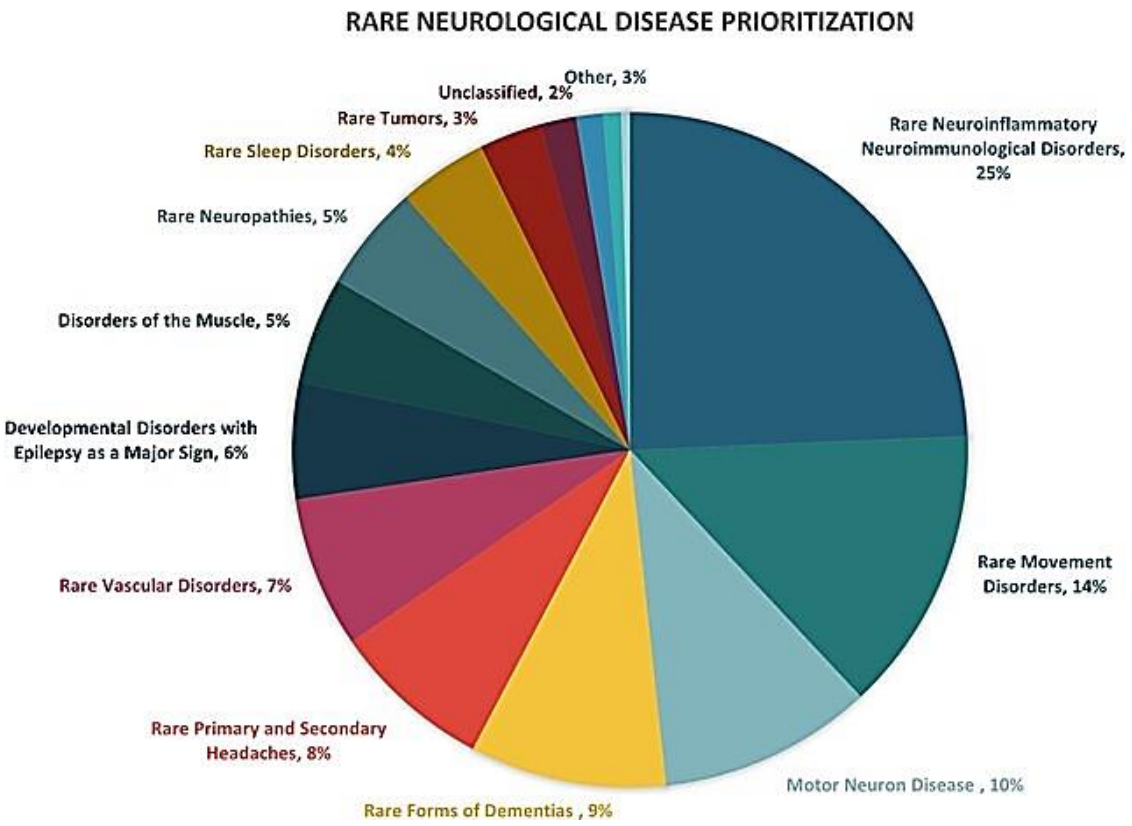
Rare Neurological Disease Animal Models

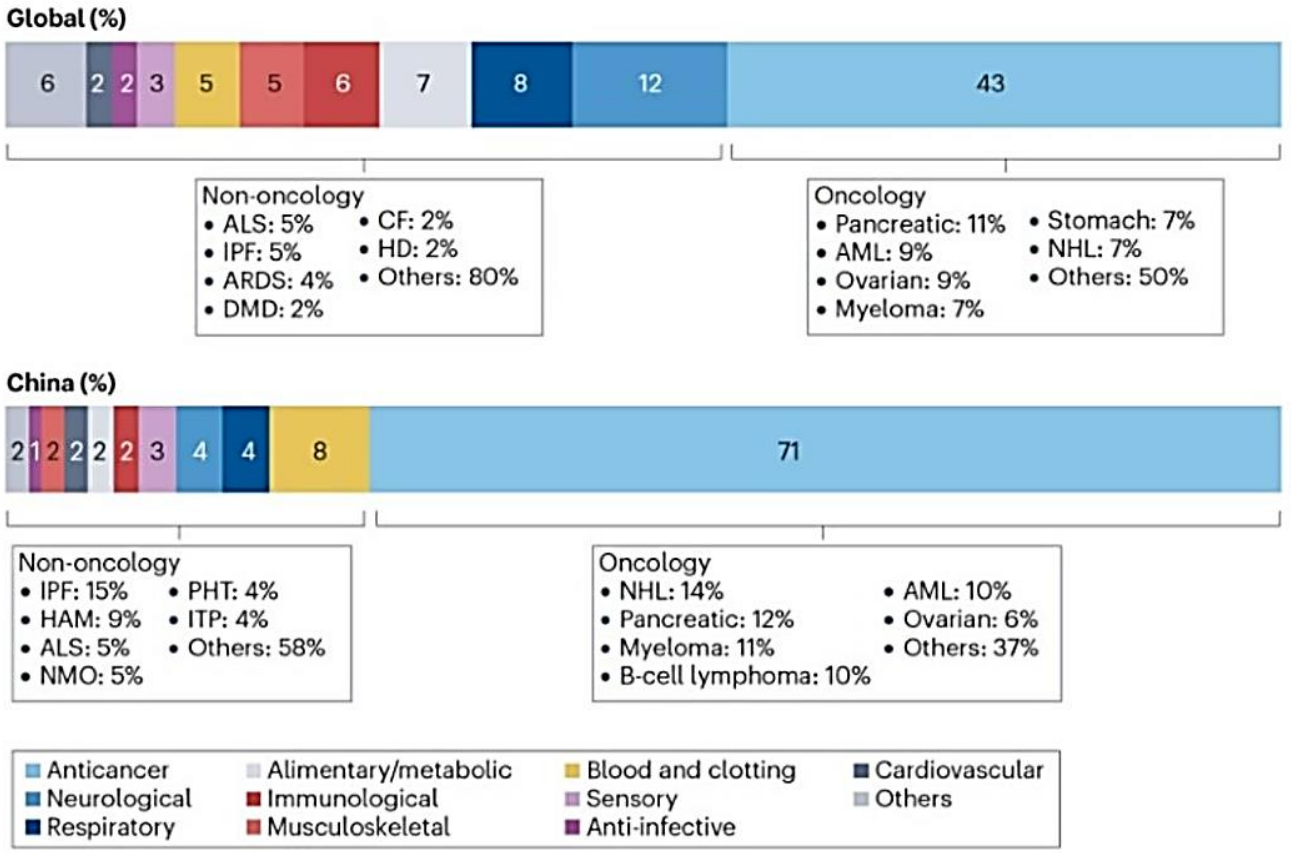
2025.02

Rare Neurological Disease Classification and Drug Development

- Rare neurological diseases can be classified into many categories based on the affected systems/organs, among which, neuroinflammatory & neuroimmunological disorders, movement disorders and motor neuron disease show higher distribution (>10%).
- Beyond oncology, neurological disease is the largest area of drug development globally (12%).



