Gene Knockout

Expedite your research with highly customizable, gene knockout mouse models that provide thorough insight into key genetic mechanisms.

Accelerate your research with customized gene knockout mouse models that provide thorough insight into key genetic mechanisms.

- Uncover gene functions and explore cellular processes
- Gain an in-depth understanding of the etiology of human diseases
- Simplify the workflow of drug candidate evaluation

Gene knockout mouse models include: :

- Conventional (constitutive) gene knockout
- Conditional gene knockout
- KO first

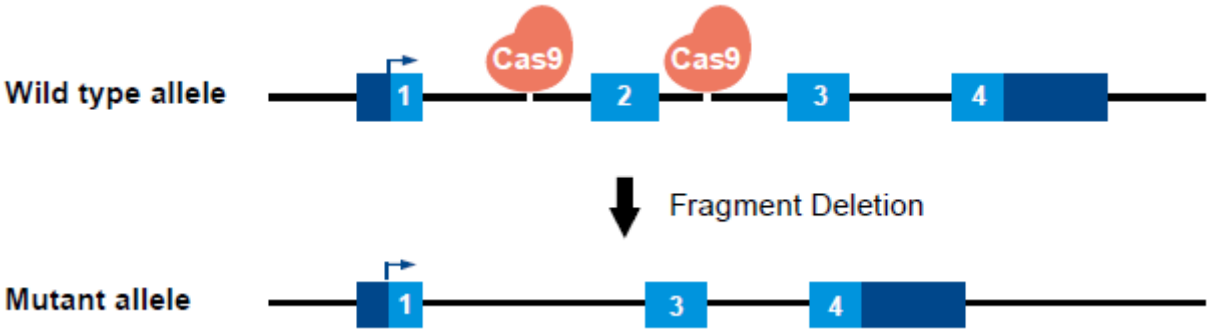
Shanghai Model Organisms Center (SMOC) has more than 6000 research-ready GEM models. Check out our website to find out whether your model of interest is available for direct purchase.

Alternatively, you may contact our technical support staff to design a customized, gene knock-out model that fits your need best.

Conventional (Constitutive) Gene Knockout

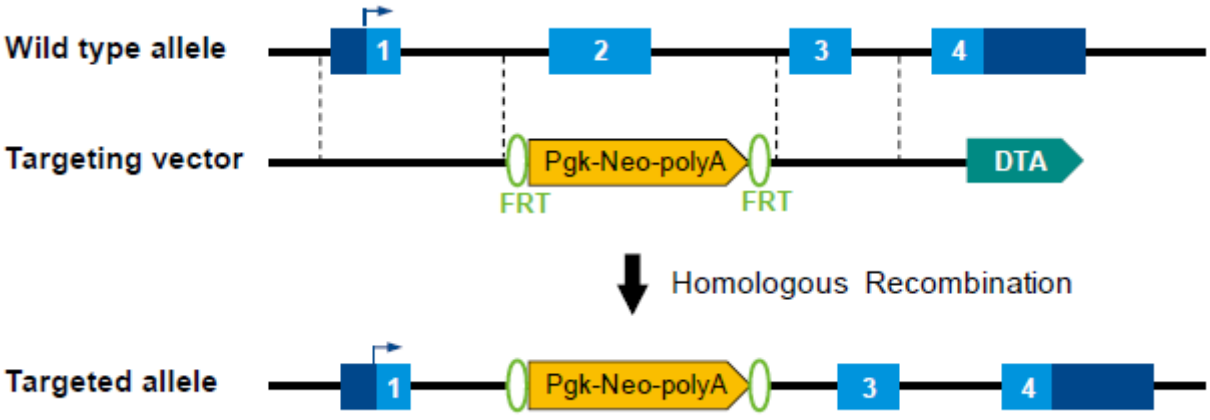
Generate a conventional (constitutive) gene knockout (KO) mouse model to permanently inactivate your target gene.

