SOD1 Rat Application Note

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Longitudinal Clinical Observations and Motor Coordination Assessments of the SOD1G93A Rat Model of Amyotrophic Lateral Sclerosis (ALS)

KEY TAKEAWAYS

- Compared to wild type controls, transgenic SOD1 rats demonstrated detectable levels of human SOD1 expression.
- The onset of ALS-like symptoms in male and female SOD1G93A rats ranged from as early as 21 weeks to as late as 30 weeks of age.
- Motor coordination deficits were evident in transgenic rats, as highlighted by their performance in beam walk and rotarod assessments.
- Transgenic SOD1 rats exhibited increased levels of neurofilament light chain, a clinical biomarker indicative of neurodegenerative disease.

Transgenic SOD1 rats expressed mutant human SOD1 at high levels

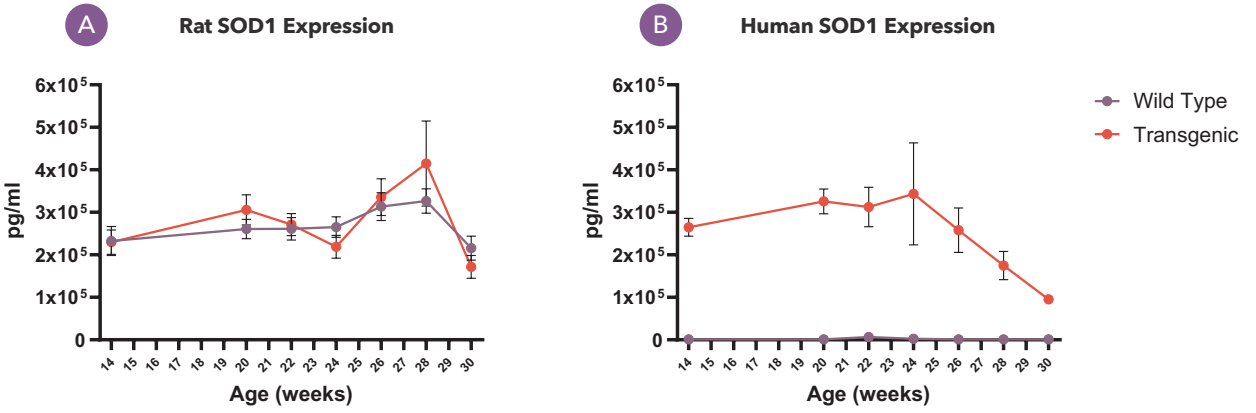

Figure 1. Quantification of Plasma Rat and Human SOD1.
(A) Levels of circulating, normal rat SOD1 were not different between the genotypes. **(B)** Concentrations of circulating, mutated human SOD1 were significantly higher [$F_{(1,272)}$ = 109.0, p<0.001] in transgenic rats compared to wild type control animals, with the data from wild types being below background levels.

