# hGLP1R

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|---|---|
| **Nomenclature** | C57BL/6Smoc-*Glp1r*$^{em2(hGLP1R)Smoc}$ |
| **Cat. NO.** | NM-HU-200220 |
| **Strain State** | Repository Live |

## Gene Summary

| | | |
|---|---|---|
| **Gene Symbol Glp1r** | **Synonyms** | GLP-1R; GLP1Rc |
| | **NCBI ID** | 14652 |
| | **MGI ID** | 99571 |
| | **Ensembl ID** | ENSMUSG00000024027 |
| | **Human Ortholog** | GLP1R |

## Model Description

The endogenous mouse Glp1r gene was completely or partially replaced by human hGLP1R gene via CRISPR/Cas9 mediated recombination.

**Research Application**:  Diabetes research; drug screening

*Literature published using this strain should indicate: hGLP1R mice (Cat. NO. NM-HU-200220) were purchased from Shanghai Model Organisms Center, Inc..
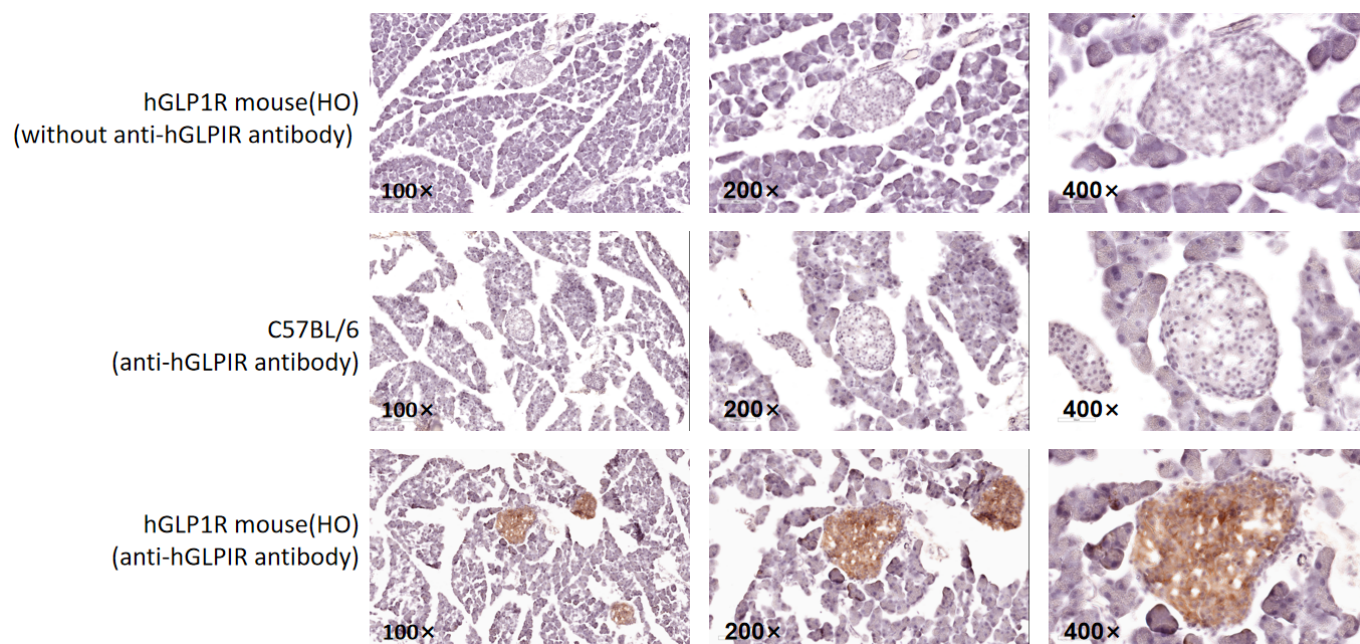
## Validation Data