Eur J Neurol. 2024;31(3):e16171



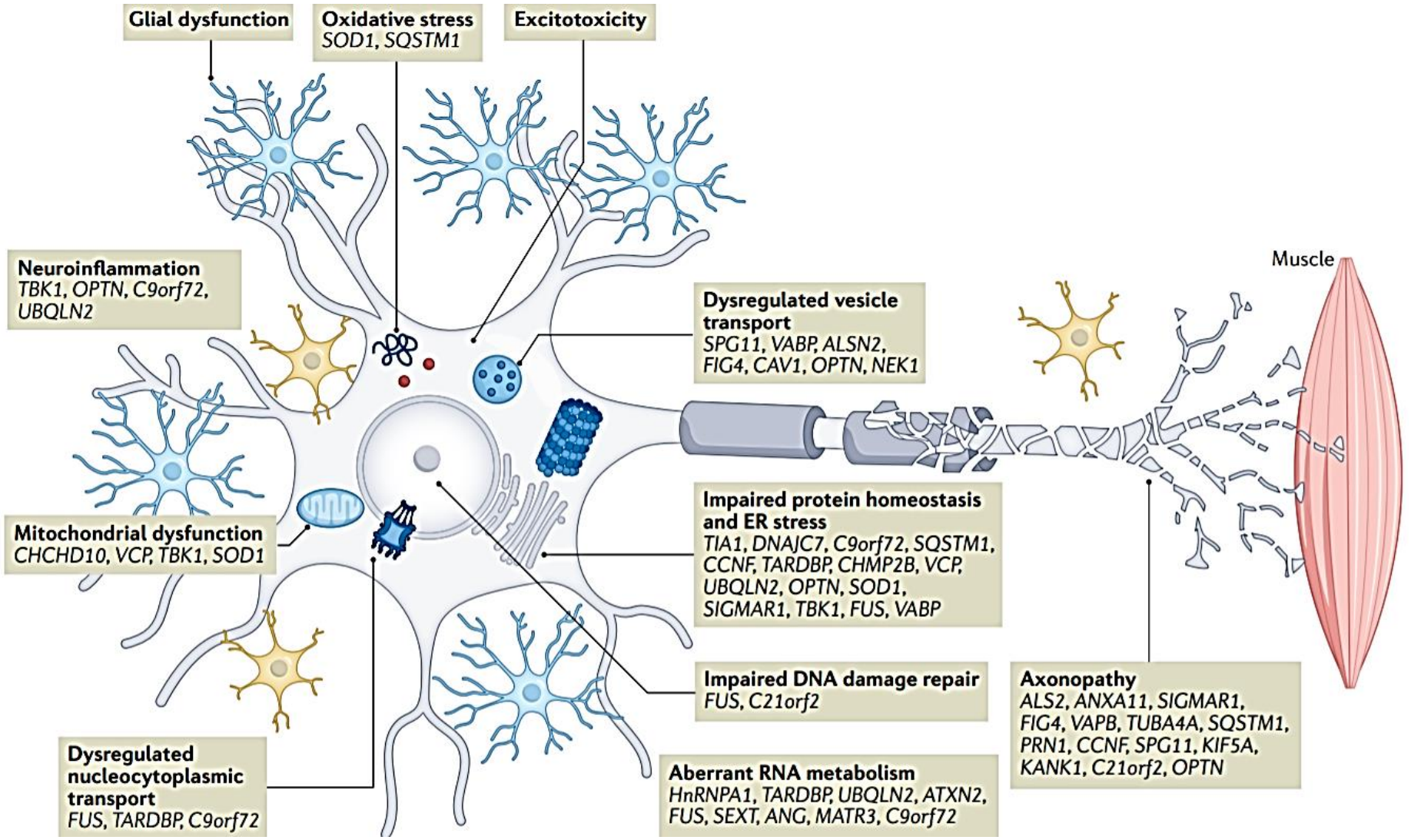
Nat Rev Drug Discov. 2024;23(3):168-169

Rare Neurological Disease Animal Models at WuXi AppTec

Disease	Animal Models
ALS (Amyotrophic Lateral Sclerosis)	*SOD1*^{G93A} rat
	SOD1^{G93A} mouse
	hTDP43 mouse
SMA (Spinal Muscular Atrophy)	SMNdelta7 mouse
	Smn1$^{-/-}$ hSMN2$^{+/+}$ mouse
Rett Syndrome	*Mecp2*$^{-/y}$ mouse
Huntington's Disease	hHTT-CAG130 mouse
GBA-associated Parkinson’s Disease	hSNCA^{A53T} mouse + CBE induced
Tourette’s Syndrome	INDP induced mouse
