

Igf1r Cas9-CKO Strategy

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Reviewer: Jinling Wang

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Overview

Target Gene Name

- Igf1r

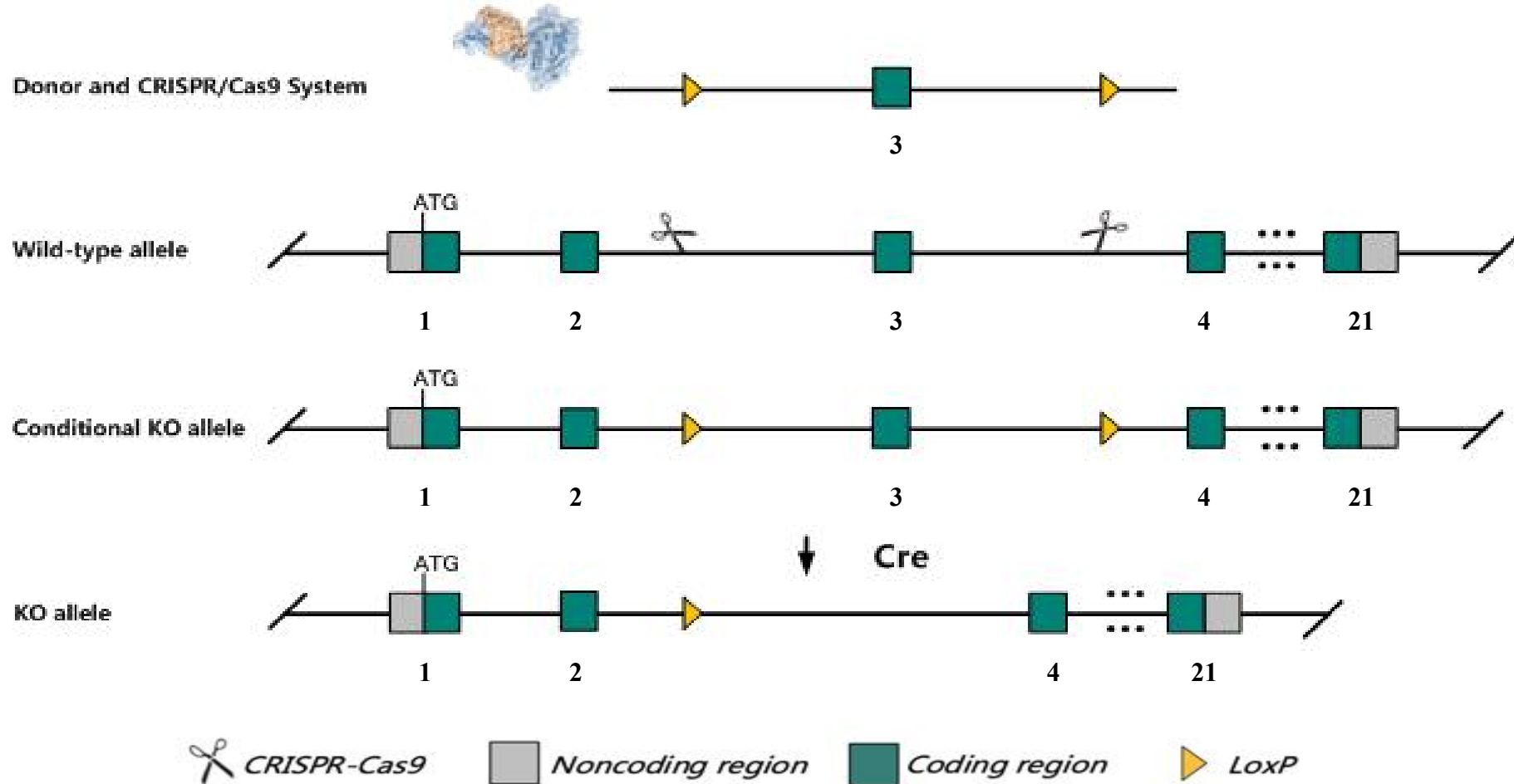
Project Type

- Cas9-CKO

Genetic Background

- C57BL/6JGpt

Strain Strategy



Schematic representation of CRISPR-Cas9 engineering used to edit the *Igflr* gene.