Fig1. Analysis of hGLP1R expression by IHC. Pancreata from wild-type and hGLP1R mice (HO) were stained using an antibody specific for human GLP1R, and only the pancreas from hGLP1R mice (HO) showed hGLP1R positive signal in pancreatic islet.
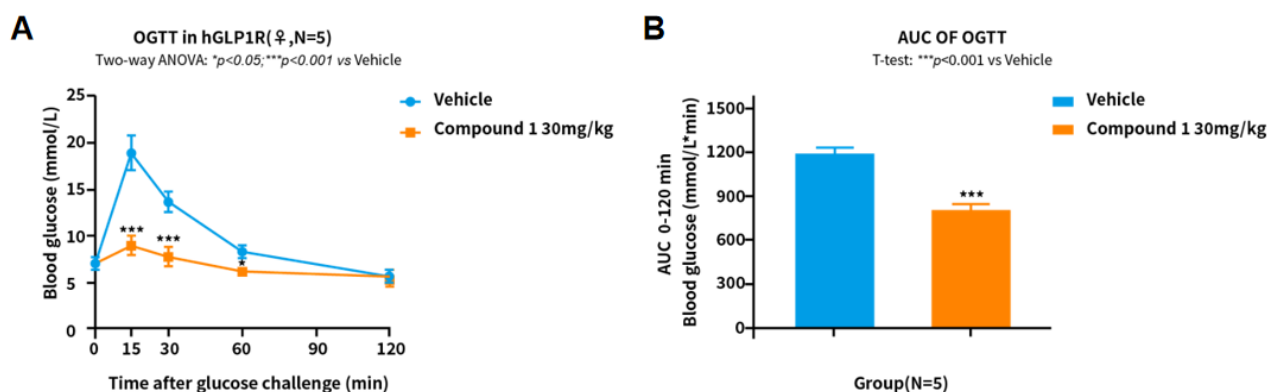


Fig2. Validation of the hypoglycemic efficacy of the test compound in humanized GLP-1R mice. The oral glucose tolerance test (OGTT) was performed (n=5), and the test compound showed a better hypoglycemic efficacy (p<0.001). The above data indicated that the GLP-1R humanized mouse is an effective model for diabetes drug screening.
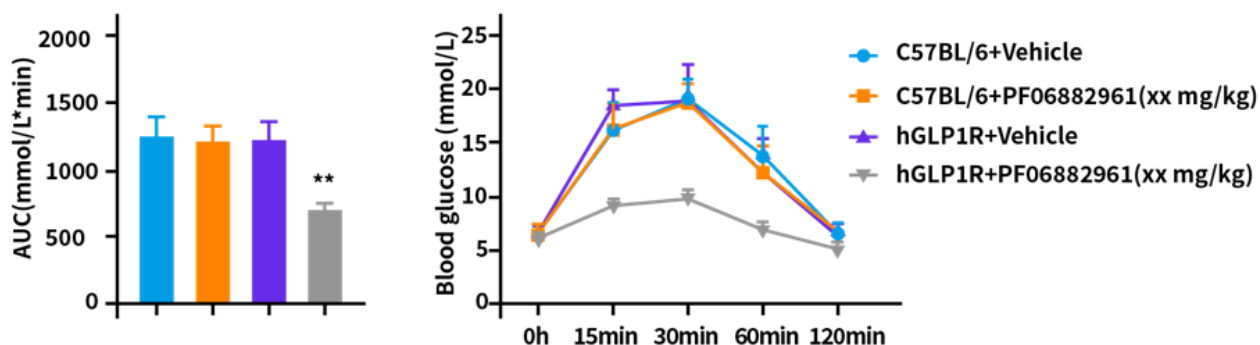
**OGTT results of different groups**



Fig 3. 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.
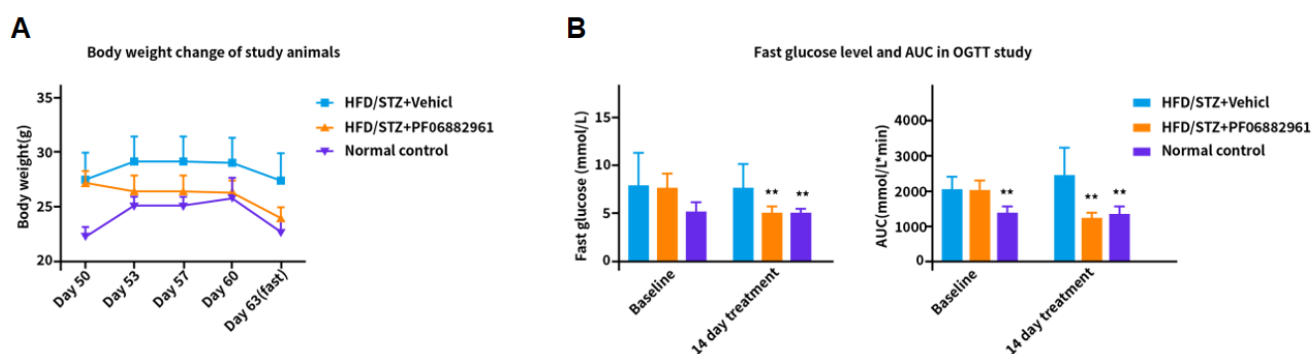


