NEURODEGENERATIVE DISEASES

Ref. 30715

ALS DISEASE

TDP43-FUS CELL LINE

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder characterized by loss of both upper and lower motoneurons in the brain and the spinal cord.

ALS and other neurodegenerative disorders, such as Alzheimer's and Parkinson's disease, are characterized by defects in protein processing resulting in protein misfolding, mislocalization and inclusion formation in motor neurons. Classical neuropathological hallmarks of ALS include ubiquitinated inclusions containing the disordered TDP-43 and FUS proteins, although pathology can be heterogeneous with the appearance of other protein aggregates.

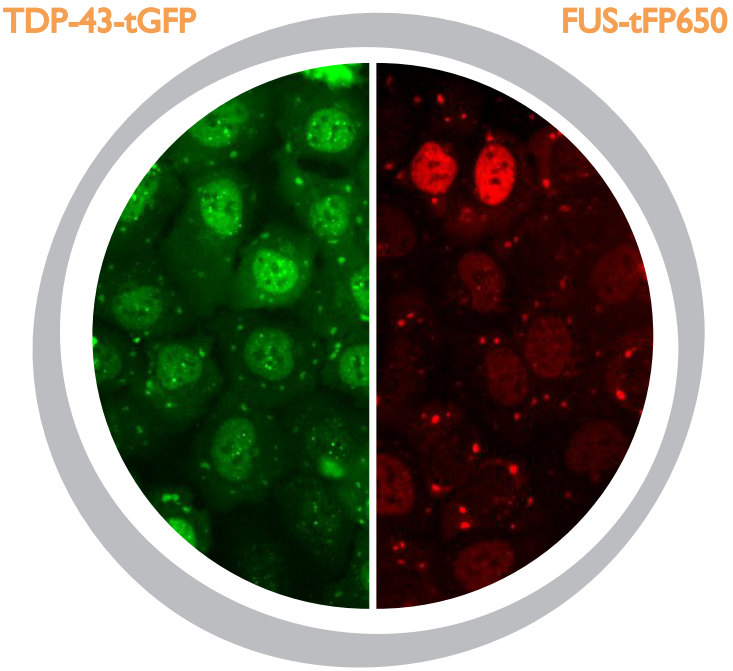
Mutations in more than forty genes have been reported to associate with ALS.

Innoprot

Background

TDP-43 is a highly-conserved, ubiquitously-expressed ribonucleoprotein with multiple roles in nucleic acid metabolism. TDP-43 mainly resides in the nucleus. However, under pathological conditions, TDP-43 mislocalizes to the cytosol. TDP-43 has been identified as one of the primary component of ubiquitinated and hyper-phosphorylated cytosolic aggregates observed in ALS patients. TDP-43 is related with both familial and sporadic forms of ALS and its aggregation is considered a hallmark of ALS as it is observed in approximately 97% of all ALS patients regardless of the mechanisms of disease onset.

Fused in sarcoma (FUS) is a multifunctional RNA-binding protein that plays a role in many RNA metabolism pathways. FUS is genetically and pathologically linked to uncommon but very aggressive forms of ALS and frontotemporal dementia (FTD). As TDP-43, FUS is mainly localized in the nucleus and under pathological conditions it is aggregated in the cytosol. To date, more than 50 different FUS mutations have been identified in patients with ALS, which together account for approximately 4% of familial cases and fewer than 2% of patients with sporadic ALS.



