InnoSer | a smart road to better health

Model Webpage

Amyotrophic Lateral Sclerosis Mouse Models

Target the distinct pathophysiological mechanisms of ALS using one of InnoSer's well-characterized mouse models

Amyotrophic Lateral Sclerosis (ALS), also known as motoneuron disease or Lou Gehrig's disease, is a severe neurodegenerative disorder that affects the motoneurons in the brain and spinal cord. This leads to progressive and rapid muscle wasting, spasticity, and eventual paralysis. To help accelerate preclinical ALS research, InnoSer offers several relevant ALS mouse models.

In combination with sensitive, standardised behavioral tests, InnoSer offers a translationally relevant platform for testing novel ALS-targeted therapies. As the models differ by pathology origin and onset, extent of neuromuscular and motor function deficits, we recommend discussing the most appropriate model with our neurology study directors.

Why work with InnoSer for your ALS research?

- InnoSer offers preclinical research services in well-established validated mouse models of ALS.
- Transgenic SOD1G93A is relevant to study efficacy of compounds aimed at reducing SOD1 aggregation, oxidative stress, motoneuron loss and motor impairments.
- The human transgenic TDP-43Q331K mouse model is relevant to study efficacy of compounds targeting TDP-43 proteinopathy, motoneuron loss and motor function in ALS or frontotemporal dementia (FTD).
- Standardized study protocols ensure consistency and reproducibility of your results.
- Work with expert study directors who take collaborative approach for your study.
- Benefit from quick study and flexible timelines.
- InnoSer's neurology expert team possesses relevant experience in working with multiple therapy types ranging from small molecules, peptides, enzymes, oligonucleotides, gene therapy (viral vectors – e.g., AAVs) and immunotherapies.

Consult available readouts

Thoroughly test your compound's efficacy with tailored readout options, providing you with translationally relevant insights to confidently advance your compound to clinical testing.

With flexible study designs and rapid start times, InnoSer neurology study experts take a collaborative approach when it comes to your research needs.

Biotechnical capabilities

- Acute and chronic administration (s.c., i.v., i.p., retro-orbital)
- Stereotaxic infusion (ICV in neonatal or adult mice)
- Cannula/osmotic minipumps

Behavioral Testing

- Motor function: Neurological scoring, Rotarod, Balance Beam, CatWalk™ gait analysis, Grip Strength, Wire Hanging, Nest Building, Spontaneous Behavior (PhenoTyper™ cages)

Analyses

- Sciatic nerve electrophysiology: compound muscle action potential (CMAP) and nerve conduction velocity (NCV) analyses
- CSF, blood and plasma collection for biomarker analyses (e.g., plasma NfL, cytokines)
- Tissue collection and histopathology analyses for biomarker analyses (e.g., TDP-43 accumulation, NfL, neuroinflammation)

Model characteristics example data

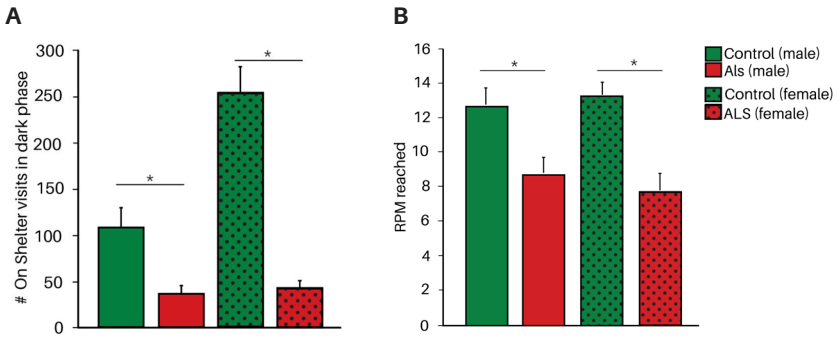

FIGURE 1. Motor impairments in 20-week old SOD1 mutant mice can be assessed in an automated home-cage and using several conventional tests, including the Rotarod. **(A)** SOD1 mutant mice show progressive behavioral changes in the PhenoTyper™ automated home-cages including a reduced frequency to climb on top of their shelter. **(B)** SOD1 mutant mice show decreased motor performance assessed by rotarod.

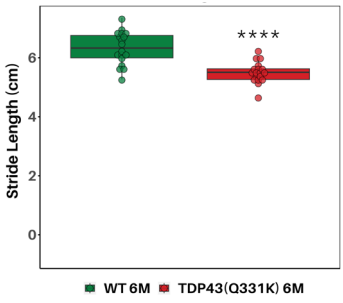

FIGURE 2. Female TDP-43 mice show progressive worsening of walking patterns in all 5 major parameter groups assessed using the CatWalk™ Gait Analysis system (one shown): temporal, spatial, run, interlimb coordination, and kinetic.

