B6;C3-Tg(NEFH-tTA)8V1e Tg(tetO-TARDBP*)4V1e/J

**Stock No:** 028412 | rNLS8 (or NEFH-hTDP-43 NLS)

- **Transgenic**

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**PLACE ORDER**

3–6 week average lead time depending on quantity and age requests are not accepted
Overview

Also Known As: rNLS8 (or NEFH-hTDP-43 NLS), rNLS8, NEFH-hTDP-43DeltaNLS

The Jackson Laboratory will not distribute double transgenic mice. Instead, we will distribute the individual transgenic lines; that is, mice having either the NEFH-ITA transgene (see Stock No. 025397) or the tetO-hTDP-43- NLS transgene (see Stock No. 014650).

This regulatable NLS (rNLS8) double transgenic line recapitulates cytoplasmic TDP-43 pathology reminiscent of amyotrophic lateral sclerosis/frontotemporal lobar degeneration in brain and spinal cord, accompanied by a progressive neurodegenerative ALS-like phenotype. The phenotype is controllable/reversible by the tetracycline analog, doxycycline (dox).

Users should be aware that mice harboring both transgenic alleles will exhibit the lethal characteristics of amyotrophic lateral sclerosis (ALS)/frontotemporal lobar degeneration and must be provided tetracycline or a suitable analog such as doxycycline for longer term maintenance.

Donating Investigator

Virginia M Lee, University of Pennsylvania

GENETIC OVERVIEW

<table>
<thead>
<tr>
<th>Genetic Background</th>
<th>Generation</th>
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<tr>
<td>Tg(tetO-TARDBP*)4Vle</td>
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<td>Allele Type</td>
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<tr>
<td>Tg(NEFH-tTA)8Vle</td>
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</tbody>
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RESEARCH APPLICATIONS

Research Tools
Neurobiology Research

BASE PRICE
Starting at:
Details

Important Note
The Jackson Laboratory will not distribute double transgenic mice. Instead, we will distribute the individual transgenic lines; that is, mice having either the NEFH-ITA transgene (see Stock No. 025397) or the tetO-hTDP-43- NLS transgene (see Stock No. 014650).

Detailed Description
These mice are useful in studying amyotrophic lateral sclerosis (ALS) / frontotemporal lobar degeneration (FTLD). The phenotype of these mice is expected to be as described in Walker et al. 2015 Acta Neuropathol 130:643; details below.

Stock No. 028412 is the regulatable NLS (rNLS8) double transgenic line created by breeding NEFH-tTA line 8 (Stock No. 025397) with TRE-promoter-driven cytoplasmic-insoluble human TDP-43 NLS transgenic mice (tetO-hTDP-43- NLS line 4; Stock No. 014650). On a mixed C57BL/6J x C3HeJ F1 genetic background, mice hemizygous for NEFH-tTA and hemizygous for tetO-hTDP-43- NLS exhibit lethal characteristics of amyotrophic lateral sclerosis (ALS) / frontotemporal lobar degeneration (FTLD) when maintained in the absence of the tetracycline analog, doxycycline (dox). Specifically, they exhibit widespread, high levels of hTDP-43 NLS expression in neurons of both the brain and spinal cord (SC) as early as 1 week off-dox. The brain/SC combination of hTDP-43- NLS expression accounts for the spinal motor neuron loss and muscle denervation; resulting in a rapid, robust and progressive neurodegenerative ALS-like phenotype (including motor deficits, denervation of neuromuscular junctions, motor neuron loss and premature death at ~8-20 weeks). Upon administration of dox, the observed TDP-43 pathology and functional deficits were found to be largely reversible, even after neurodegeneration was underway (~8 weeks of hTDP-43- NLS expression).

Stock No. 028413 is the regulatable control double transgenic line created by breeding NEFH-tTA line 8 (Stock No. 025397) with TRE-promoter-driven human TDP-43 wildtype transgenic mice (tetO-hTDP-43-WT line 12; Stock No. 016841). On a mixed C57BL/6J x C3HeJ F1 genetic background, mice hemizygous for NEFH-tTA and hemizygous for tetO-hTDP-43-WT exhibit broad nuclear hTDP-43-WT expression in the brain and spinal cord, without the formation of cytoplasmic TDP-43 pathology.

Importantly, the donating investigator reports that the human NEFH promoter in NEFH-tTA line 8 drives slightly higher levels of tTA expression in the cortex compared to their experiences with the mouse Camk2a promoter used in Camk2a-tTA mice (greater than ~10-fold higher than endogenous NEFH versus ~8-fold higher than endogenous CAMK2A). In addition, the human NEFH promoter directs tTA expression in spinal cord (whereas the mouse Camk2a promoter did not).

Development

Expression Data

Control Suggestions

Selected References

Genetics

Tg(tetO-TARDBP*)4Vle

Tg(NEFH-tTA)8Vle
Genotyping Protocols
Genotyping resources and troubleshooting

Breeding Considerations
Mice hemizygous for NEFH-tTA and hemizygous for tetO-hTDP-43- NLS maintained in the absence of the tetracycline analog, doxycycline will exhibit the lethal characteristics of amyotrophic lateral sclerosis/frontotemporal lobar degeneration. To avoid prenatal and postnatal developmental effects of the transgenes’ expression, single allele females carrying bi-allelic offspring should be provided with doxycycline.

The Jackson Laboratory will not distribute double transgenic mice. Instead, we will distribute the individual transgenic lines; that is, mice having either the NEFH-tTA transgene (see Stock No. 025397) or the tetO-hTDP-43- NLS transgene (see Stock No. 014650).

Additional Breeding and Husbandry Support

Mating System
The Jackson Laboratory will not distribute double transgenic mice. Instead, we will distribute the individual transgenic lines that is, mice having either the NEFH-tTA transgene (see Stock No. 025397) or the tetO-hTDP-43- &Delta
NLS transgene (see Stock No. 014650)

Citation
When using the rNLS8 (or NEFH-hTDP-43 NLS) mouse strain in a publication, please cite the originating article(s) and include JAX stock #028412 in your Materials and Methods section.

Pricing & Availability
3–6 week average lead time depending on quantity and age requests are not accepted

Repository Live

Domestic International
Pricing effective for USA, Canada and Mexico shipping destinations
Breeder Pair

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<tr>
<th>SEX</th>
<th>GENOTYPE</th>
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- By Allele
- By Gene
- By Collection

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TOMORROW'S CURES

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