Infantile Spasms	Betamethasone + NMDA induced rat
Angelman Syndrome	*Ube3a*$^{-/-}$ mouse
Leigh Syndrome	*Ndufs4*$^{-/-}$ mouse

Amyotrophic Lateral Sclerosis (ALS)

Introduction



Nat Rev Drug Discov. 2023;22(3):185-212

Showcase: Amyotrophic Lateral Sclerosis (ALS)

SOD1^{G93A} rat

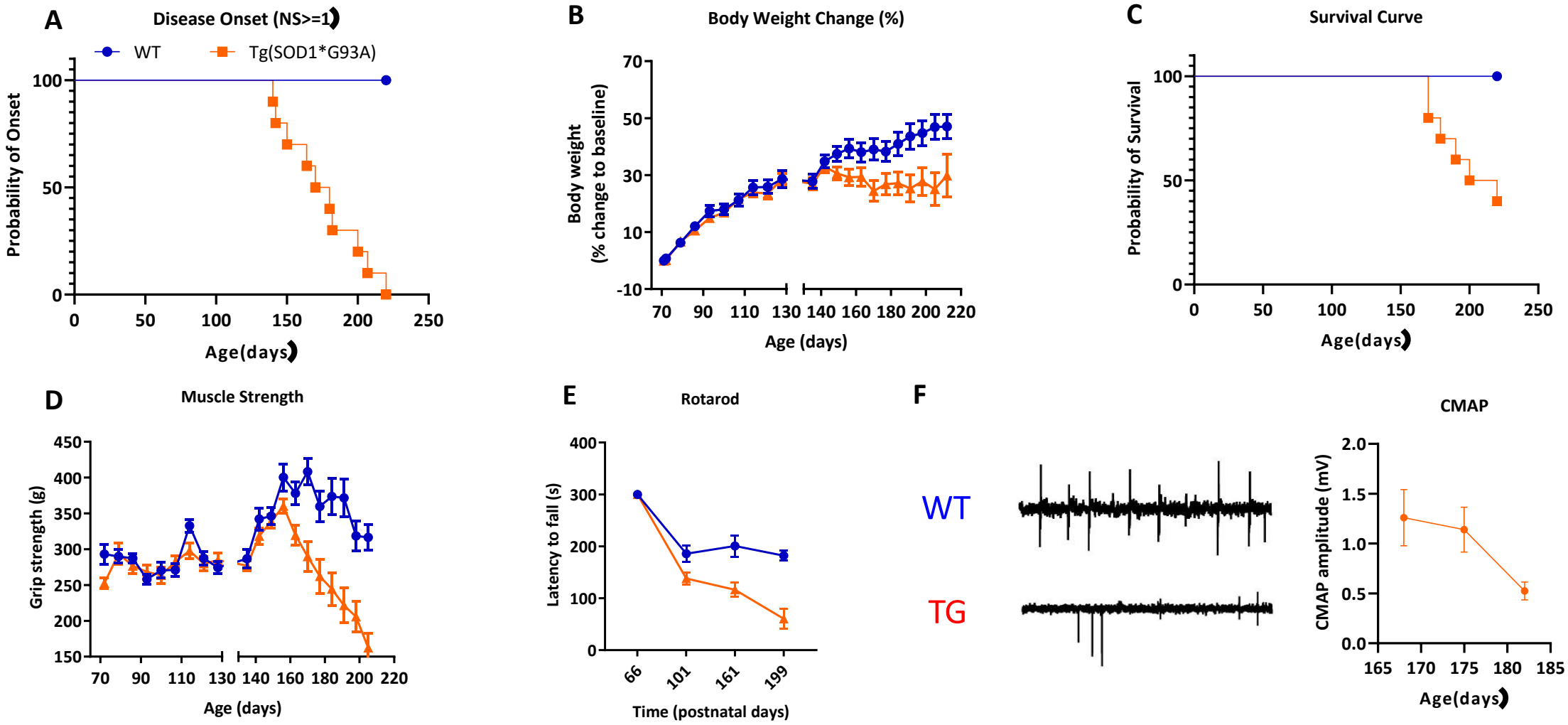


Figure: Disease onset curve **(A)**, body weight gain **(B)** and survival rate **(C)** of TG model and WT; Decreased muscle strength **(D),** latency to fall in Rotarod **(E),** and CMAP **(F)** after disease onset in TG model.