Technical Information

- The *Igf1r* gene has 6 transcripts. According to the structure of *Igf1r* gene, exon3 of *Igf1r*-201 (ENSMUST00000005671.10) transcript is recommended as the knockout region. The region contains 313bp coding sequence. Knocking out the region will result in disruption of protein function.
- In this project we use CRISPR-Cas9 technology to modify *Igf1r* gene. The brief process is as follows: CRISPR-Cas9 system and Donor were microinjected into the fertilized eggs of C57BL/6JGpt mice. Fertilized eggs were transplanted to obtain positive F0 mice which were confirmed by PCR and on-target amplicon sequencing. A stable F1-generation mouse strain was obtained by mating positive F0-generation mice with C57BL/6JGpt mice and confirmation of the desired mutant allele was carried out by PCR and on-target amplicon sequencing.
- The flox mice will be knocked out after mating with mice expressing Cre recombinase, resulting in the loss of function of the target gene in specific tissues and cell types.

Gene Information

Igf1r insulin-like growth factor I receptor [*Mus musculus* (house mouse)]

Download Datasets

Gene ID: 16001, updated on 26-Jun-2024

Summary

Official Symbol [Igf1r](#) provided by [MGI](#)
Official Full Name [insulin-like growth factor I receptor](#) provided by [MGI](#)
Primary source [MGI:MGI:96433](#)
See related [Ensembl:ENSMUSG00000005533](#) [AllianceGenome:MGI:96433](#)
Gene type protein coding
RefSeq status VALIDATED
Organism [Mus musculus](#)
Lineage Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Myomorpha; Muroidea; Muridae; Murinae; Mus; Mus
Also known as [hytt](#); [CD221](#); [IGF-1R](#); [D930020L01](#); [A330103N21Rik](#)
Summary Enables insulin-like growth factor binding activity. Involved in several processes, including adrenal gland development; positive regulation of cold-induced thermogenesis; and positive regulation of meiotic cell cycle. Acts upstream of or within several processes, including gland development; peptidyl-tyrosine autophosphorylation; and regulation of intracellular signal transduction. Located in T-tubule. Is integral component of membrane. Is expressed in several structures, including alimentary system; brain; genitourinary system; limb; and lung. Human ortholog(s) of this gene implicated in several diseases, including dementia (multiple); kidney cancer (multiple); liver disease (multiple); nervous system cancer (multiple); and neurodegenerative disease (multiple). Orthologous to human IGF1R (insulin like growth factor 1 receptor). [provided by Alliance of Genome Resources, Apr 2022]
Expression Ubiquitous expression in limb E14.5 (RPKM 10.6), kidney adult (RPKM 10.1) and 27 other tissues [See more](#)
Orthologs [human](#) [all](#)
NEW Try the new [Gene table](#)
Try the new [Transcript table](#)

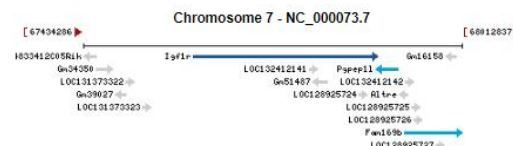
Genomic context

Location: 7 C; 7 37.27 cM

See Igf1r in [Genome Data Viewer](#)

Exon count: 24

Annotation release	Status	Assembly	Chr	Location
RS_2024_02	current	GRCm39 (GCF_000001635.27)	7	NC_000073.7 (67601486..67883416)
108.20200622	previous assembly	GRCm38.p6 (GCF_000001635.26)	7	NC_000073.6 (67952257..68233668)



Source: <https://www.ncbi.nlm.nih.gov/>

Transcript Information

The gene has 6 transcripts, all transcripts are shown below:

