BALB/c-hGPC3

Strain Name: BALB/cJGpt-*GPC3*$^{em1Cin(hGPC3)}$/Gpt
Strain Type: Knock-in
Strain Number: T054198
Background: BALB/cJGpt

Description

Glypican 3 (GPC3) is a member of the family of glypican heparan sulfate proteoglycans (HSPGs), located on chromosome X of human [1]. GPC3 is highly expressed during human embryonic development, while only expressed in lung, ovaries, mammary epithelium, and mesothelium in adult [2]. It has been confirmed that GPC3 is highly expressed in esophageal carcinoma, glioblastoma multiforme, hepatocellular carcinoma, pancreatic cancer, thymic cancer and uterine cancer [3]. Especially in hepatocellular carcinoma, GPC3 exhibits higher expression than AFP (alpha-fetoprotein) [4]. Patients with GPC3 low-expression hepatocellular carcinoma had a longer median overall survival compared with the patients with GPC3 high-expression [3]. GPC3 accelerates HCC progression via involving in Wnt signaling pathway, Hippo signaling pathway and FGF signaling pathway. There are many effective treatment that target GPC3, such as GPC3 monoclonal antibody, GPC3/CD3 double-antibody, GPC3 CAR-T therapy and so on. Despite its effective anticancer efficacy, GPC3 antibody exerts many undesirable adverse effects, including cytokine release syndrome (CRS), hyperpyrexia, liver failure even death. Attention must be paid to toxicity issues during the development of GPC3 antibody.

GemPharmatech used CRISPR/Cas9 gene editing technology to substitute the partial region of mouse GPC3 with the CDS region of human GPC3 on BALB/cJGpt background. This model can successfully express human GPC3 protein. These mice are suitable models for evaluating anti-GPC3 drug efficacy and toxicy, in particular anti-GPC3 drug safety in vivo.

Strategy

Fig.1 Schematic diagram of BALB/c-hGPC3 model strategy.

Applications

1. Efficacy evaluation of human anti-GPC3 drugs.
2. Drug safety evaluation of human anti-GPC3 drugs.

Data support

1. mRNA expression of human GPC3

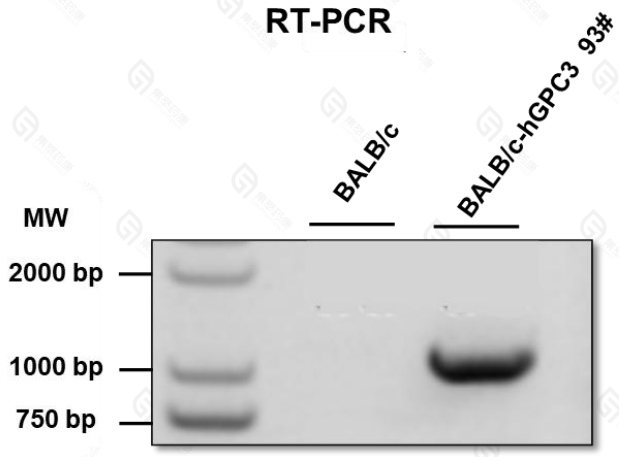

Fig 2. Detection of human GPC3 mRNA expression on kidney of heterozygous BALB/c-hGPC3. Human GPC3 mRNA can be detected in kidney of heterozygous BALB/c-hGPC3 by RT-PCR, while that can't be detected on wild-type BALB/c mouse.

2. Protein expression of human GPC3

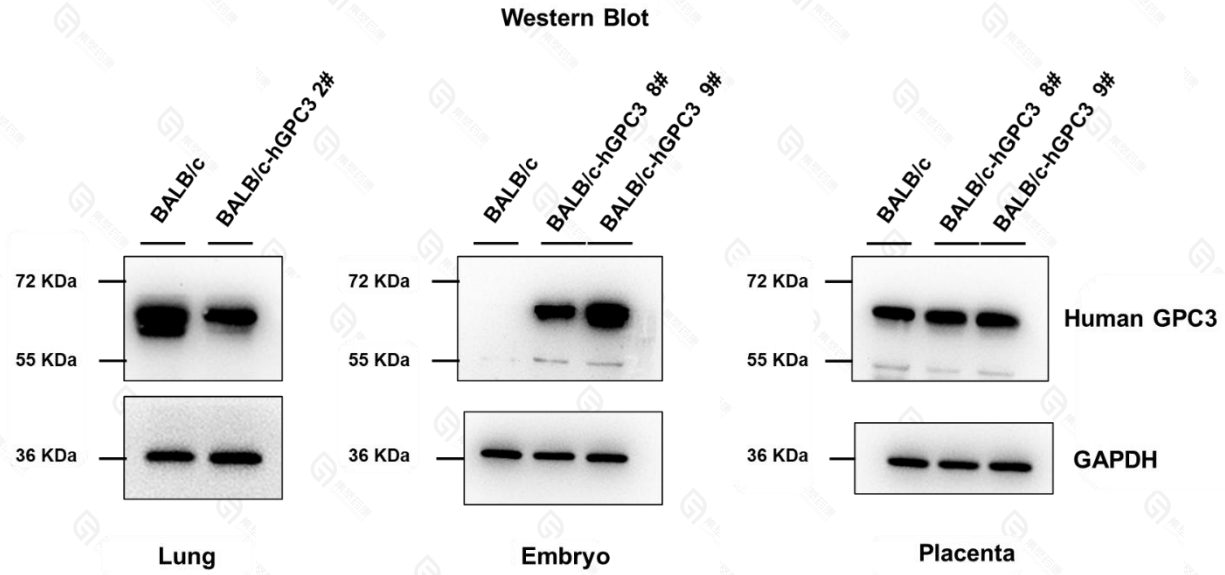

Fig 3. Detection of human GPC3 protein expression on lung, embryos and placenta of homozygous BALB/c-hGPC3.

Human GPC3 protein can be detected in lung, embryos and placenta of homozygous BALB/c-hGPC3 successfully. (Anti-human GPC3 antibody can cross-react with mouse GPC3 protein)

References

1. Hattab, E.M., 18 - Germ Cell Tumors, in Practical Surgical Neuropathology: A Diagnostic Approach (Second Edition), A. Perry and D.J. Brat, Editors. 2018, Elsevier. p. 423-442.
2. Walesky, C. and U. Apte, Chapter 7 - Mechanisms of Termination of Liver Regeneration, in Liver Regeneration, U. Apte, Editor. 2015, Academic Press: Boston. p. 103-111.
3. Zheng, X., et al., Glypican-3: A Novel and Promising Target for the Treatment of Hepatocellular Carcinoma. Frontiers in Oncology, 2022. 12.
4. Hsu, H.C., W. Cheng, and P.L. Lai, Cloning and expression of a developmentally regulated transcript MXR7 in hepatocellular carcinoma: biological significance and temporospatial distribution. Cancer Res, 1997. 57(22): p. 5179-84.