Showcase: Amyotrophic Lateral Sclerosis (ALS)

SOD1^{G93A} rat

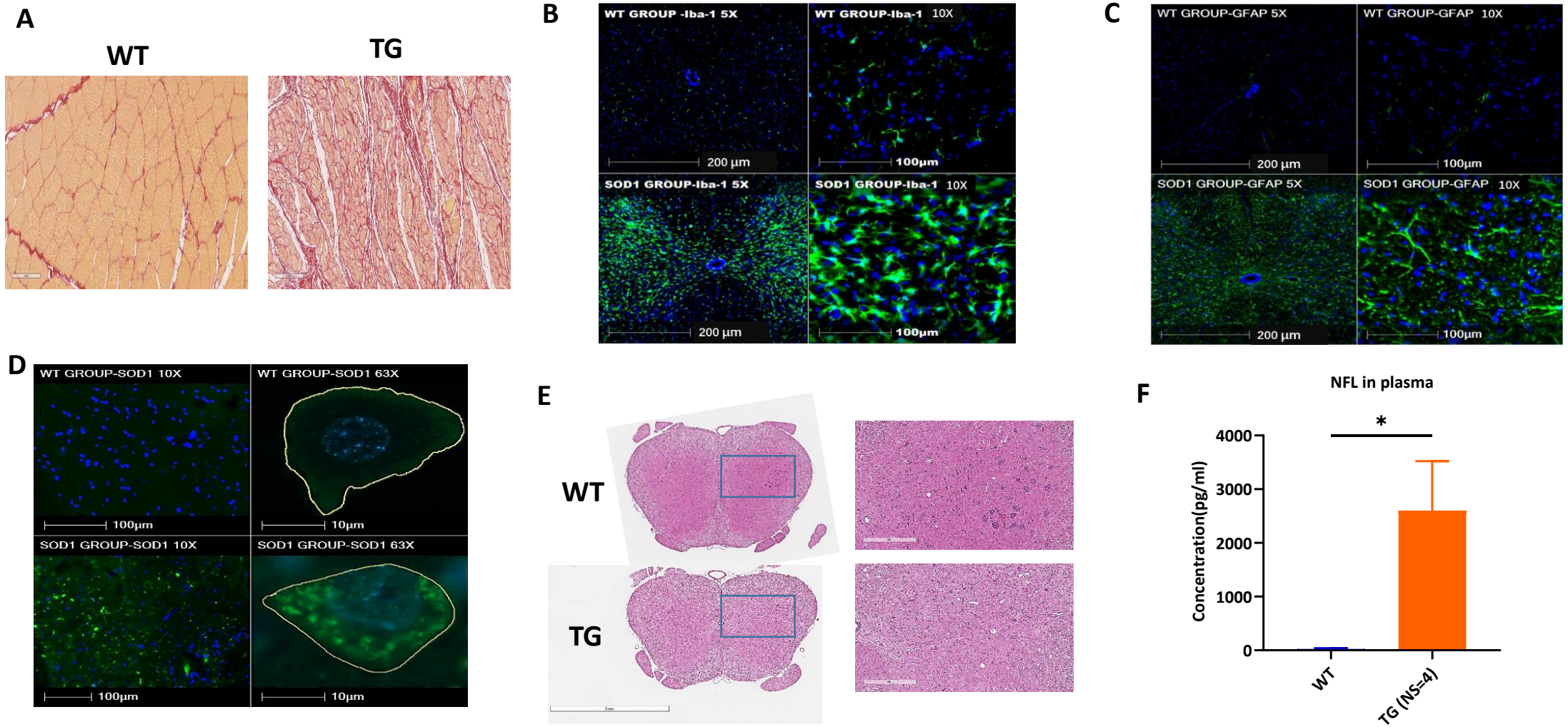
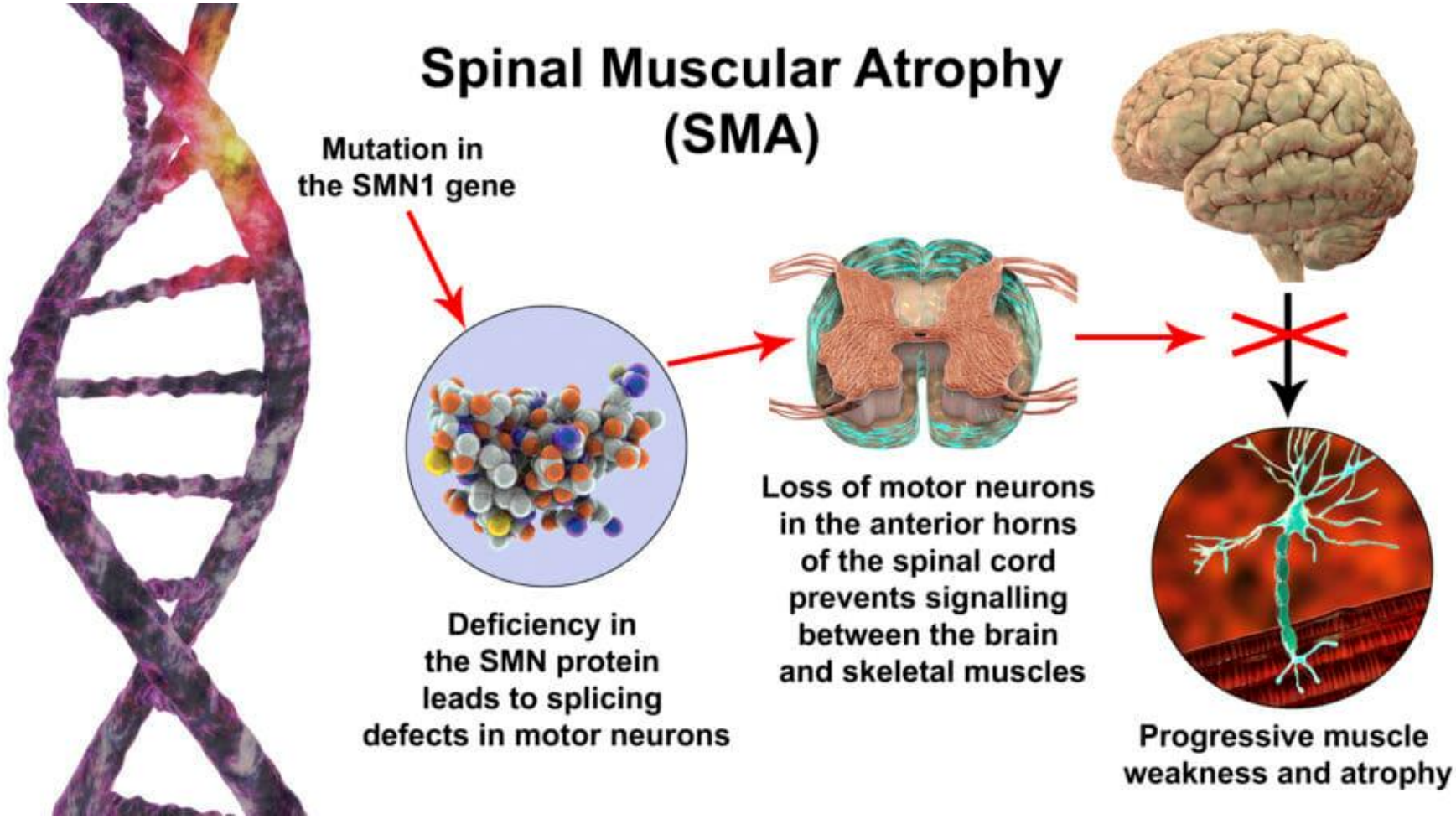