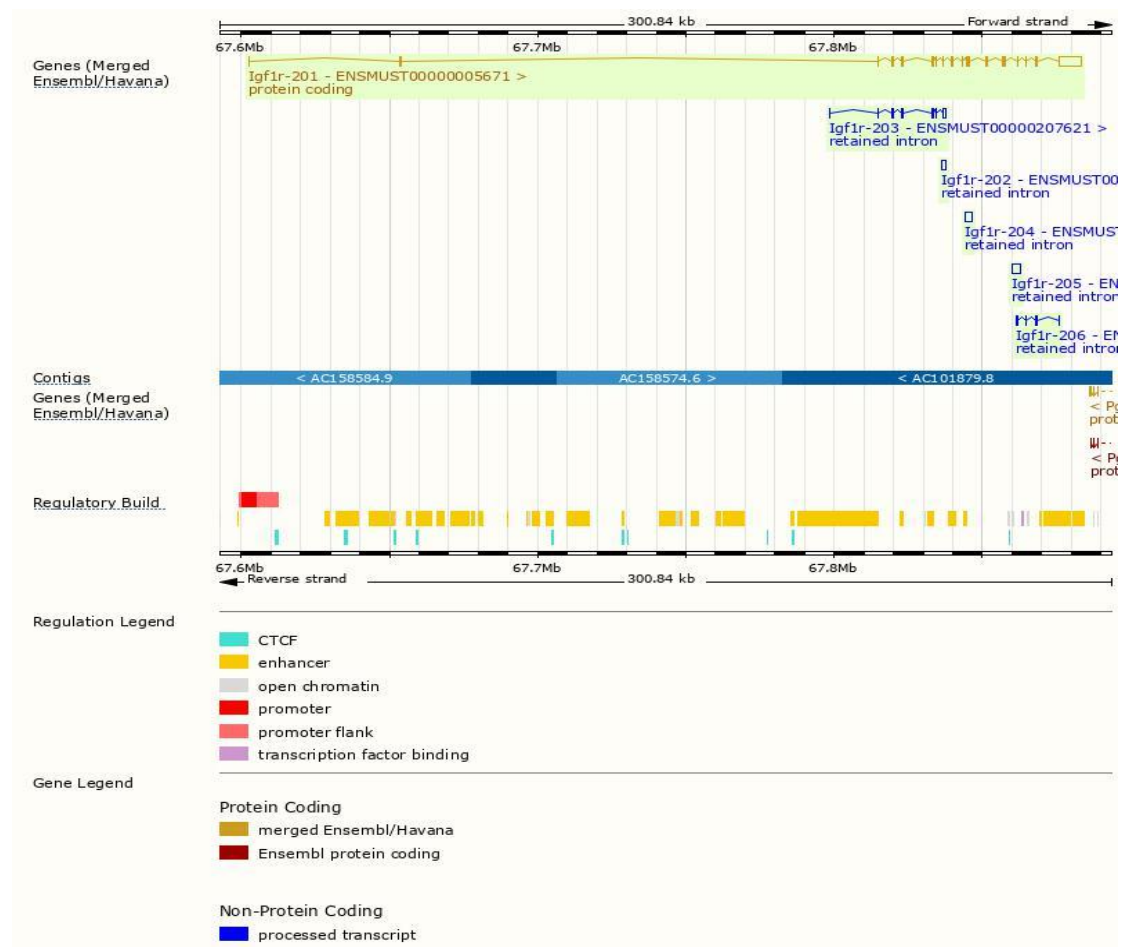
Transcript ID	Name	bp	Protein	Biotype	CCDS	UniProt Match	Flags
ENSMUST00000005671.10	Igf1r-201	11409	1369aa	Protein coding	CCDS21355	E9QNX9	Ensembl Canonical Gencode basic APPRIS P1 TSL:1
ENSMUST00000208731.2	Igf1r-205	2668	No protein	Retained intron		-	TSL:NA
ENSMUST00000207621.2	Igf1r-203	2050	No protein	Retained intron		-	TSL:2
ENSMUST00000208348.2	Igf1r-204	1945	No protein	Retained intron		-	TSL:NA
ENSMUST00000207487.2	Igf1r-202	1350	No protein	Retained intron		-	TSL:NA
ENSMUST00000208871.2	Igf1r-206	733	No protein	Retained intron		-	TSL:1

The strategy is based on the design of *Igf1r-201* transcript, the transcription is shown below:

