

B6.Cg-Tg(Chat-COP4*H134R/EYFP,Slc18a3)5Gfng/J

Stock No: 014545

 Congenic, Transgenic

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of cholinergic neuronal populations, or for studying the consequences of overactive cholinergic signaling in information processing, memory, behavior and physical fitness.

Donating Investigator

Guoping Feng, Massachusetts Institute of Technology

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GENETIC OVERVIEW

Genetic Background

Generation

Tg(Chat-COP4*H134R/EYFP,Slc18a3)5Gfng

Alele Type

Transgenic (Reporter)

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\$2,854.50 Domestic price Cryo Recovery

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Details

Important Note

The vesicular acetylcholine transporter gene (*Slc18a3* or VACht) within the *Chat* locus on the BAC transgene was not disrupted. The donating investigator reports that these ChAT-mhChR2-YFP line 5 mice are expected to have a similar VACht overexpression phenotype as reported for ChAT-mhChR2-YFP line 6 (Stock No. [014546](#)). That is, VACht overexpression in hippocampus and brainstem results in increased cholinergic tone; the functional consequence of which is increased physical endurance but severe cognitive deficits in attention, working memory and spatial memory.

Detailed Description

Mice hemizygous for the ChAT-ChR2-YFP BAC transgene are viable and fertile (see note below), with expression of the mhChR2::YFP fusion protein directed to cholinergic neuronal populations by the mouse choline acetyltransferase (*Chat* or ChAT) promoter/enhancer regions on the BAC transgene. The mhChR2::YFP fusion protein is composed of a mammalian codon-optimized *Chlamydomonas reinhardtii*-derived channelrhodopsin-2 that was modified to harbor a gain-of-function H134R substitution (mhChR2; also called hChR2-H134R) fused in-frame with an enhanced yellow fluorescent protein (EYFP). The mhChR2 is designed to cause larger stationary photocurrents compared to ChR2. The bacterial opsins are retinal-binding proteins that provide light-dependent ion transport and sensory functions to a family of halophilic bacteria; and this mhChR2 functions as a blue light-driven cation channel that depolarizes the cell and causes action potentials. As such, illuminating mhChR2-expressing neurons with blue light (450-490 nm) leads to rapid and reversible photostimulation of action potential firing/neural activity in these cells.

The donating investigator reports that EYFP expression is only weakly visible by direct fluorescence (epifluorescence microscope), but can be amplified by antibody enhancement in fixed brain sections. ChAT-mhChR2-YFP mice derived from founder line 5 (ChAT-ChR2-YFP line 5) exhibit moderate EYFP expression in striatum, trochlear nucleus, medial habenula, interpeduncular nucleus and various brainstem motor neuron nuclei. Lower EYFP expression is found in cortex, hippocampus, and other brain regions. Functional activation of neurons with blue laser light has only been confirmed in striatal cholinergic neurons in this founder line. ChAT co-staining shows precise co-localization with mhChR2-EYFP expression neurons; suggesting mhChR2-EYFP labeled neurons in this line are cholinergic neurons. Moderate EYFP fluorescence is also observed in the ventral gray horn in transverse section of the spinal cord. The donating investigator also reports that these ChAT-mhChR2-YFP line 5 mice exhibit a similar, but less bright expression pattern as ChAT-mhChR2-YFP line 6 (Stock No. [014546](#)).

Because the vesicular acetylcholine transporter gene (*Slc18a3* or VACht) within the *Chat* locus on the BAC transgene was not disrupted, VACht protein is overexpressed. The VACht overexpression phenotype is reported for ChAT-mhChR2-YFP line 6 (Stock No. [014546](#)), and the donating investigator expects a similar phenotype for ChAT-mhChR2-YFP line 5 mice. That is, VACht overexpression in hippocampus and brainstem results in increased cholinergic tone; the functional consequence of which is increased physical endurance but severe cognitive deficits in attention, working memory and spatial memory. ChAT-ChR2-EYFP line 6 mice also consume more food and water during the dark cycle compared to control mice. Compared to wildtype animals, ChAT-ChR2-EYFP line 6 mice show no changes in metabolic profile, locomotor activity in a novel environment, anxiety-like behavior, depression-like behavior, gross sensorimotor function, and ability to use cues to learn a task.

This optogenetic strain is one of many from the same transgene creator/donating investigator with light-inducible neurobiology applications; including Thy1-ChR2-YFP line 18 (Stock No. [007612](#)),

Thy1-ChR2-YFP line 9 (Stock No. [007615](#)),
Thy1-eNpHR-YFP line 2 (Stock No. [012332](#)),
Thy1-eNpHR-YFP line 4 (Stock No. [012334](#)),
Thy1-vChR1-YFP line 1 (Stock No. [012341](#)),
Thy1-vChR1-YFP line 4 (Stock No. [012344](#)),
Thy1-vChR1-YFP line 8 (Stock No. [012348](#)),
Thy1-mhChR2-YFP Line 20 (Stock No. [012350](#)),
Prv-mhChR2-YFP Line 15 (Stock No. [012355](#)),
ChAT-ChR2-YFP line 6 (Stock No. [014546](#)),
VGAT-ChR2-YFP line 8 (Stock No. [014548](#)),
and TpH2-ChR2-YFP line 5 (Stock No. [014555](#)).

[+ Development](#)

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[+ Tg\(Chat-COP4*H134R/EYFP,Slc18a3\)5Gfng](#)

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[- Technical Support](#)

Genotyping Protocols

Standard PCR: [Tg\(Chat-COP4*H134R/EYFP\)](#)

Standard PCR: [Tg\(Chat-COP4*H134R/EYFP\)](#)

[Genotyping resources and troubleshooting](#)

Breeding Considerations

When maintaining a live colony, hemizygous mice may be bred with wildtype (noncarrier) mice from the colony or with C57BL/6J inbred mice (Stock No. [000664](#)).

[Additional Breeding and Husbandry Support](#)

Citation

When using the B6.Cg-Tg(Chat-COP4*H134R/EYFP,Slc18a3)5Gfng/J mouse strain in a publication, please [cite the originating article\(s\)](#) and include JAX stock #014545 in your Materials and Methods section.

Animal Health Reports

[Facility Barrier Level Descriptions](#)

Production of mice from cryopreserved embryos or sperm occurs in a maximum barrier room, [G200](#)

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Frozen Mouse Embryo	B6.Cg-Tg(Chat-COP4*H134R/EYFP Slc18a3)5Gfng/J Frozen Embryo	\$2595.00
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