Product Name: TDP43-FUS cell line
Green variant reference: P30715
Prot. Official Full Name: TAR DNA-binding protein 43 (TDP-43) and RNA-binding protein FUS/TLS
Host Cell: U2OS
Resistance: G418+Puromycin
Quantity: > 3 x 10^6 cells / vial
Storage: Liquid Nitrogen

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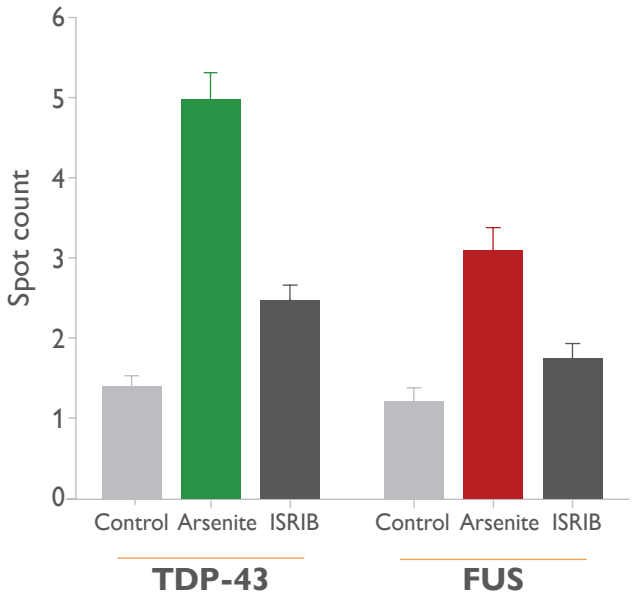
Assay Description

Innoprot´s TDP43-FUS cell line has been designed to assay compounds or analyze their capability to modulate TDP-43 and FUS tendency to form cytosolic aggregates inside the cell.

TDP-43 and FUS are mainly localized in the nucleus. The addition of sodium arsenite, produces the mislocalization of both proteins to the cytosol and the formation of pathological aggregates.

U2OS cell line stably expressing green (TurbotGFP) fluorescent tagged TDP-43 and red (TurboFP650) fluorescent tagged FUS proteins was induced with 250 μM sodium arsenite during 2 h. Previously, the cell culture had been incubated with 1 μM ISRIB overnight as an assay´s positive control.

TDP-43 and FUS aggregates formation are quantified with an image analysis algorithm.



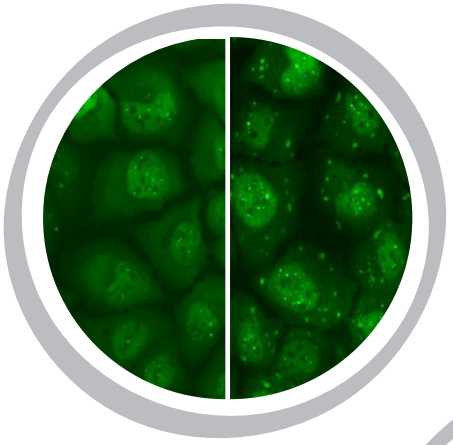
The addition of 250 μM sodium arsenite increases TDP-43 and FUS cytosolic aggregates number 3.55-fold and 2.54-fold, respectively. 1 μM ISRIB treatment reduces to 1.77 and 1.44-fold the number of aggregates of TDP-43 and FUS, respectively.

Applications

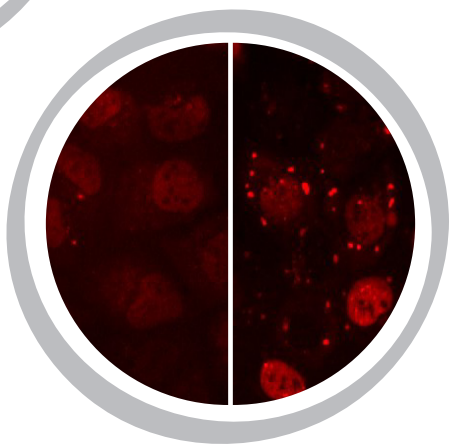
The stably transfected TDP43-FUS cell line can be used in drug discovery for the search of inhibitors of the pathological inclusions formation.

This model allows the evaluation of test compounds in living cells.

This cellular model has been adapted to HCS analyses based on image algorithms to analyze the number of TDP-43 and FUS aggregates.



TDP-43-tGFP



FUS-tFP650

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