NEURODEGENERATIVE DISEASES

Ref. 30726

ALS DISEASE

SOD1-A4V AGGREGATION ASSAY 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.

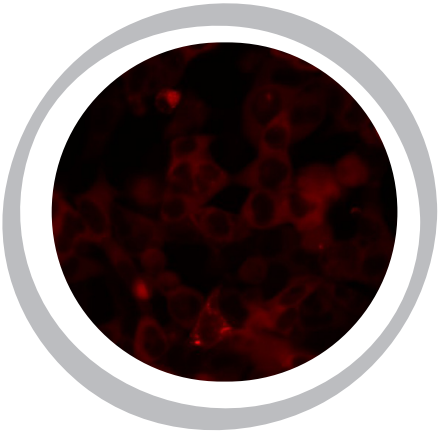
Innoprot

Background

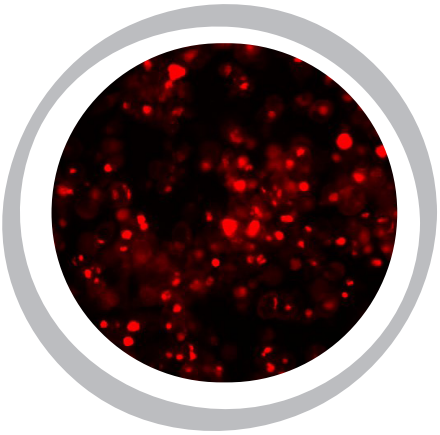
Mutations in the gene encoding superoxide dismutase 1 (SOD1) were the first discovered to cause ALS, and elicit approximately 20% of all familiar ALS cases in the world and up to 50% in China.

The alanine to valine mutation at codon 4 (A4V) of SOD1 causes a rapidly progressive dominant form of ALS with exclusively lower motor neuron disease and is one of the most common mutations worldwide responsible for 50% of SOD1 mutations associated with familial ALS in North America.

Usually, the genes associated with ALS are related with misfolded and aggregated proteins. In the case of SOD1-A4V mutant, it has an increased tendency to aggregate and form aberrant depositions. Misfolded and aggregated SOD1-A4V elicits many toxic properties and has been linked with cell death.



Basal conditions



SOD1-A4V aggregates

Product Name: SOD1-A4V-FP602 cell line
Product reference: P30726
Prot. Official Full Name: Human Superoxide Dismutase [Cu-Zn]
Host Cell: HEK 293
Resistance: Puromycin
Quantity: > 3 x 10^6 cells / vial
Storage: Liquid Nitrogen

NEURODEGENERATIVE DISEASES

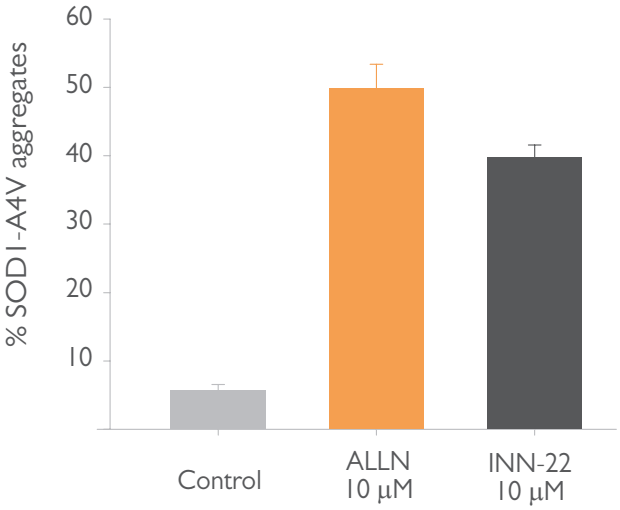
Assay Description

Innoprot´s SOD1-A4V-FP602 cell line has been designed to assay compounds or analyze their capability to modulate superoxide dismutase 1 tendency to form aggregates inside the cell.

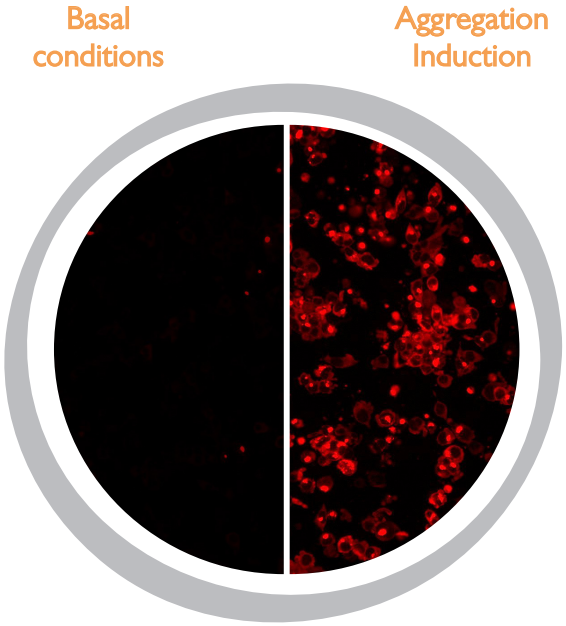
SOD1 is a soluble Cu/Zn enzyme that is mainly localized in the cytosol. The addition of proteasome inhibitor ALLN, produces the aggregation of the protein in HEK293 cells.

HEK293 cell line stably expressing red fluorescent tagged (TurboFP602) SOD1-A4V protein was induced overnight with 10 µM ALLN to form SOD1 aggregates. Previously, the cell culture was incubated overnight with INN-22, a compound that reduces the number of cells with inclusions, as an assay´s positive control.

After an overnight treatment, the cells are fixed and the SOD1-A4V aggregates are quantified with an image analysis algorithm.



The addition of ALLN 10 µM increases aggregates formation 6-fold. INN-22 reduces to 4.5-fold the percentage of SODI-A4V aggregates



Applications

The stably transfected SOD1-A4V 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 test the percentage of cells in the culture with SOD1-A4V aggregates.

INNOVATIVE TECHNOLOGIES IN BIOLOGICAL SYSTEMS, S.L.
Parque Tecnológico Bizkaia, Edifício 502, 1ª Planta | 48160 | Derio | Bizkaia
Tel.: +34 944005355 | Fax: +34 946579925
innoprot@innoprot.com | www.innoprot.com

Innoprot