Figure: Muscle Sirius Red staining **(A)** of TG model and WT; Increased microglia **(B),** astrocyte **(C),** and SOD1 aggregation **(D)** in cortex of TG model; **(E)** Increased motor neurons loss in of TG model; **(F)** Increased NFL in plasma of TG model.

Spinal Muscular Atrophy (SMA)

Introduction



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Showcase: Spinal Muscular Atrophy (SMA)

SMNdelta7 mouse

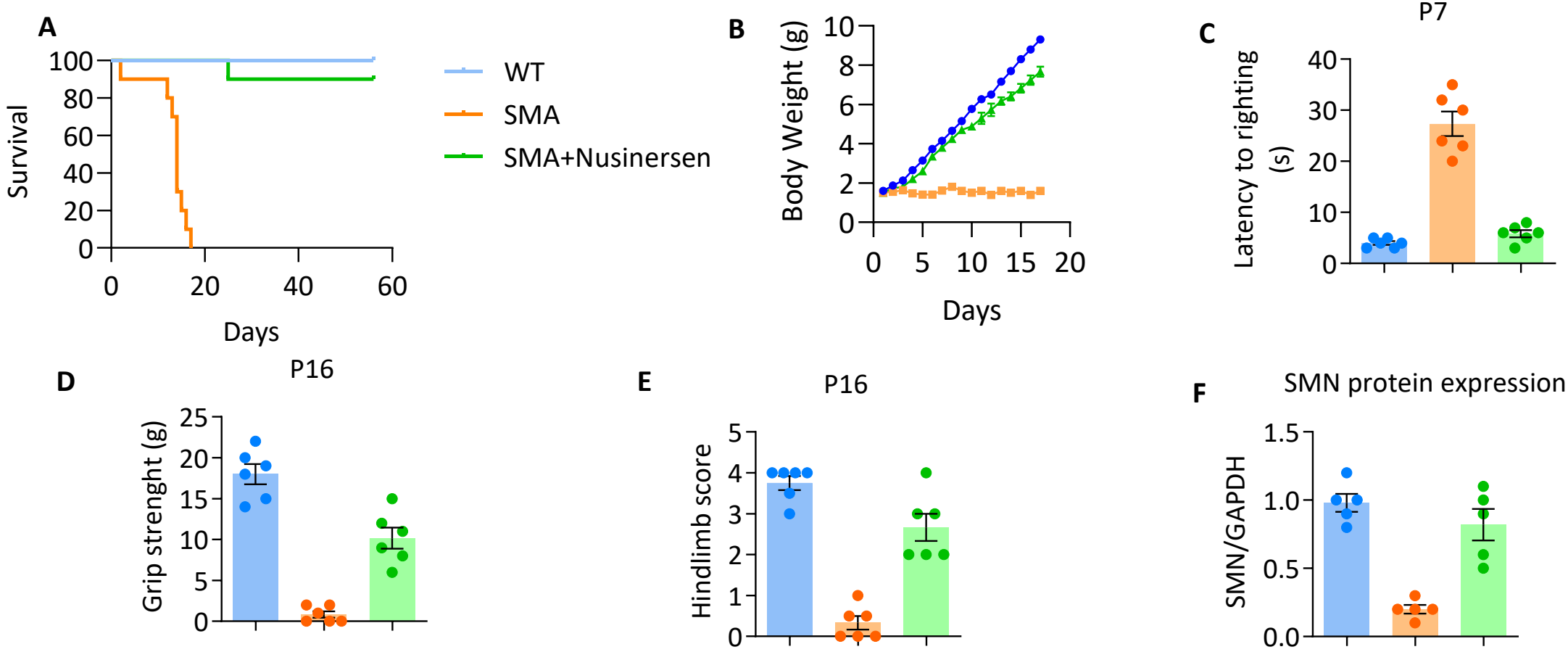


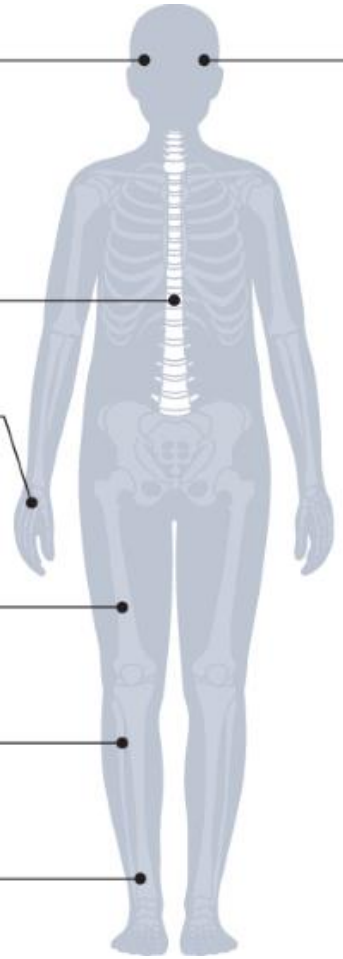
Figure: Nusinersen rescued the survival rate **(A),** increased the body weight **(B),** decreased the latency of righting reflex **(C),** elevated the strength **(D),** improved the hindlimb splay **(E)** and resulted in upregulated expression of SMN **(F)** in SMA mice.

Rett Syndrome

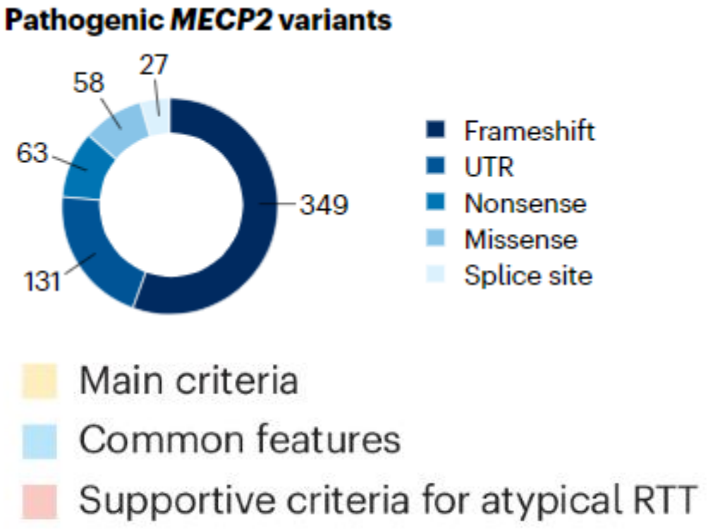
Introduction

MECP2 dysfunction

- Loss of acquired spoken language
- Bruxism (when awake)
- Breathing irregularities
- Scoliosis and/or kyphosis
- Loss of acquired purposeful hand skills
- Stereotypic hand movements
- Gait abnormalities
- Growth failure
- Abnormal muscle tone
- Peripheral vasomotor disturbances
- Cold extremities



- Impared sleep pattern
- Abnormal psychomotor development
- Intense eye communication
- Diminished response to pain
- Seizures
- Deceleration of head growth