Fig 4. Efficacy study of PF06882961 in HFD/STZ induced type II diabetes model in hGLPIR mice. PF06882961 could significant decreases the body weight(A); PF06882961 could significantly decrease fast blood glucose level and AUC in OGTT study (B).
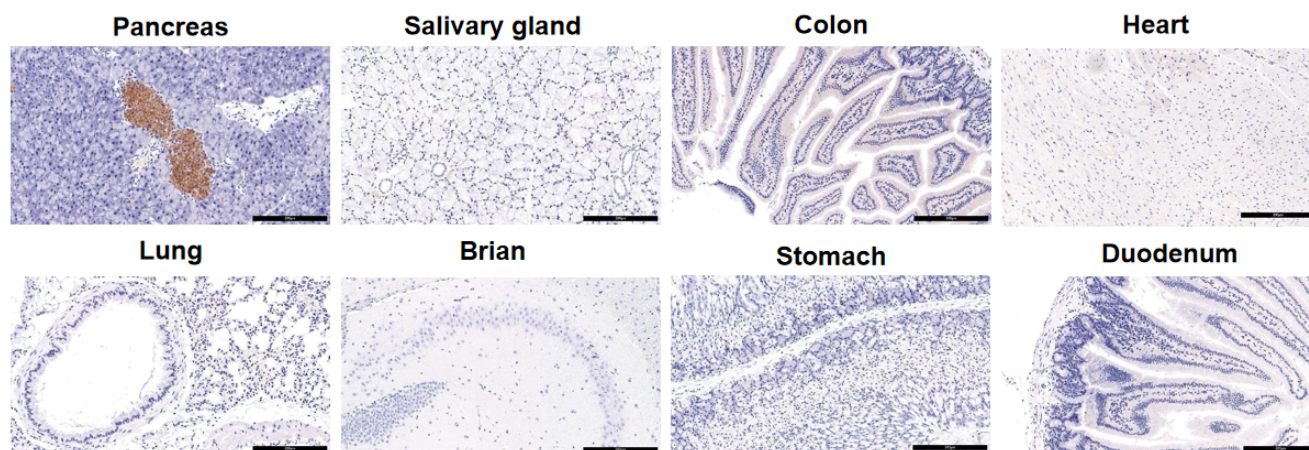


Fig5. Detection of human GLP-1R expression in HO hGLP-1R knockin mice by IHC. Pancreas, salivary gland, colon, heart, lung, brian, stomach and duodenum were collected from

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. Abbr. HO/HO, homozygous.

Table1. Blood routine test results of Hom hGLP-1R mice (Data are presented as mean and ± SEM).