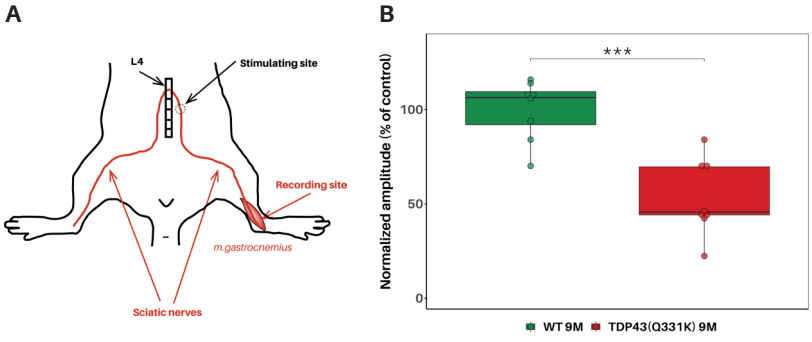

FIGURE 3. Sciatic nerve conduction electrophysiology in gastrocnemius muscle of TDP-43Q331K mice. **(A)** Experimental set-up for sciatic nerve conduction electrophysiology recording which includes compound muscle action potentials (CMAP) recordings. CMAP represents the summed electrical response generated by a group of muscle fibers in response to nerve stimulation. **(B)** Mutant TDP-43 mice show reduction of CMAP amplitude.

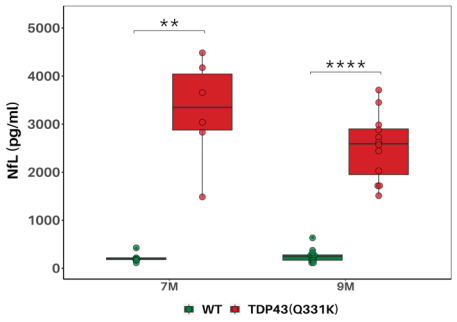

FIGURE 4. TDP-43Q331K mice show elevated plasma Neurofilament light chain (NfL) levels in the plasma. Compared to WT littermates, TDP-43 mice show significantly higher concentrations of plasma NfL at 7 months and 9 months of age.

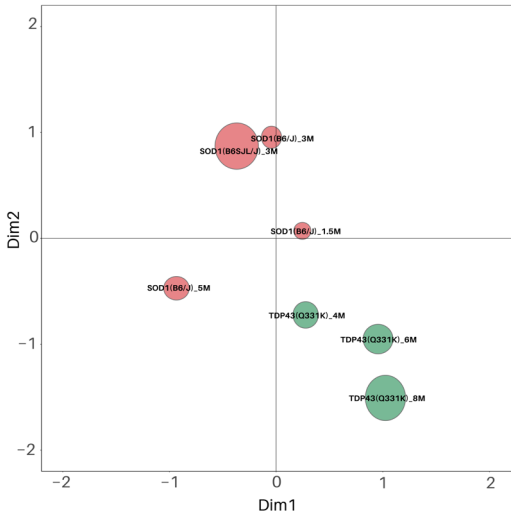

FIGURE 5. Principal component analysis (PCA) on multiple parameters in the PhenoTyper™ automated home-cage reveals consistent progression of the neurodegenerative phenotype of TDP-43 ALS mice. PCA bubble plot shows spontaneous behaviors of 2 ALS models (SOD1 and TDP43) progressively deteriorated by aging. SOD1 ALS models (both males and females) were tested at 1.5, 3 and 5M. While the 1.5M group showed small deviation vs control (center 0 point of the plot), the 3M groups showed a large deviation, with consistent results in 2 different SOD1 backgrounds (B6/J and B6SJL/J). At 5M, SOD1 model reached humane endpoint by paralysis symptoms, resulted in a bubble in different direction from the 1.5M and 3M. TDP43 ALS model (females) were tested at 4, 6 and 8M. The bubbles moved gradually further away from the center in the same quadrant, indicating the phenotype aggravated consistently in the same direction in this model, with the 8M showing the most pronounced phenotype.

Other neurodegenerative disease models

Our ALS models are a part of our large neurodegenerative disease portfolio, including multiple Alzheimer's disease (APP/PS1 transgenic as well as Tau transgenic and seeding models) and Parkinson's disease mouse models (MPTP-induced as well as transgenic and seeding alpha synuclein mouse modles)). Talk to our team to discover how you can benefit from our innovative services using one of the models.