Nat Rev Dis Primers. 2024;10(1):84

Showcase: Rett Syndrome

Mecp2$^{-/Y}$ mouse

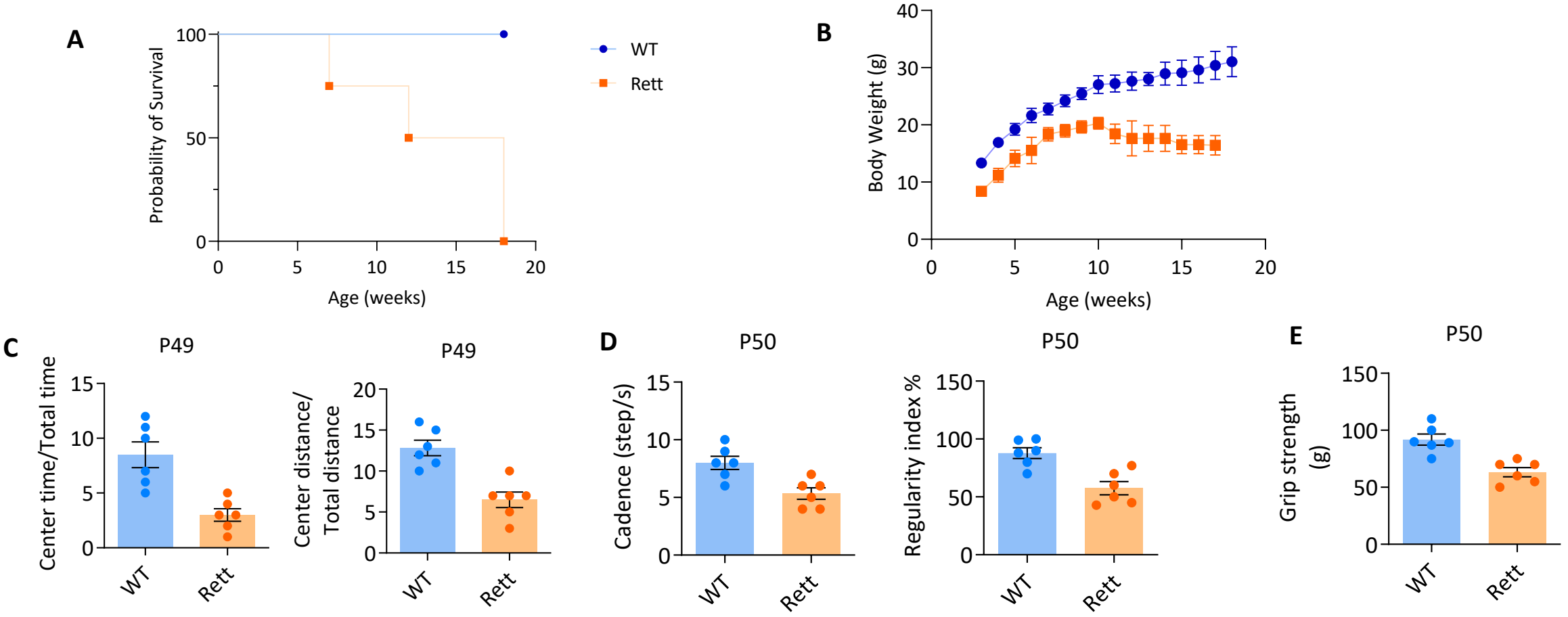
