GENETICALLY ENGINEERED MODELS (GEM)

NATURAL IMMUNO-DEFICIENT

WILD TYPE

NATURAL MUTANTS

MICE
Humanized

B6 hGLP-1R Mouse

Strain name:
C57BL/6Smoc-*Glp1r*$^{em2(hGLP1R)}$/SmocRj

Type: Humanized mouse, GMO

Origin: Shanghai Model Organism Center

Colour and related genotype:
Black mouse

Presentation of the model

The hGLP-1R mouse is a genetically engineered knock-in (KI) model, homozygous for the human Glucagon-Like Peptide-1 Receptor (hGLP-1R), developed to support translational research in diabetes, obesity, and metabolic disorders, particularly for therapeutic modalities specifically targeting the human receptor.

The model carries a humanized GLP-1R allele, in which the murine Glp1r coding sequence is replaced by or functionally substituted with the human GLP-1R gene, while preserving physiological expression patterns.

The GLP-1 receptor is a key regulator of glucose homeostasis, insulin secretion, appetite control, and energy balance. While murine and human GLP-1R share significant homology, species-specific differences exist in receptor sequence, ligand affinity, signaling dynamics, and pharmacological responsiveness, which can limit the predictive value of standard mouse models when evaluating human-specific GLP-1–based therapies.

To address this limitation, the hGLP-1R mouse has been engineered to express the human GLP-1R, allowing:
- Accurate assessment of human-specific agonists, antagonists, antibodies, and biologics (Figure 3 and 4)
- Improved translational relevance for PK/PD and efficacy studies
- Reduced risk of species-related false negatives during preclinical development

Key characteristics:
- Homozygous expression of human GLP-1R under endogenous regulatory control
- Preservation of tissue-specific expression (pancreatic β-cells, CNS, gut, peripheral tissues)

The model remains otherwise fully immunocompetent.

Main application and research fields

METABOLIC DISEASE

DIABETES RESEARCH

OBESITY PHARMACOLOGY

INCRETIN BIOLOGY

DRUG DISCOVERY

Our added value

- The «JANVIER LABS Genetic Policy», specific programme, guarantees homozygosity of autosomal pairs
- Animals with the SPF or SOPF standards
- A gentling policy for docile and easy-to-handle animals
- Optimal stability conditions of our models during shipments, thanks to our dedicated and internal transport service
- A scientific support with a team of Veterinarians and PhD

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Validation data:

Parameter	Units	C57BL6 F WT	C57BL6 M WT	C57BL6 hGLP1R F	C57BL6 hGLP1R M
WBC	(10^3/uL)	9.8±0.63	9.41±0.23	10.37±0.24	9.58±0.43
RBC	(10^6/uL)	10.97±0.08	10.39±0.21	9.43±0.27	9.18±0.25
HGB	(g/dL)	16.77±0.2	15.87±0.33	14.27±0.36	14.2±0.46
HCT	(%)	52.13±0.32	51.1±0.92	49.43±0.95	48.3±0.9
MCV	(fL)	47.5±0.17	49.1±0.36	52.6±0.17	52.67±0.41
MCH	(pg)	15.3±0.1	15.27±0.02	15.38±0.18	15.43±0.25
MCHC	(g/dL)	32.17±0.19	31.03±0.08	28.87±0.48	29.37±0.41
PLT	(10^3/uL)	1330.33±30.74	1649.67±76.12	1512±74.13	1807±57.73
RDW-SD	(fL)	28.43±0.1	30.97±0.2	36.77±1.85	33.2±1.13
RDW-CV	(%)	21.07±0.1	21.13±0.2	22.13±0.42	20.6±0.18
PDW	(fL)	7.4±0.03	7.5±0.09	7.23±0.18	6.97±0.1
MPV	(fL)	6.67±0.05	6.77±0.02	6.63±0.13	6.37±0.04
P-LCR	(%)	4.37±0.19	5.23±0.13	4.73±0.59	3.57±0.17
PCT	(%)	0.89±0.02	1.12±0.05	0.99±0.03	1.15±0.04
NEUT#	(10^3/uL)	0.85±0.07	1.6±0.22	0.45±0.02	0.47±0.03
LYMPH#	(10^3/uL)	8.3±0.57	7.07±0.08	9.47±0.23	8.67±0.42
MONO#	(10^3/uL)	0.41±0.02	0.62±0.07	0.28±0.01	0.31±0.02
EO#	(10^3/uL)	0.24±0.02	0.12±0.01	0.16±0.01	0.12±0.0
BASO#	(10^3/uL)	0.01±0.0	0±0	0.01±0.0	0.01±0.0
NEUT	(%)	8.6±0.41	16.7±2.05	4.37±0.08	4.97±0.39
LYMPH	(%)	84.57±0.59	75.43±2.52	91.33±0.11	90.43±0.41
MONO	(%)	4.33±0.54	6.5±0.64	2.67±0.14	3.23±0.25
EO	(%)	2.43±0.1	1.33±0.17	1.57±0.17	1.3±0.09
BASO	(%)	0.07±0.02	0.03±0.02	0.07±0.02	0.07±0.02

Table 1. Hematological parameters comparing C57BL6 wild-type mice to C57BL6 hGLP1R mice (Data are presented as mean and ± SEM).

