The Jackson Laboratory

STOCK *Shank3* $^{tm5.1Gfng}$ /J

Stock No: **028800** | Shank3 ^{fx} (FLexed PDZ domain inverted)

Targeted Mutation

Typically mice are recovered in 10-14 weeks. Contact Customer Service to place an order or for more information.

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homozygotes exhibit autistic-like characteristics. Subsequent exposure to Cre recombinase that places the *Shank3* PDZ domain into the proper orientation for expression results in restored expression of most major SHANK3 isoforms in those cells. These mice allow *cre*-inducible restoration of SHANK3 expression, and may be useful for studying autism spectrum disorder (ASD), Phelan-McDermid syndrome and schizophrenia.

Donating Investigator

Guoping Feng, Massachusetts Institute of Technology

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GENETIC OVERVIEW

Genetic Background	Generation

Shank3$^{tm5.1Gfng}$

Allele Type	Gene Symbol	Gene Name
Targeted (Conditional ready (e.g. floxed), Null/Knockout)	*Shank3*	SH3 and multiple ankyrin repeat domains 3

VIEW GENETICS

RESEARCH APPLICATIONS

Research Tools
Neurobiology Research
Developmental Biology Research

VIEW ALL RESEARCH APPLICATIO

BASE PRICE

Starting at:

$2,854.50 Domestic price Cryo Recovery

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Details

Detailed Description

SHANK3 is a synaptic scaffolding protein, expressed in the postsynaptic density (PSD) of excitatory synapses. SHANK3 mutations have been identified in cases of intellectual disability such as autism spectrum disorder (ASD), Phelan-McDermid syndrome and schizophrenia.

The Shank3^{fx} allele has an inverted *Shank3* PDZ domain (exons 13-16) that is flanked with the FLEx cassette (inward-facing *lox2272*:*loxP* sites), all replacing the corresponding endogenous *Shank3* sequences. Prior to Cre recombinase exposure, the Shank3^{fx} allele functions as a knockout. No protein expression of most major SHANK3 isoforms (including the putative α, β and γ forms) is observed from this allele in striatal postsynaptic density. Homozygous mice (Shank3$^{fx/fx}$) recapitulate several autistic-like characteristics, including significant deficits in exploratory behavior, anxiety and motor coordination. The presence of open wound lesions is also suggestive of repetitive grooming behavior. In addition, they show impaired neurotransmission in the dorsal striatum.
When exposure to Cre recombinase places the Shank3 PDZ domain into the proper orientation for expression, the resulting mice have restored expression of most major SHANK3 isoforms (with the exception of the putative SHANK3 γ isoform).

Specifically, Shank3$^{fx/fx}$ mice with widespread expression of tamoxifen-inducible Cre recombinase (Shank3$^{fx/fx}$:CreER$^{+/-}$) allow temporal restoration of SHANK3 expression following tamoxifen treatment.
Prior to tamoxifen, they exhibit the same autistic-like phenotype as Shank3$^{fx/fx}$ mice.
Tamoxifen induction as adult mice (2-4.5 months) rescued the repetitive grooming behavior and social interaction deficit, as well as improved synaptic protein composition, spine density and neural function in the striatum. Adult restoration did not rescue anxiety or motor coordination deficits.

Earlier *cre*-induced restoration of SHANK3 expression yielded more behavioral improvement than adult treatment. When Shank3$^{fx/fx}$ mice are bred to have constitutive, widespread *cre* expression staring at the germ-cell stages (β-actin Cre mice), restoration of SHANK3 rescues the behavioral abnormal behavioral phenotype (normal striatal physiology, exploratory behavior, anxiety and motor coordination).

The two *lox* variants, *lox2272* and *loxP*, are compatible only with a *lox* sequence identical to self; they do not recombine with each other. Based on the design of the Shank3^{fx}, several *cre*-mediated recombination outcomes are possible based on which *lox* sites are recombined. The outcomes are described below. In addition, because inward-facing *lox* sequences result in *cre*-mediated inversion rather than excision, *cre*-expressing cells may be able to reversibly switch back-and-forth from the SHANK3-expressing orientations (outcomes i and ii, below) and original knockout orientation as long as Cre recombinase is active in the cell.

i. Inversion of the Shank3^{fx} allele at the *lox2272* sites places the Shank3 PZD domain sequence into the proper orientation for restored SHANK3 expression in the *cre*-expressing cell type. The Shank3 PZD domain is still flanked by inward-facing *lox2272* sites, but the 3' *lox2272* site is itself flanked by *loxP* sites now in the same direction.

ii. Inversion of the Shank3^{ix} allele at the *loxP* sites places the Shank3 PZD domain sequence into the proper orientation for restored SHANK3 expression in the *cre*-expressing cell type. The Shank3 PZD domain is still flanked by inward-facing *loxP* sites, but the 5' *loxP* site is itself flanked by *lox2272* sites now in the same direction.

iii. Recombination of outcome i at the *loxP* sites now deletes the 3' *lox2272* site, without interruption of SHANK3 expression. This results in permanent SHANK3 expression because the PDZ domain is now flanked with non-compatible *lox* sites.

iv. Recombination of outcome ii at the *lox2272* sites now deletes the 5' *loxP* site, without interruption of SHANK3 expression. This results in permanent SHANK3 expression because the PDZ domain is now flanked with non-compatible *lox* sites.

v. Both the inversion of outcome i at the inward-facing *lox2272* sites, as well as the inversion of outcome ii at the inward-facing *loxP* sites reverts to the original Shank3^{fx} allele; resulting in disrupted SHANK3 expression.

- Development
- Control Suggestions
- Selected References

Genetics

- *Shank3$^{tm5.1Gfng}$*

Disease/Phenotype

- Disease Terms
- Research Areas By Phenotype
- Mammalian Phenotype Terms by Genotype
- References

Technical Support

CONTACT TECHNICAL SUPPORT

Genotyping Protocols

Standard PCR:Shank3

Genotyping resources and troubleshooting

Breeding Considerations

Homozygous mice are viable and fertile, with several autistic-like characteristics. When maintaining a live colony, heterozygous mice may be bred together, to wildtype littermates, or to C57BL/6J inbred mice (Stock No. 000664).

Additional Breeding and Husbandry Support

Citation

When using the Shank3^{fx} (FLexed PDZ domain inverted) mouse strain in a publication, please cite the originating article(s) and include JAX stock #028800 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

Pricing & Availability

Cryo Recovery

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Domestic **Internatio**

Pricing effective for USA, Canada and Mexico shipping destinations

Cryorecovery - Domestic Pricing

SERVICE/PRODUCT	DESCRIPTION	PRICE
Cryo Recovery	Heterozygous or wildtype for Shank3<tm5.1Gfng>	$2,854.50

Related Products and Services

Frozen Mouse Embryo	STOCK Shank3<tm5.1Gfng>/J	$2595.00

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