B6-hGLP-1R

Strain Name： B6/JGpt-*Glp1r*$^{em1Cin(hGLP1R)}$/Gpt
Strain Type： Knock-in
Strain Number： T053832
Background： C57BL/6JGpt

Description

Glucagon like peptide 1 receptor, also known as GLP-1,GLP-1R and GLP-1-R. GLP-1R belongs to the glucagon receptor subfamily of G protein-coupled receptor cluster B and is typically characterized by a seven-transmembrane core domain and a large extracellular domain[1]. GLP-1 is exteracted from intestines, can promote glucose-dependent insulin secretion, than GLP-1 is classified as an incretin hormone[2]. Currently, long-acting GLP-1 analogs are used as pharmacological therapies for Type 2 diabetes[3]. Furthermore, GLP-1 can inhibit the release of glucagon and cause satiety. Until 2021, incretin hormone drugs are all based on GLP-1 in clinical. GLP-1R is widely distributed in the brain, small intestine, heart, lung and other tissues. It exerts physiological functions when it is activated by GLP-1 or GLP-1R agonists[4]. Studies have found that GLP-1R signaling can reduce food intake and body weight by action through multiple brain regions in the neuraxis[5]. In the gastrointestinal tract, GLP-1R can play a variety of functions such as inhibit the secretion of gastric juice and the intestinal peristalsis, delay gastric emptying, increase satiety, and reduce food intake[6]. In addition, GLP-1R can prevent oxidative stress-mediated apoptosis of human cardiac progenitor cells, improve cardiovascular function, and play a cardioprotective role[7]. Therefore, targeted GLP-1R can develop a variety of metabolic diseases drugs to meet more indications.

GemPharmatech use CRISPR/Cas9 technology to modify the GLP-1R gene, replacing the mouse GLP-1R gene with human GLP-1R and carrying the human 3'UTR. This strain can successfully express human GLP-1R, the humanized model of GLP-1R is an ideal animal model for drug development of metabolic diseases such as obesity and type II diabetes.

Strategy

This model will use CRISPR/Cas9 technology to edit the mouse *Glp1r* gene. The schematic diagram is as follows:

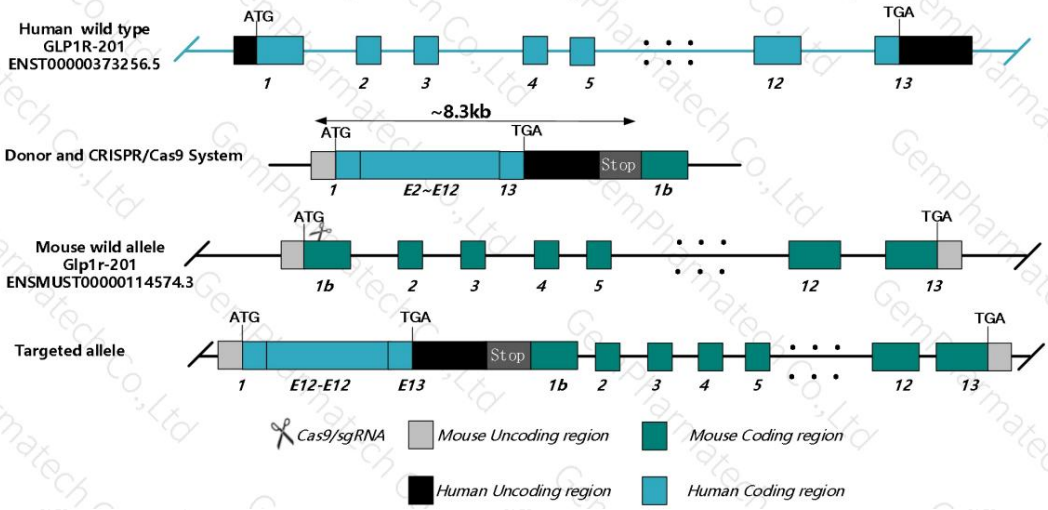

Fig.1 Schematic diagram of B6-hGLP-1R model strategy

Applications

1. Type II diabetes or obesity research;
2. The drug development of type II diabetes or obesity: GLP-1 analogs, small molecule non-peptide GLP-1R agonists, dual/triple agonists.