Parameter	Units	C57BL6 F WT	C57BL6 M WT	C57BL6 hGLP1R F	C57BL6 hGLP1R M
ALT	(U/L)	28.67±0.96	38.67±1.07	24.67±0.69	26.67±0.51
AST	(U/L)	56±1.2	62.67±0.96	54.67±0.38	54.33±1.26
UREA	(mmol/L)	11.23±0.47	11.27±0.68	9.53±0.08	10.73±0.25
CRE	(µmol/L)	13.49±0.51	8.4±0.08	14.85±0.23	15.67±0.08
HDL-C	(mmol/L)	1.67±0.01	1.84±0.04	1.78±0.05	2.03±0.02
LDL-C	(mmol/L)	0.56±0.01	0.44±0	0.57±0.01	0.46±0.01
TCHO	(mmol/L)	2.25±0.01	2.58±0.05	2.49±0.04	2.76±0.02
TG	(mmol/L)	0.9±0.04	1.55±0.05	1.27±0.07	1.67±0.05
UA	(µmol/L)	148.93±2.59	117.9±3.15	114.3±5.05	105.93±1.93

Table 2. Biochemical blood parameters comparing C57BL6 wild-type mice to C57BL6 hGLP1R mice (Data are presented as mean and ± SEM).

Validation data:

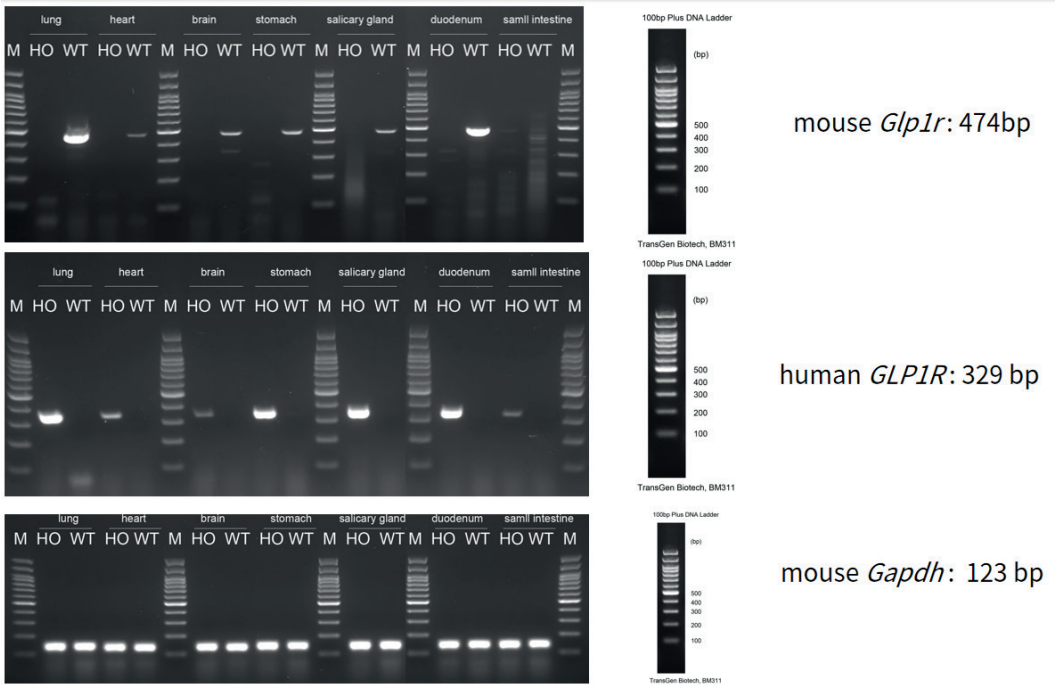

Fig 1. Detection of GLP1R and Gapdh expression in lung, heart, brain, stomach, salivary gland, duodenum and samll intestine by RT-PCR.

