

BALB/c-hMSLN

Strain Name: BALB/cJGpt-*Msln*^{em1Cin(hMSLN)}/Gpt

Strain Type: Knock-in

Strain Number: T036851

Background: BALB/cJGpt

Description

Mesothelin (MSLN) is a glycosylphosphatidylinositol (GPI)-linked cell surface protein, which is normally expressed in mesothelial cells that line the pleura, peritoneum, and pericardium at a low level^[1]. The biologic function of MSLN is not well known, however, currently no detectable abnormalities were reported in growth and reproduction in MSLN deficient mouse model^[2].

MSLN is highly expressed in several types of malignant tumors, such as mesothelioma, pancreatic cancer, ovarian cancer, and lung adenocarcinomas^[1,3]. What's more, recent studies indicated that MSLN may play an important role in cancer cell adherence, cancer cell survival/proliferation, tumor progression and chemoresistance^[3,4]. Thus, MSLN is a promising target for antibody-based cancer therapy and CAR-T therapy.

GemPharmatech use gene editing technology to replace the MSLN transcript of BALB/c mice with the corresponding fragment of human MSLN, and developed BALB/c-hMSLN humanized model. These mice are ideal models for evaluation of the efficacy and safety of MSLN targeting drugs.

Strategy



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

Applications

1. Efficacy Evaluation of MSLN Targeted Drugs
2. Safety study of MSLN targeted drugs

Data support

1. Detection of *MSLN* expression

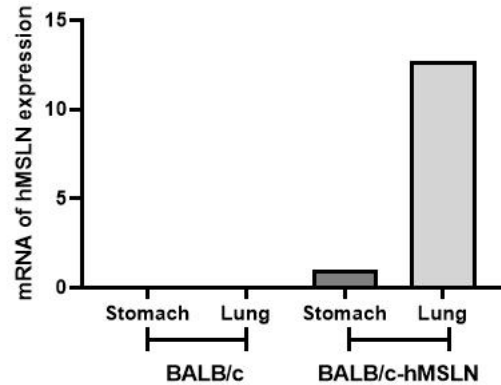


Fig 2. Detection of *hMSLN* expression in BALB/c-hMSLN mice.

mRNA expression of human *MSLN* were detected in stomach and lung of BALB/c-hMSLN mice but not BALB/c wild type mice.