Data support

1. The expression of *hGLP-1R* in brain and lung

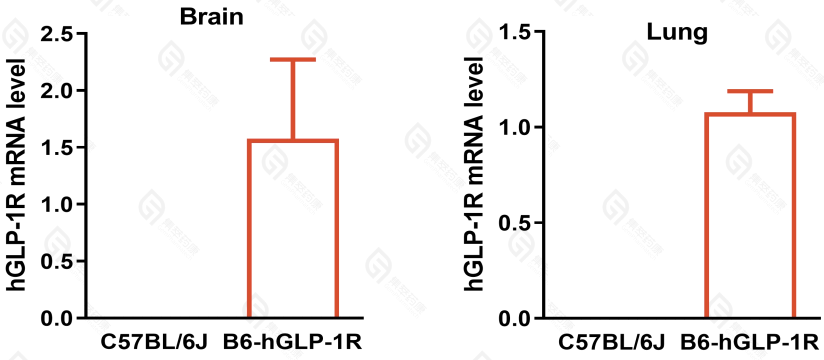

Fig 2. The expression of *hGLP-1R* in brain and lung

hGLP-1R expresses in brain and lung of homozygous B6-hGLP-1R mice. C57BL/6J mice (n=3-6, 8 weeks), B6-hGLP-1R mice (n=3-6, 8 weeks).

2. The expression of *mGlp-1r* in brain and lung

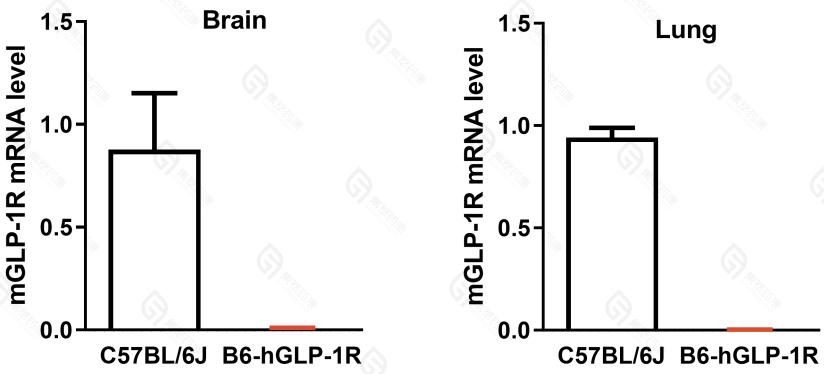

Fig 3. The expression of *mGlp-1r* in brain and lung

mGlp-1r does not express in brain and lung tissues of homozygous B6-hGLP-1R mice. C57BL/6J mice (n=3-6, 8 weeks), B6-hGLP-1R mice (n=3-6, 8 weeks).

3. The level of hGLP-1R protein in pancreas by IHC

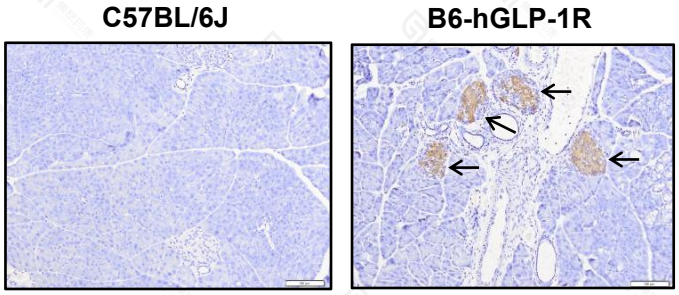

Fig 4. The level of hGLP-1R protein in pancreas

The human GLP-1R is highly expressed in pancreas tissues of homozygous B6-hGLP-1R mice. C57BL/6J mice (n=2, female, 5 weeks), B6-hGLP-1R mice (n=2, female, 5 weeks). Scale Bar=100 μm.

Risk alarm

The human GLP-1R protein level of this strain expressed highly in pancreatic tissue, and the GLP-1R protein level in other tissues has no data.

References

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