Transgenic SOD1 rats demonstrated physical changes and increased mortality

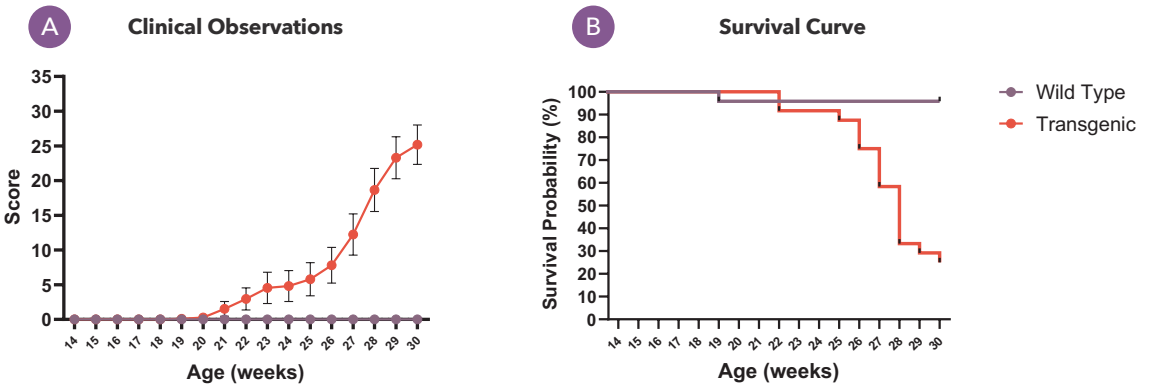

Figure 2. Clinical Observation Scores and Survival Curves.
(A) Weekly clinical observations including provoked behavior, locomotion, sneezing, respiration, posture, body condition, skin/fur, eyes, presence of tumors or infections, and body weight loss were recorded from 14 to 30 weeks of age. A two-way ANOVA (time x genotype) detected a significant interaction. An unpaired t-test of the data collapsed across time was used to demonstrate that transgenic animals had significantly higher observations than wild type controls [$T_{(32)}$= 3.07, p= 0.004). **(B)** Kaplan-Meier survival probability curves across the experimental period for male and female SOD1G93A rats aged to paralysis. As with the clinical observation data, the survival data required an unpaired t-test for analysis [$T_{(32)}$= 2.69, p = 0.011].

Transgenic SOD1 rats exhibited significant motor function challenges

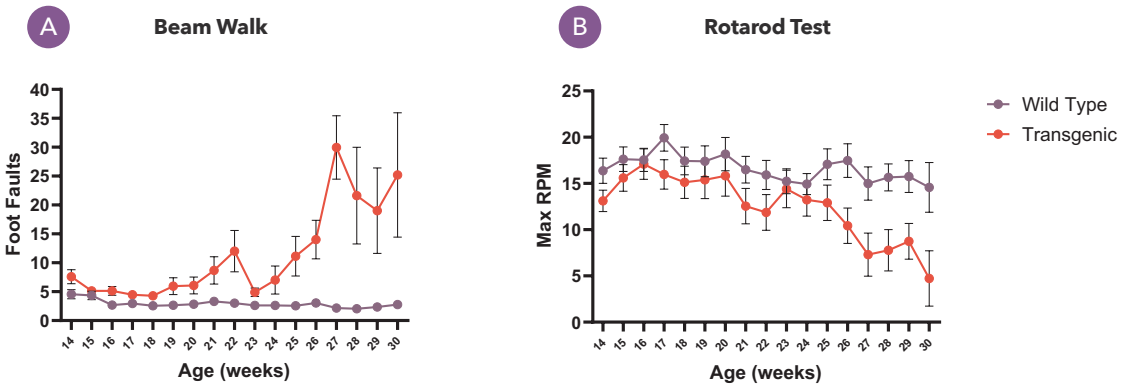

Figure 3. Motor Coordination Assessment of SOD1G93A Rats.
(A) SOD1G93A rats exhibited significantly more foot faults than wild type controls during the beam walk test [$T_{(32)}$= 4.32, p < 0.001].
(B) SOD1G93A rats achieved lower maximum revolutions per minute (RPM) than wild type controls in the rotarod test [$F_{(1,681)}$=15.9, p < 0.001].

Neurofilament light chain, a key neurodegenerative marker, was present in plasma of transgenic SOD1 rats

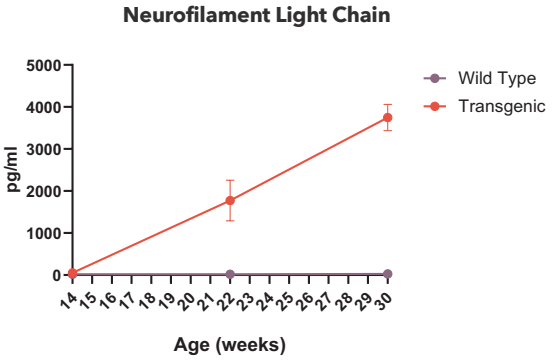

Figure 4. Quantification of Plasma Neurofilament Light Chain. Circulating neurofilament light chain (pg/ml) was detected in the plasma of SOD1G93A rats but not in the plasma from wild type control animals [$F_{(1,68)}$= 48.1, p<0.001].

The SOD1G93A rat model expresses mutant human SOD1 protein and develops motor problems, which correlate with measurable levels of a key clinical biomarker of neurodegeneration.

Learn more about the SOD1 rat model

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