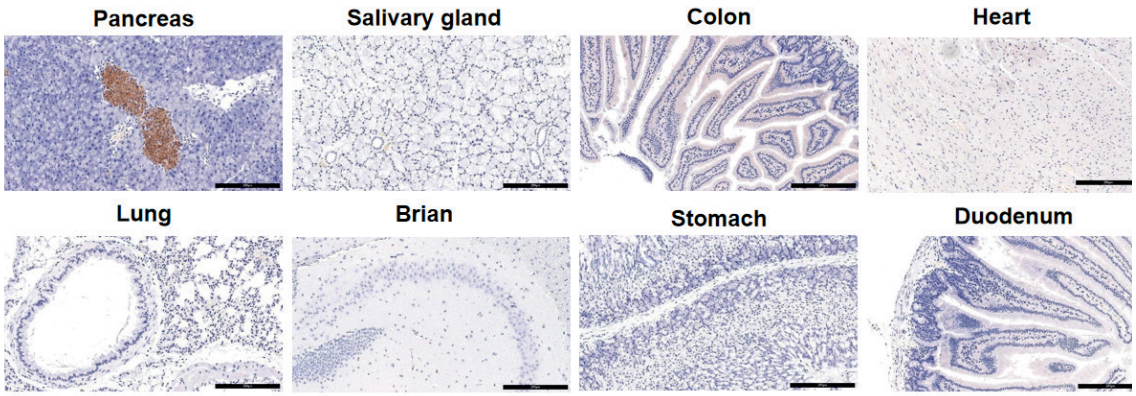

Fig 2. Detection of human GLP-1R expression in hGLP-1R mice by IHC. Pancreas, salivary gland, colon, heart, lung, brian, stomach and duodenum were collected from homozygous hGLP-1R mice (HO/HO), and analyzed by IHC with anti-human GLP-1R antibody. Human GLP-1R is specifically expressed in islets of the pancreas.

Validation data:

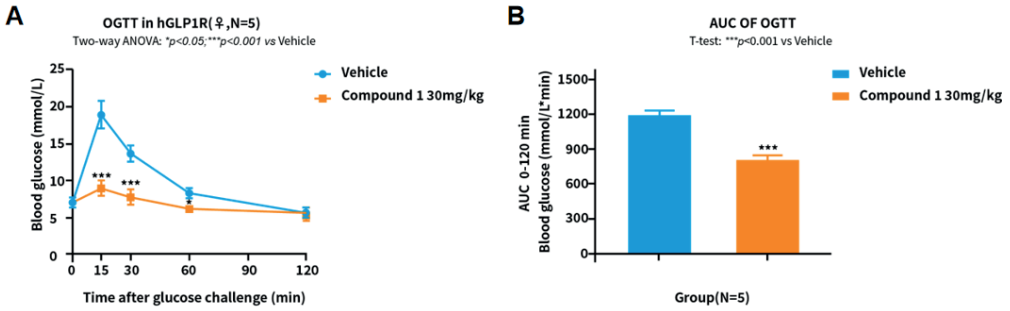

Fig 3. Validation of the hypoglycemic efficacy of the test compound in humanized GLP-1R mice. The oral glucose tolerance test (OGTT) was performed (n=5), and the test compound showed a better hypoglycemic efficacy (p<0.001). The above data indicated that the GLP-1R humanized mouse is an effective model for diabetes drug screening.

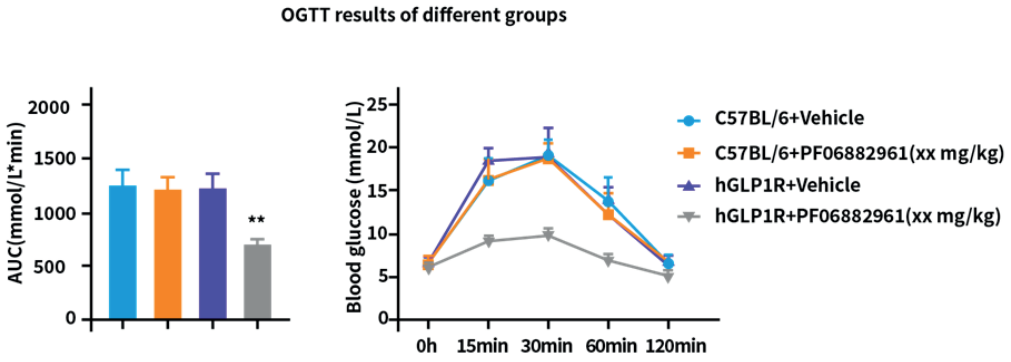

Fig 4. Efficacy study of PF06882961 in hGLP1R mice. PF06882961 has shown significant effect in hGLP1R mice in OGTT study, but no effect in C57BL/6 mice.

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