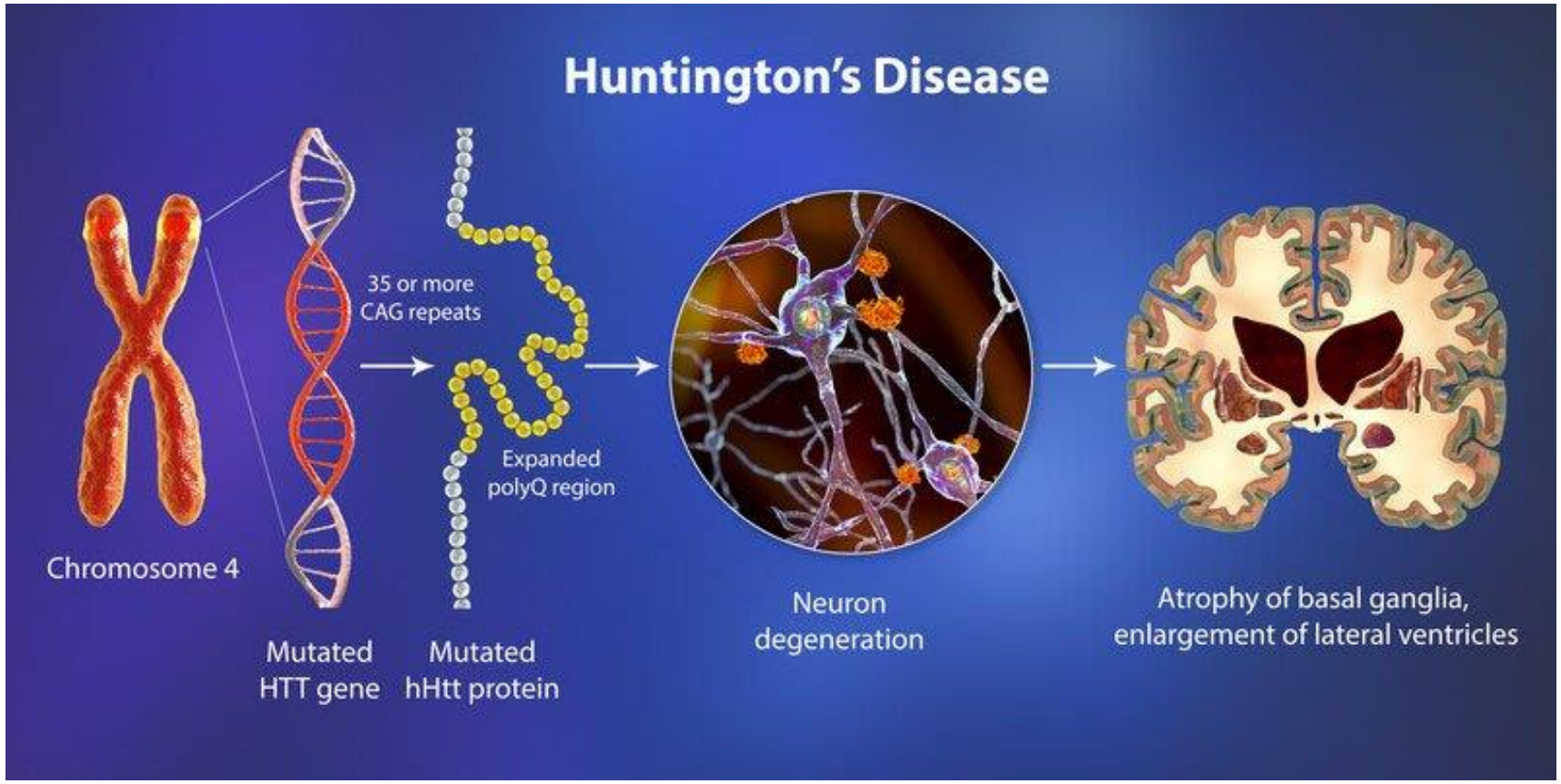
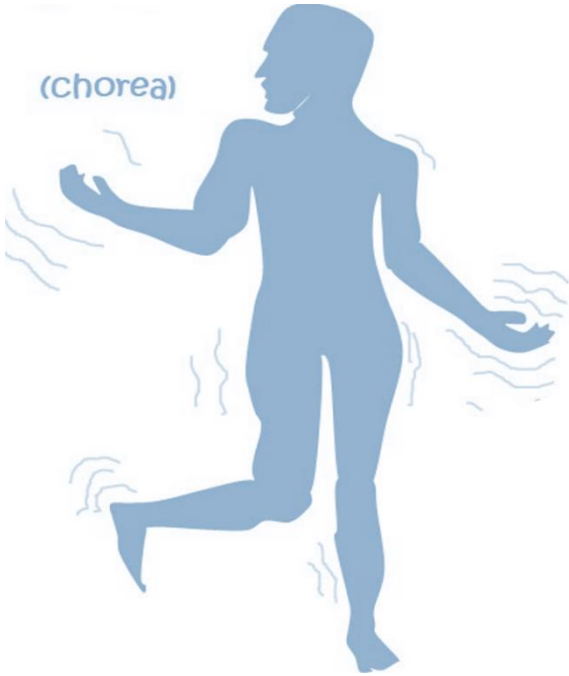