2. Detection of protein expression of *MSLN*

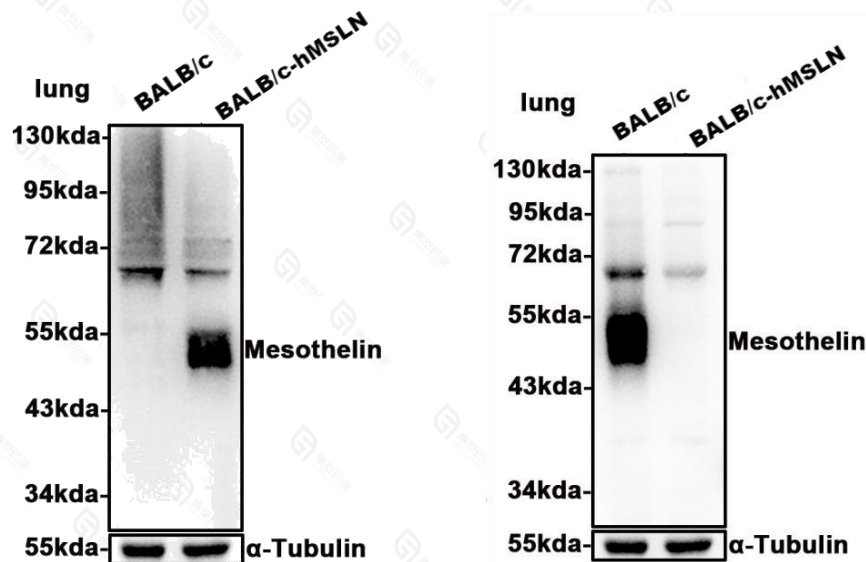
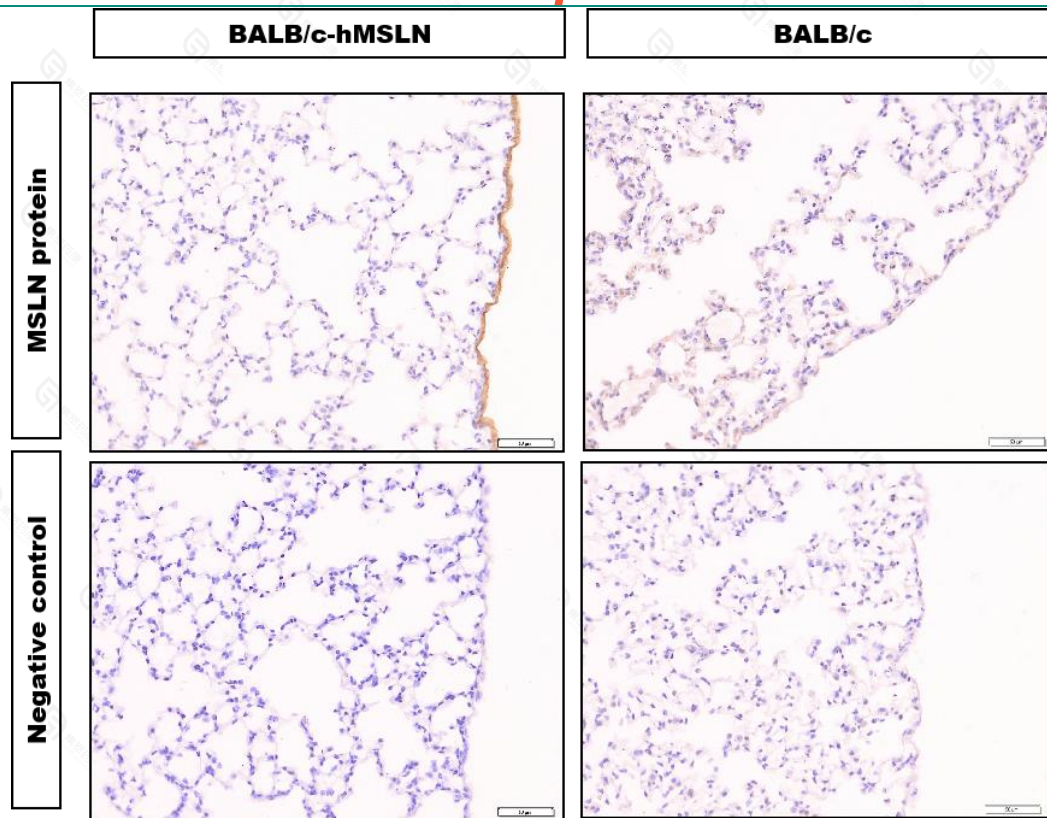


Fig 3. Expression detection of hMSLN (left) and mMSLN (right) in BALB/c-hMSLN mice

The expression of human *MSLN* protein can be detected in homozygous BALB/c-hMSLN but not BALB/c wild type mice (left) through western blot; the expression of murine *MSLN* protein can be detected in BALB/c wild type mice but not homozygous BALB/c-hMSLN mice (right).



Notes: Scale Bar=50 μm

Fig 4. The immunohistochemical staining of MSLN protein in the lung tissues

The expression of human MSLN protein can be detected in homozygous BALB/c-hMSLN but not BALB/c wild type mice.

References

1. Inaguma S , Wang Z , Lasota J , et al. Comprehensive immunohistochemical study of mesothelin(MSLN) using different monoclonal antibodies 5B2 and MN-1 in 1562 tumors with evaluation of itsprognostic value in malignant pleural mesothelioma[J]. *Oncotarget*, 2017, 8(16):26744-26754.
2. Bera T K , Pastan I . Mesothelin Is Not Required for Normal Mouse Development or Reproduction[J]. *Molecular and Cellular Biology*, 2000, 20(8):2902-2906.
3. Ho M , Qian M , Tang Z . The Role of Mesothelin in Tumor Progression and Targeted Therapy[J]. *Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry - Anti-Cancer Agents)*,2013, 13(2).
4. Paolo B , Sara C . Amatuximab and novel agents targeting mesothelin for solid tumors[J]. *OncoTargets and Therapy*, 2017, Volume 10:5337-5353.