-tagged recombinant protein from the C-terminal of human TDP-43 (aa 208-414).		
Species Reactivity:	Human		
Applications:	ELISA	IHC 1:200	WB 1:1000 ICC 1:200

Additional Information

Subcellular location:	Nucleus	MW: 43kDa
Gene ID	23435	Uniprot ID: Q13148



ALS patient line showing proteinopathy. - Images courtesy of Dr Laura Ferraiuolo and Mr Marco Destro at the University of Sheffield

TDP43: Cat No: AX17-10010 (Lot AX17-1808-0002)

Technique: ICC Secondary Ab: Alexa 488 Primary Ab dilution: 1:200

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).
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).

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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)*