Figure: Survival curve **(A)** and body weight gain **(B)** of Rett mice and WT; Open field test **(C)**, Catwalk test **(D)** and Grip strength **(E)** test of Rett mice and WT at week 7.

Huntington's Disease

Introduction





https://www.fcneurology.net/what-is-huntingtons-disease/

Showcase: Huntington's Disease

hHTT-CAG130 mouse

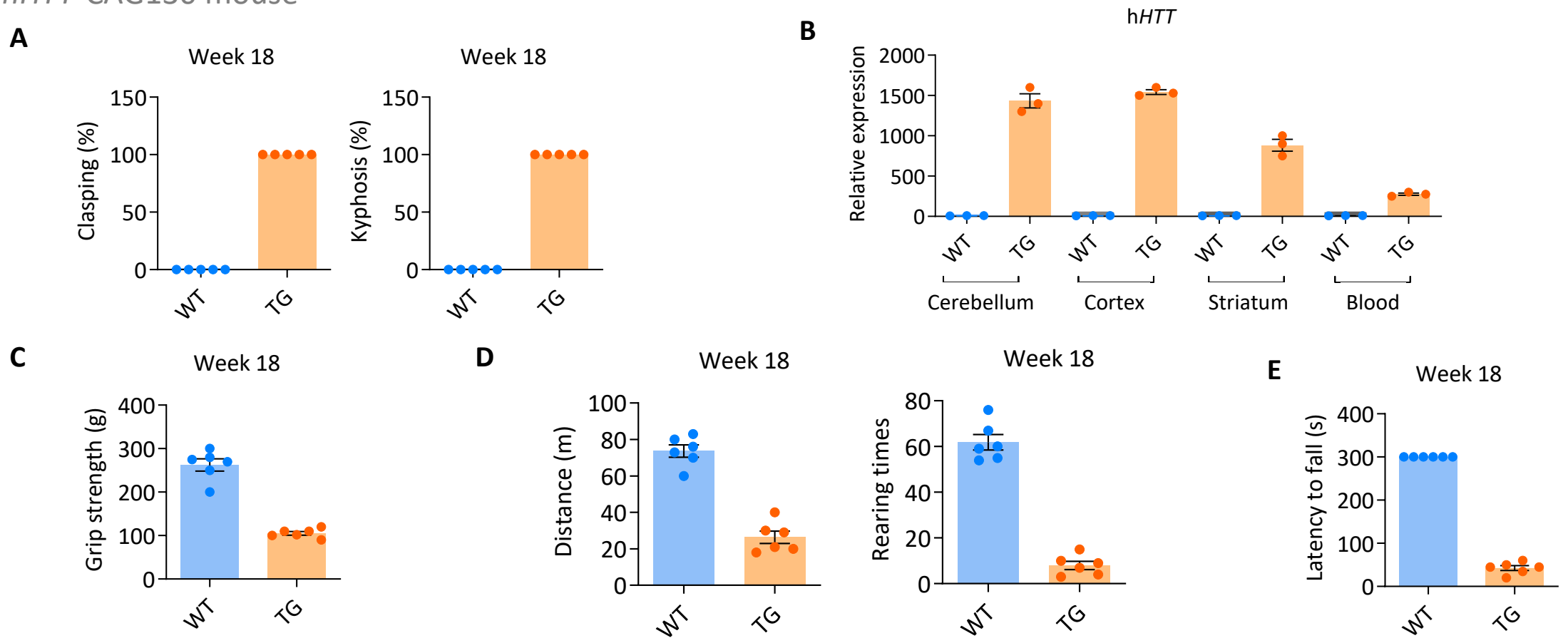


Figure: (A) Clasping and kyphosis were observed on TG mice; **(B)** *HTT* expression was elevated in TG mice; Decreased grip strength **(C)** and locomotion activity in open field test **(D),** as well as shorter latency to fall in rotarod test **(E)** were found in TG mice.

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