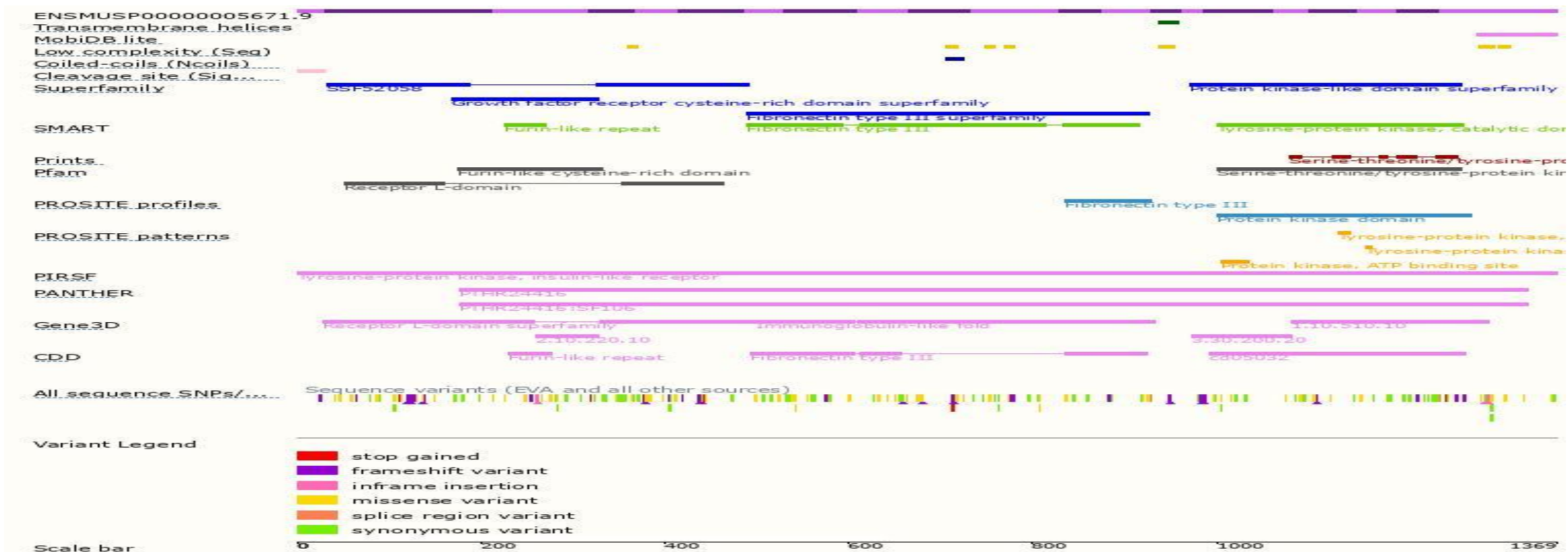


Source: <https://www.ensembl.org>

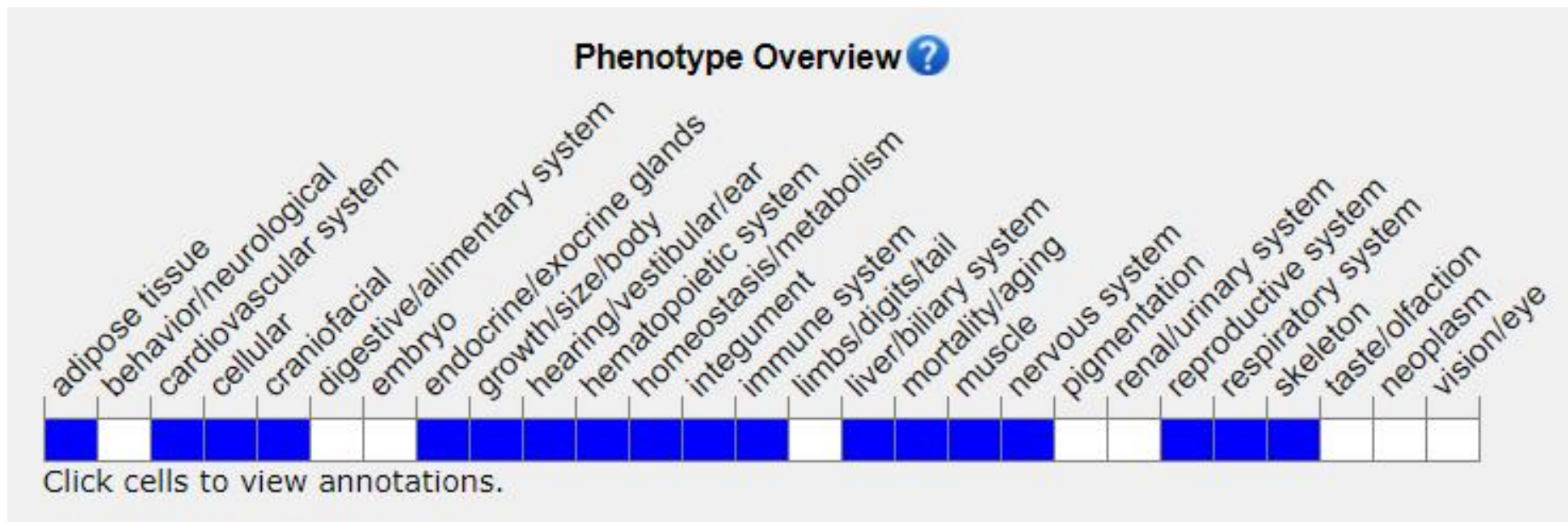
Genomic Information



Protein Information



Mouse Phenotype Information (MGI)

