BALB/c-hLRRC15

Strain Name: BALB/cJGpt-*Lrrc15*$^{em1Cin(hLRRC15)}$/Gpt
Strain Type: Knock-in
Strain Number: T056083
Background: BALB/cJGpt

Description

One of the most studied components of the tumor microenvironment, cancer-associated fibroblasts (CAF), play a crucial role in increased tumorigenesis and resistance to therapy through immunomodulation, promoting angiogenesis[1]. The protein leucine-rich repeat-containing 15 (LRRC15), is highly expressed in TGF/β–driven CAFs and serves as a marker of this CAF subpopulation in the tumor microenvironment. Normally, LRRC15 displays a highly restricted expression pattern, but is expressed in areas that make up innate immune barriers such as the placenta, skin, activated fibroblasts in wounds, and lymphoid tissues such as the spleen. LRRC15 is also expressed in the cells of multiple tumor types. ADC drug targeting LRRC15 was demonstrated to suppress the tumor development[2].

GemPharmatech used CRISPR/Cas9 gene editing technology to substitute the extracellular region of mouse LRRC15 with the corresponding region of human LRRC15 on BALB/cJGpt background, and normal intracellular signal transduction was retained. Developed the BALB/c-hLRRC15 humanized mouse model, this model can successfully express human LRRC15. These mice are suitable models for evaluating anti-LRRC15 drug efficacy and toxicy, in particular anti-LRRC15 drug safety in vivo.

Strategy

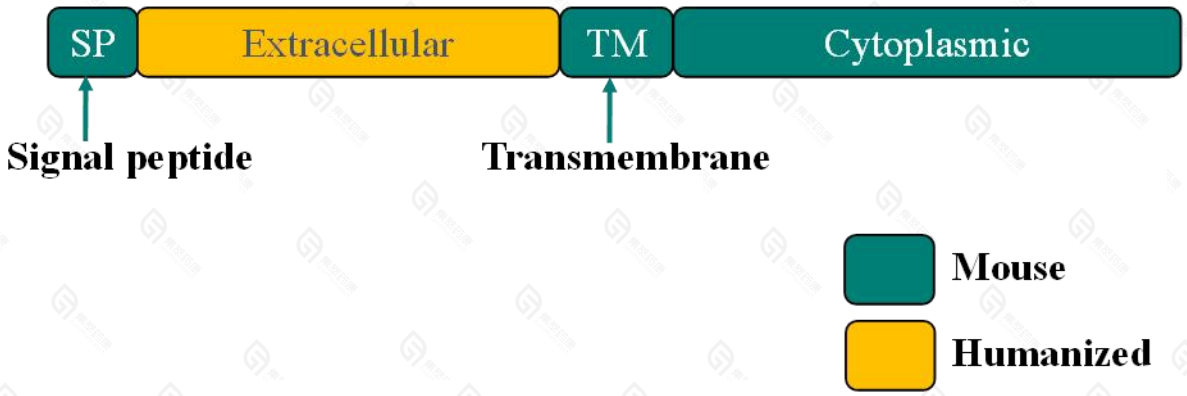

Fig.1 Schematic diagram of BALB/c-hLRRC15 model strategy.