It usually takes 4-6 months to generate a conventional (constitutive) gene knockout mouse model via CRISPR gene editing technology.



Synthetic sgRNAs and Cas9 mRNA are co-injected into mouse fertilized eggs. sgRNAs targeting specific loci in the genome guide Cas9 enzyme to the locus of interest, where Cas9 nuclease cuts the target site. Without the presence of donor template, random repair through the non-homologous end joining (NHEJ) pathway usually results in a frameshift of the gene coding sequence. Since NHEJ repair may create distinct mutations in different cells, F0 mice need to be bred with WT in order to obtain hterozygous animals with stably inherited genotype.

It usually takes 9-12 months to generate a conventional (constitutive) gene knockout mouse model by ES cell targeting technology.



A homologous recombination vector in which one or more exons of the target gene were replaced with a neomycin (Neo) gene was generated and transformed into ESC clones. The targeted ES cells were injected into blastocysts to obtain a partial ES-derived chimeric mouse. Then the chimeric mouse was mated with the wild type to finally obtain a heterozygous mouse derived from the recombinant ES cell. Specific exon(s) of target gene on one chromosome of heterozygous mice have been replaced by a Neo gene, and then homozygous, KO mice were obtained by mating between heterozygous mice.

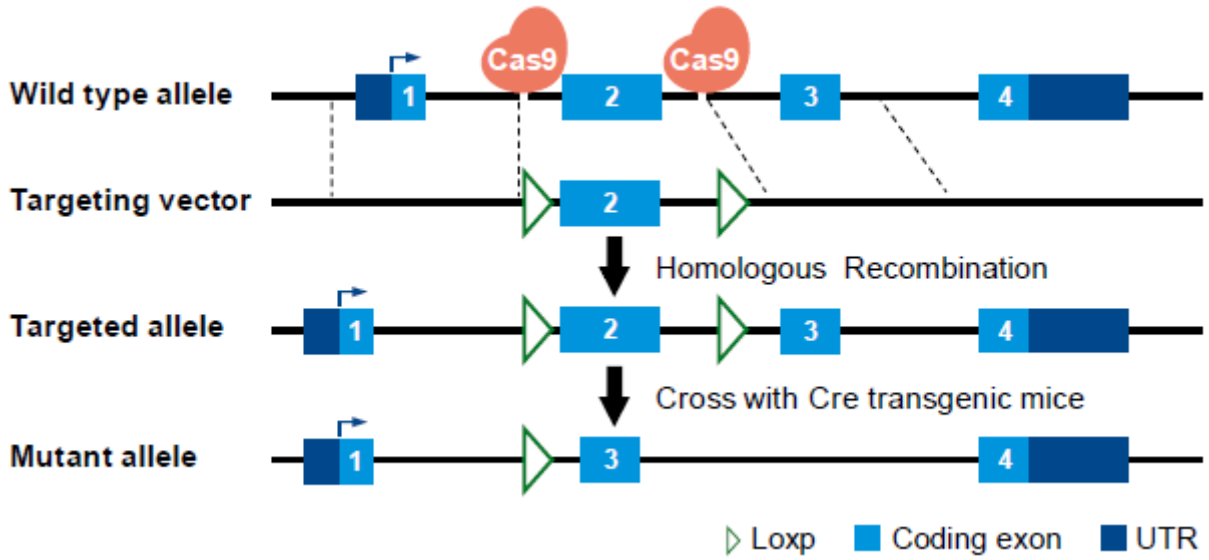
Conditional Gene Knockout

Conditional knockout (CKO) can be used to knock out a target gene of interest in a temporal- or spatial-specific pattern, enabling more accurate gene knockout and more focused research.