| Parameter | Full Name | Units | WT C57BL/6 ♀ 7 weeks; n=3 | WT C57BL/6 ♂ 7 weeks; n=3 | HO hGLP1R ♀ 7 weeks; n=3 | HO hGLP1R ♂ 7 weeks; n=3 |
|---|---|---|---|---|---|---|
| WBC | White blood cell count | (10^3/uL) | 9.8±0.63 | 9.41±0.23 | 10.37±0.24 | 9.58±0.43 |
| RBC | Red blood cell count | (10^6/uL) | 10.97±0.08 | 10.39±0.21 | 9.43±0.27 | 9.18±0.25 |
| HGB | Hemoglobin | (g/dL) | 16.77±0.2 | 15.87±0.33 | 14.27±0.36 | 14.2±0.46 |
| HCT | Hematocrit | (%) | 52.13±0.32 | 51.1±0.92 | 49.43±0.95 | 48.3±0.93 |
| MCV | Mean corpuscular volume | (fL) | 47.5±0.1 | 49.2±0.12 | 52.6±1.44 | 52.67±0.41 |
| MCH | Mean corpuscular hemoglobin | (pg) | 15.3±0.1 | 15.27±0.02 | 15.13±0.18 | 15.43±0.08 |
| MCHC | Mean corpuscular hemoglobin concentration | (g/dL) | 32.17±0.19 | 31.03±0.08 | 28.87±0.48 | 29.37±0.41 |
| PLT | Platelet count | (10^3/uL) | 1330.33±30.74 | 1649.67±76.12 | 1512±74.13 | 1807±57.73 |
| RDW-SD | Red blood cell distribution width-standard deviation | (fL) | 28.43±0.1 | 30.97±0.2 | 36.77±1.85 | 33.2±1.13 |
| RDW-CV | Red blood cell distribution width-coefficient of variation | (%) | 21.07±0.1 | 21.13±0.2 | 22.13±0.42 | 20.6±0.18 |
| PDW | Platelet volume distribution width | (fL) | 7.4±0.03 | 7.5±0.09 | 7.23±0.18 | 6.97±0.08 |
| MPV | Mean platelets volume | (fL) | 6.67±0.05 | 6.77±0.02 | 6.63±0.13 | 6.37±0.04 |
| P-LCR | Platelet-larger cell ratio | (%) | 4.37±0.19 | 5.23±0.13 | 4.73±0.59 | 3.57±0.17 |
| PCT | Platelet hematocrit | (%) | 0.89±0.02 | 1.12±0.05 | 0.99±0.03 | 1.15±0.04 |
| NEUT# | Neutrophil count | (10^3/uL) | 0.85±0.07 | 1.6±0.22 | 0.45±0.02 | 0.47±0.03 |
| LYMPH# | Lymphocyte count | (10^3/uL) | 8.3±0.57 | 7.07±0.08 | 9.47±0.23 | 8.67±0.42 |
| MONO# | Monocyte count | (10^3/uL) | 0.41±0.02 | 0.62±0.07 | 0.28±0.01 | 0.31±0.02 |
| EO# | Eosinophil count | (10^3/uL) | 0.24±0.02 | 0.12±0.01 | 0.16±0.02 | 0.12±0 |
| BASO# | Basophil count | (10^3/uL) | 0.01±0 | 0±0 | 0.01±0 | 0.01±0 |
| NEUT% | Neutrophil ratio | (%) | 8.6±0.41 | 16.7±2.05 | 4.37±0.08 | 4.97±0.39 |
| LYMPH% | Lymphocyte ratio | (%) | 84.57±0.59 | 75.43±2.52 | 91.33±0.11 | 90.43±0.41 |
| MONO% | Monocyte ratio | (%) | 4.33±0.54 | 6.5±0.64 | 2.67±0.14 | 3.23±0.25 |
| EO% | Eosinophil ratio | (%) | 2.43±0.1 | 1.33±0.17 | 1.57±0.17 | 1.3±0.09 |
| BASO% | Basophil ratio | (%) | 0.07±0.02 | 0.03±0.02 | 0.07±0.02 | 0.07±0.02 |

Table2. Biochemistry examinations results of Hom hGLP-1R mice (Data are presented as mean and ± SEM).

| Parameter | Full Name | Units | WT C57BL/6 ♀ 7 weeks; n=3 | WT C57BL/6 ♂ 7 weeks; n=3 | HO hGLP1R ♀ 7 weeks; n=3 | HO hGLP1R ♂ 7 weeks; n=3 |
|---|---|---|---|---|---|---|
| ALT | Alanine Aminotransferase | (U/L) | 28.67±0.96 | 38.67±1.07 | 24.67±0.69 | 26.67±0.51 |
| AST | Aspartate Aminotransferase | (U/L) | 56±1.2 | 62.67±0.96 | 54.67±0.38 | 54.33±1.26 |
| UREA | Urea | (mmol/L) | 11.23±0.47 | 11.27±0.68 | 9.53±0.08 | 10.73±0.25 |
| CRE | Creatinine | (μmol/L) | 13.49±0.51 | 8.4±0.08 | 14.85±0.23 | 15.67±0.08 |
| HDL-C | High Density Lipoprotein Cholesterol | (mmol/L) | 1.67±0.01 | 1.84±0.04 | 1.78±0.05 | 2.03±0.02 |
| LDL-C | Low Density Lipoprotein Cholesterol | (mmol/L) | 0.56±0.01 | 0.44±0 | 0.57±0.01 | 0.46±0.01 |
| TCHO | Total Cholesterol | (mmol/L) | 2.25±0.01 | 2.58±0.05 | 2.49±0.04 | 2.76±0.02 |
| TG | Triglyceride | (mmol/L) | 0.9±0.04 | 1.55±0.05 | 1.27±0.07 | 1.67±0.05 |
| UA | Uric acid | (μmol/L) | 148.93±2.59 | 117.9±3.15 | 114.3±5.05 | 105.93±1.93 |