Applications

1. Efficacy evaluation of human anti-LRRC15 drugs.
2. Drug safety evaluation of human anti-LRRC15 drugs.

Data support

1. mRNA expression of human LRRC15

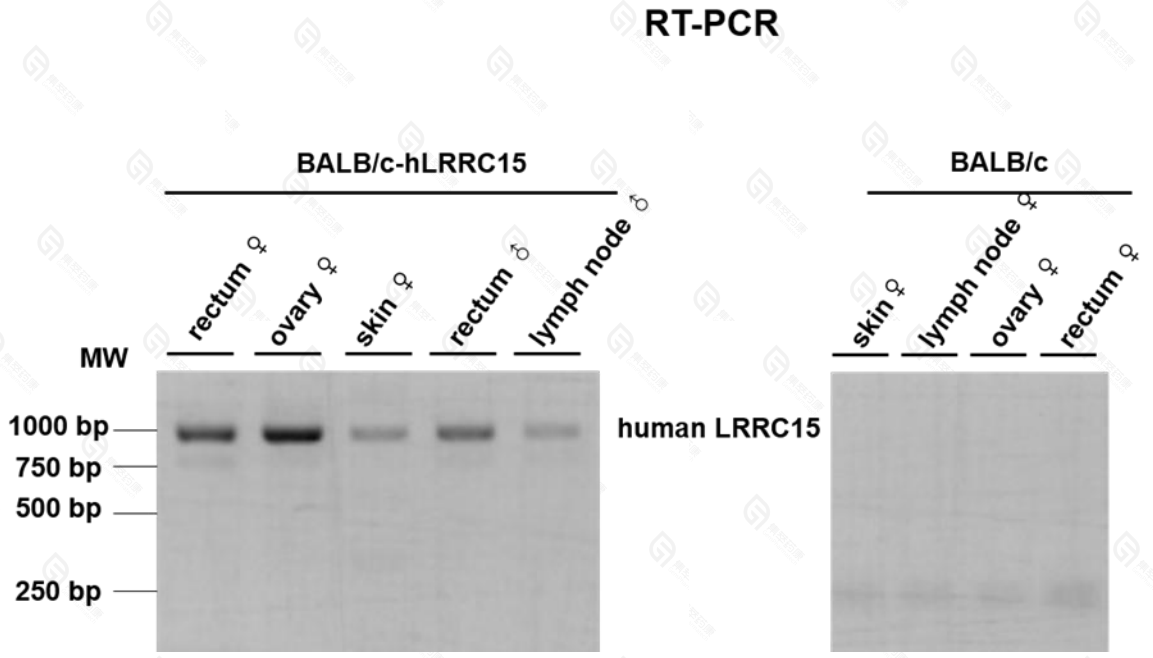

Fig 2. Detection of human LRRC15 mRNA expression on heterozygous BALB/c-hLRRC15. Rectum, ovary, skin and lymph node of heterozygous adult BALB/c-hLRRC15 can successfully express human LRRC15 mRNA.

2. Protein expression of human LRRC15

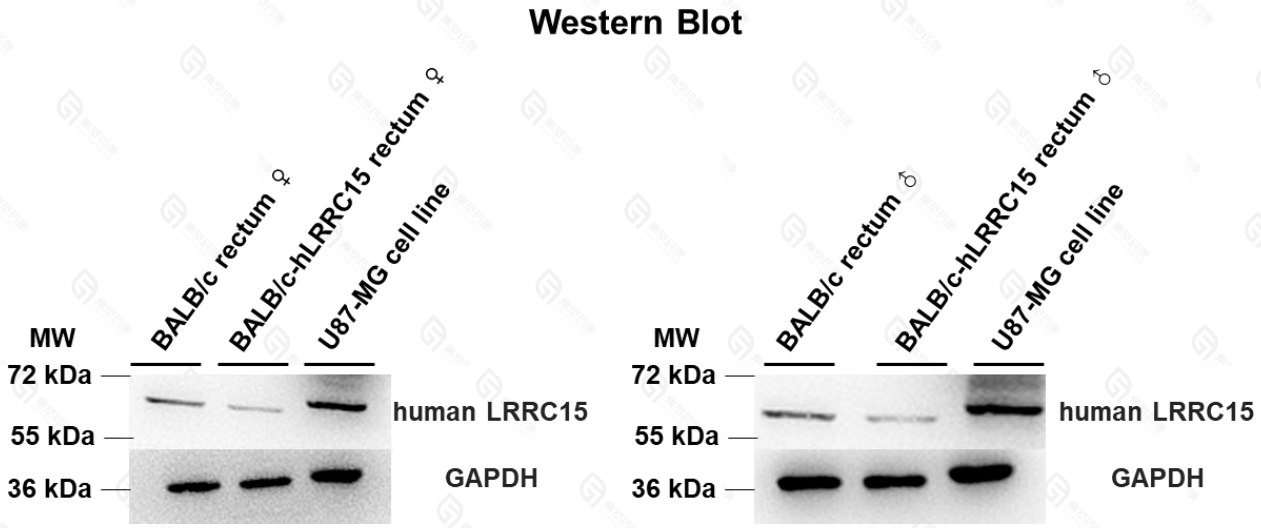

Fig 3. Detection of human LRRC15 protein expression on homozygous BALB/c-hLRRC15. Human U87-MG cell line was incorporated as positive control. Human LRRC15 protein can be detected in the homozygous BALB/c-hLRRC15 rectum. (Anti-human LRRC15 antibody can cross-react with mouse LRRC15 protein)

References

1. Ray, U., et al., Exploiting LRRC15 as a Novel Therapeutic Target in Cancer. Cancer Res, 2022. 82(9): p. 1675-1681.
2. Hingorani, P., et al., ABBV-085, Antibody-Drug Conjugate Targeting LRRC15, Is Effective in Osteosarcoma: A Report by the Pediatric Preclinical Testing Consortium. Mol Cancer Ther, 2021. 20(3): p. 535-540.