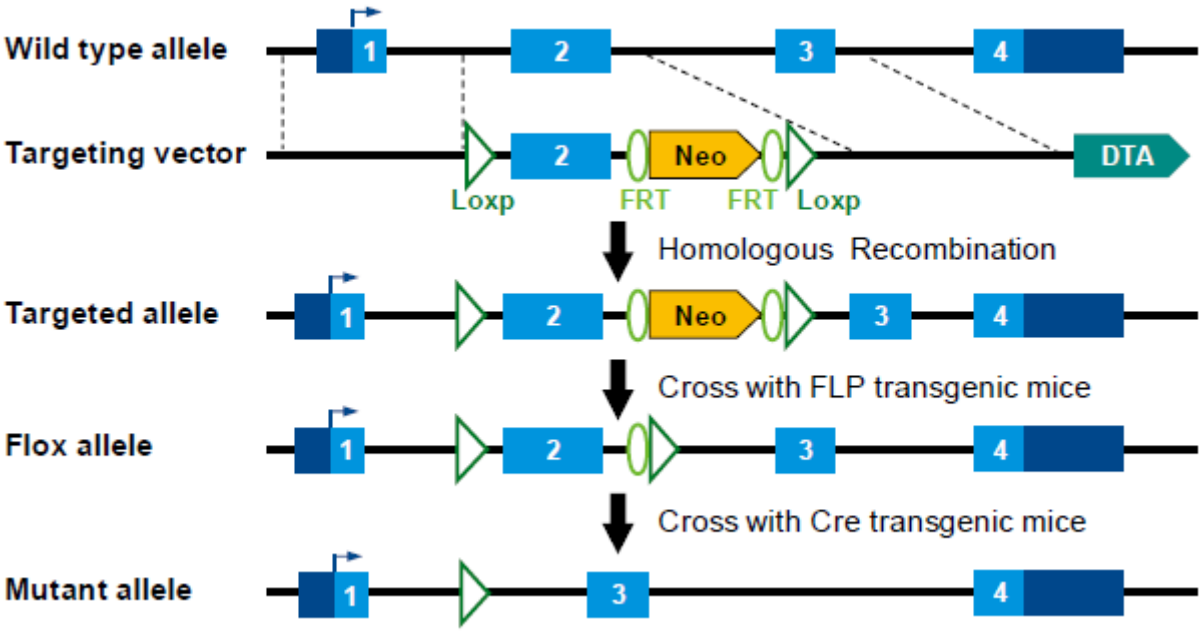
Conditional gene knockout is mainly achieved by site-specific recombinase systems such as Cre-LoxP, FLP-Frt and Dre-Rox. Among those approaches, the Cre-LoxP system is most frequently used, whereby a LoxP sequence is placed at each end of a DNA sequence to be deleted to generate a Flox (flanked by LoxP) mouse. Flox mice are crossed with Cre-expressing mice to achieve a tissue- or cell-specific gene knockout.

Such Flox mice may be less likely to develop embryonic or neonatal lethality, relative to the models devloped by the conventional KO method. By crossing with different Cre-expressing mice, we can generate offsprings in which the target gene can be inactivated at any developmental stage or in any specific cell type. Moreover, when combined with other inducible Cre systems, target gene can be temporally and spatially regulated simultaneously.

It usually takes 6-9 months to generate a conditional gene knockout mouse model by CRISPR gene editing technology.



It usually takes 9-12 months to generate a conditional gene knock-in mouse model by ES cell targeting technology.



KO first

KO first (Conditional Ready) is a multipurpose, CKO-like model in which LoxP sites with the same orientation flank the target fragment and the SA-IRES-reporter fragment flanked by FRT sites is placed within the 5' end intron. This type of mouse model has two main applications:

1) Mating with Cre-expressing mice results in the deletion of Neo gene and Flox region. This leads to the expression of the reporter gene (SA-IRES-reporter), accompanied with the loss of the endogenous gene. As the reporter is under the control of the endogenous promoter, we can track where the endogenous gene is expressed by monitoring the reporter expression in the mouse model.

2) Mating with Flp-expressing mice results in the deletion of SA-IRES-reporter fragment to obtain conventional Flox mice. Flox mice are then mated with various tissue-specific Cre-expressing mice to obtain a range of conditional knockout models.