

BALB/c-hCD3E/hMSLN

Strain Name: BALB/cJGpt-Tg(hCD3E)102/Gpt-*Msln*^{em1Cin(hMSLN)}/Gpt

For short : BALB/c-hCD3E/hMSLN

Strain Type: Knock in

Strain ID: T050041

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 used gene editing technology to replace the *Msln* transcript of BALB/c-hCD3E mice with the corresponding fragment of human *MSLN*, and developed BALB/c-hCD3E/hMSLN humanized model. These mice are ideal models for evaluation of the efficacy and safety of MSLN targeting drugs especially the CD3E bispecific antibody that targeting for MSLN.

Strategy





Fig.1 Schematic diagram of BALB/c-h MSLN/hCD3E humanized strategy

Application

1. Efficacy evaluation of MSLN targeted drugs.
2. Safety study of MSLN targeted drugs.

Data supports

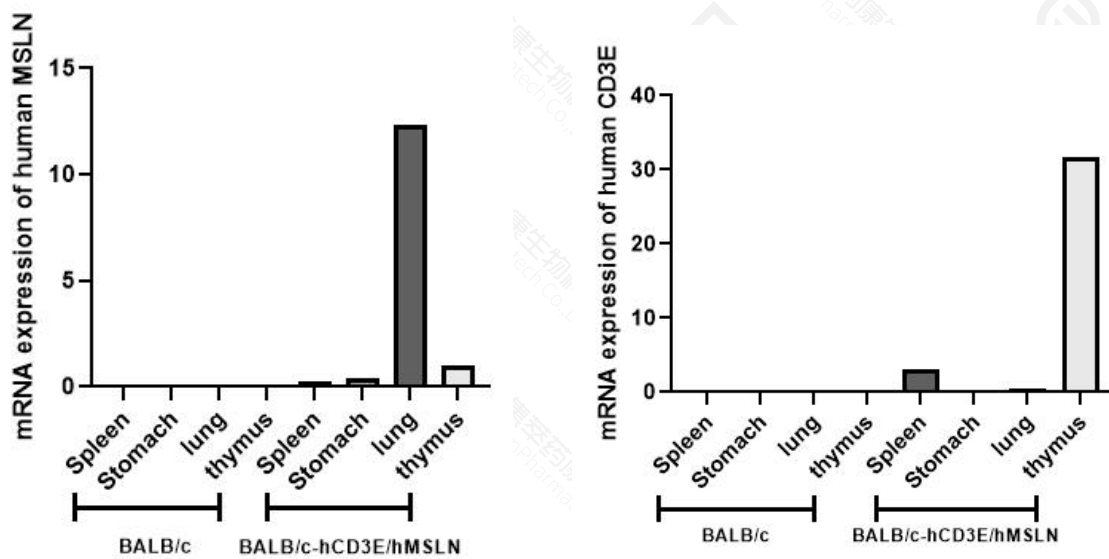


Fig. 2 Detection of human MSLN and CD3E expression. mRNA expression of human MSLN and CD3E were detected in several tissues of BALB/c-hMSLN/hCD3E(H/+;H/+) mice but not BALB/c wild type mice.

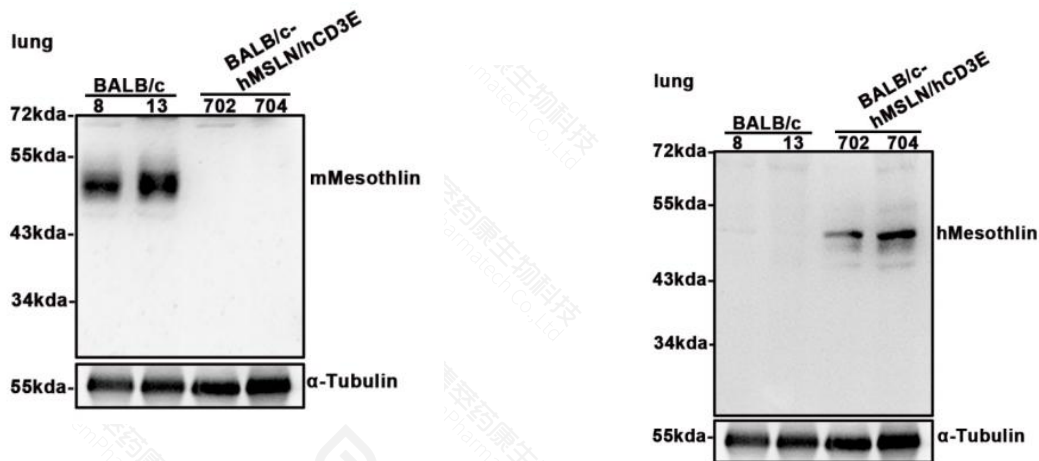


Fig. 3 Detection of human MSLN protein expression. Human MSLN expression were detected in the lung of BALB/c-hMSLN/hCD3E(H/H;H/+) but not WT mice, and mouse MSLN were only detected in the lung of WT mouse but not in humanized mice.

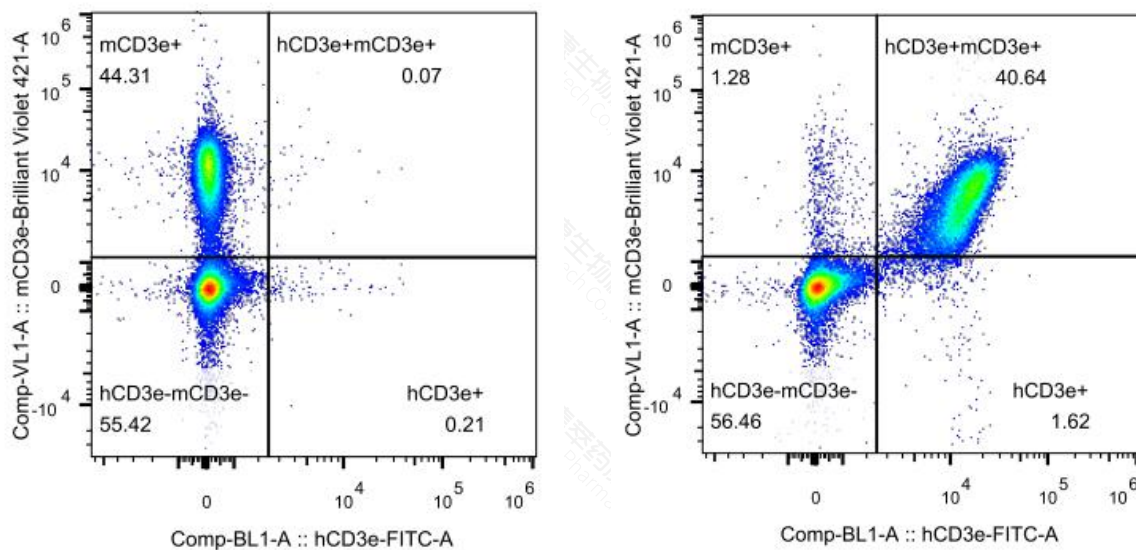


Fig. 4 CD3E expression were detected by flow cytometry. Splenocytes were collected from wild type BALB/c mice and BALB/c-hMSLN/hCD3E mice (H/H;H/+),and analyzed with strain specific antibody detection with CD3E. Human and mouse CD3E were detected in BALB/c-hMSLN/hCD3E mice (H/H;H/+) and only mouse CD3E were expression in BALB/c 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 its prognostic 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.