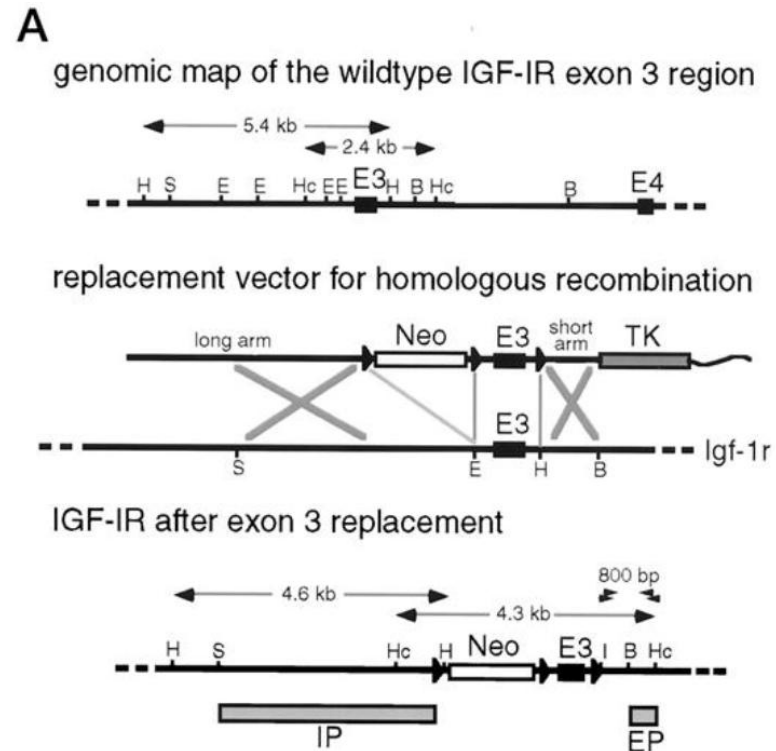


- Targeted null mutants die at birth of respiratory failure; fetuses exhibit retarded growth, organ hypoplasia, ossification delay and nervous system and epidermal abnormalities. hyft homozygous fetuses are growth retarded and exhibit hydrops fetalis and focal hepatic ischemia.

Important Information

- According to MGI information, targeted null mutants die at birth of respiratory failure; fetuses exhibit retarded growth, organ hypoplasia, ossification delay and nervous system and epidermal abnormalities. *hyft* homozygous fetuses are growth retarded and exhibit hydrops fetalis and focal hepatic ischemia.
- This strategy is designed based on existing literature, but does not guarantee a consistent phenotype.
- *Igf1r* is located on Chr7. If the knockout mice are crossed with other mouse strains to obtain double homozygous mutant offspring, please avoid the situation that the second gene is on the same chromosome.
- This Strategy is designed based on genetic information in existing databases. Due to the complexity of biological processes, all risk of loxp insertion on gene transcription, RNA splicing and protein translation cannot be predicted at the existing technology level.

Reference



To target the IGF-IR locus, we used a genomic region between the *SalI* site 4.3 kb upstream from exon 3 and the *Bam*HI site 850 bp downstream from exon 3 (Fig. 1A). A neomycin selection cassette, driven by a PGK promoter and equipped with *loxP* sites on both sides, was inserted into the *Eco*RI site 154 bp upstream from exon 3. A third *loxP* site, associated with an I-*Sce*I site, was inserted into the *Hind*III site 350 bp downstream from exon 3. The *Bam*HI site 0.5 kb downstream from *Hind*III was used to insert a PGK promoter-driven TK (thymidine kinase) cassette. The TK and *neo* genes were inserted in the opposite orientation to the IGF-IR gene. This construct was amplified in a 2.9-kb plasmid backbone (details of the construction

Holzenberger M, Leneuve P, Hamard G, Ducos B, Perin L, Binoux M, Le Bouc Y. A targeted partial invalidation of the insulin-like growth factor I receptor gene in mice causes a postnatal growth deficit. *Endocrinology*. 2000 Jul;141(7):2557-66. doi: 10.1210/endo.141.7.7550. PMID: 10875258.