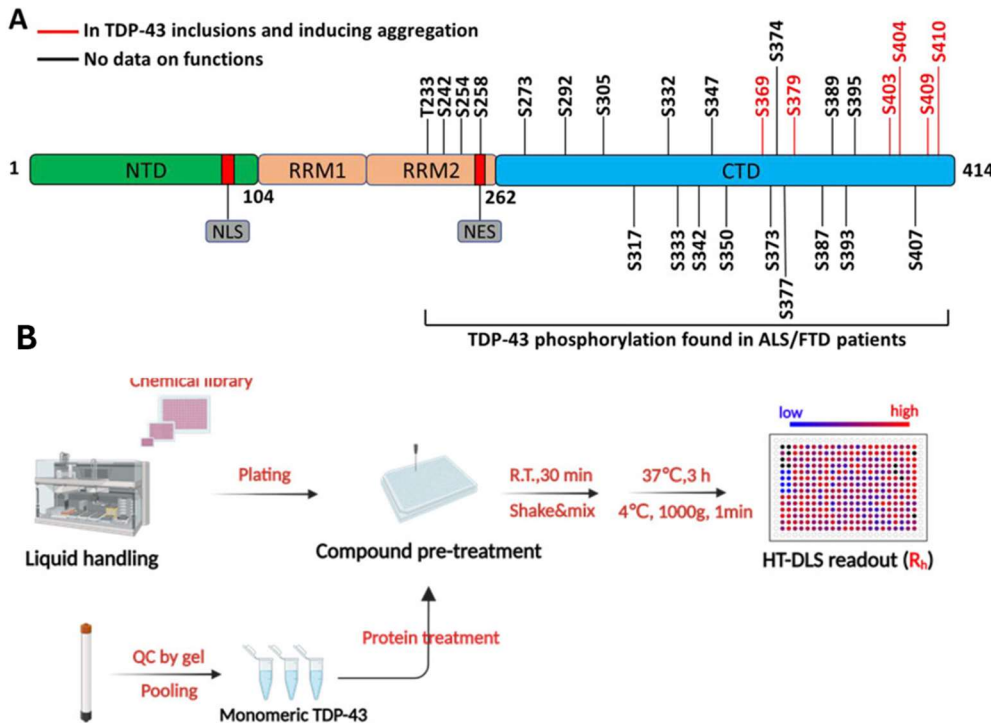


# Native state stabilisation of TDP-43 using phosphomimetic mutants



Ref. Nr

6.2368

Keywords

TPD-43, DNA-binding protein 43 kDa, Amyotrophic Lateral Sclerosis (ALS, Parkinson Diseases, neurodegenerative diseases

Intellectual Property

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A. phosphomimetic variants based on finding that TDP-43 domains and ALS/FTD-relevant phosphorylation sites are found in C-domain of TP43, B. high throughput screening design using the phosphomimetic variants that are monomeric at RT and aggregate at 37 °C.

## Description

Transactive response DNA binding protein with 43 kDa (TDP-43) misfolding and aggregates have been associated with ALS as well as other neurodegenerative diseases. Stabilising the monomeric form of the TDP-43 variant offers the unique opportunity to identify inhibitors and modulators of TPD-43 aggregation.

The technology relies on TPD-43 variants with phosphomimetic mutations of the C-terminus. The variants are monomeric for days at 4 °C or RT and be induced to

aggregate and form TDP-43 fibrils by increasing the temperature to 37 °C.

## Advantages

The phosphomimetic substitutions preserve the basic functions or cellular properties of TDP-43.

## Applications

- Therapeutic screening of aggregation inhibitors of TP-43
- ALS, Parkinson, Alzheimer's disease and other neurodegenerative diseases.