BALB/c-hSEMA4D

Strain Name： BALB/cJGpt-*Sema4d*$^{em1Cin(hSEMA4D)}$/Gpt
Strain Type： Knock-in
Strain Number： T054490
Background： BALB/cJGpt

Description

Sema4D, also known as CD100, is a homodimeric transmembrane glycoprotein first identified in immune cells, and later classified as a member of class 4 semaphorin based on its distinctive structure [1]. SEMA4D is widely expressed in a variety of tissues and organs in the human body, both in embryonic and adult tissues, including non-lymphoid tissues (heart, brain, and kidney) and lymphoid tissues (spleen, thymus, and lymph nodes) [2]. Studies have shown that SEMA4D not only plays an important role in axon guidance, the immune system including autoimmune diseases and cardiovascular system diseases, but also participates in tumor growth and progression, such as tumor angiogenesis and invasion [3].

A large number of studies have confirmed that when SEMA4D/Plexin-B1 is abnormally expressed, it will induce autoimmune diseases such as multiple sclerosis and various cancers such as squamous cell carcinoma of the head and neck [4,5]. Plexin-B1 is one of the important members of the transmembrane protein plexins family. As a high-affinity receptor of SEMA4D, Plexin-B1 can activate ERBB2, Met or RON tyrosine kinase pathway after binding to SEMA4D, thereby inducing ERBB2, Met and Phosphorylation of signaling molecules downstream of RON (such as Gab1 and Shc), ultimately mediating cell proliferation, migration and invasion [1]. In head and neck squamous cell carcinoma, lung cancer , and breast cancer models, SEMA4D/Plexin-B1 is highly expressed, and silencing SEMA4D expression can significantly inhibit tumor cell proliferation; therefore, SEMA4D can be used as a new target for autoimmune diseases and cancer therapy point [6,7].

GemPharmatech used gene editing technology to replace the extracellular domain of mouse SEMA4D in BALB/c mice with the human counterpart, and developed BALB/c-hSEMA4D humanized model. This strain is an ideal animal model for related disease studies.

Strategy

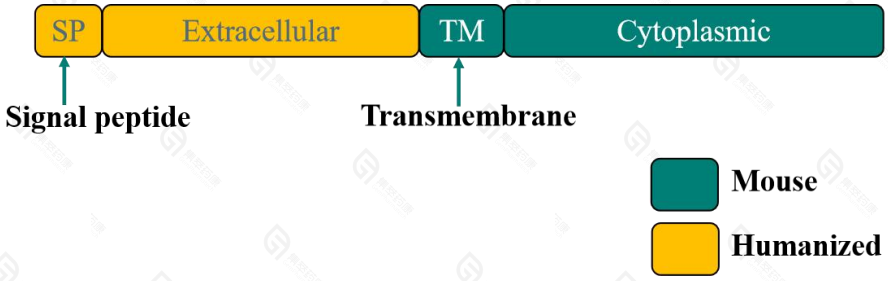

Fig.1 Schematic diagram of BALB/c-hSEMA4D model stratery.

Applications

1. Screening and Efficacy Evaluation of Antibody Drugs Targeting SEMA4D
2. Anti-cancer drug research and development
3. Immune system-related research

Supporting Data

1. Detection mRNA expression of *SEMA4D*

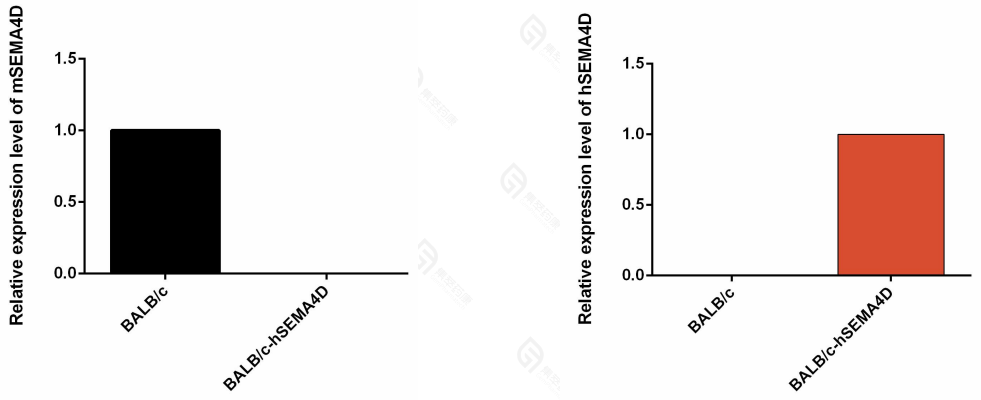

Fig 2. Detection of *SEMA4D* expression in BALB/c-hSEMA4D mice.

mRNA expression of human *SEMA4D* were detected in spleen of BALB/c-hSEMA4D mice but not BALB/c wild type mice.

2. Detection of protein expression of SEMA4D

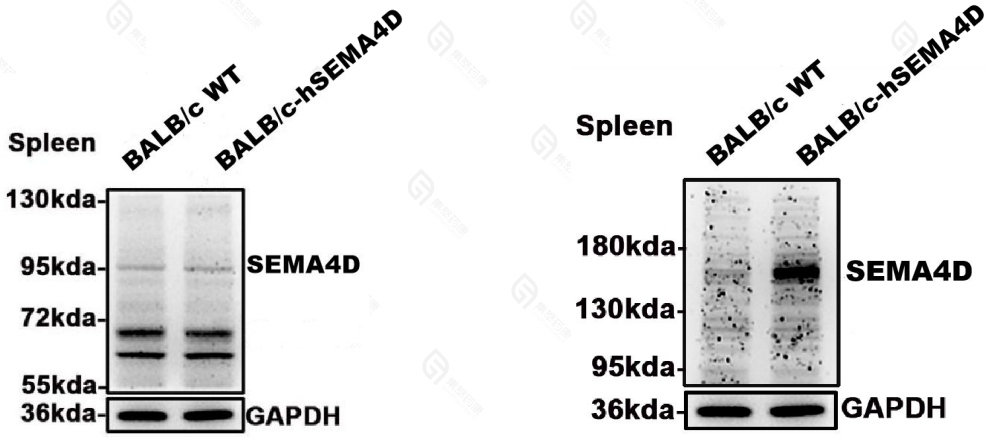

Fig 3. Expression detection of mSEMA4D (left) and hSEMA4D (right) in BALB/c-hSEMA4D mice. The expression of human SEMA4D protein can be detected in homozygous BALB/c-hSEMA4D but not BALB/c wild type mice (right) through western blot; murine SEMA4D was detectable in both homozygous BALB/c-hSEMA4D and wild-type mice due to the cross-reactivity of the antibody (left) The mSEMA4D consists of 861 amino acids and the non-modification protein is estimated to be 96 kDa. The actual molecular weight is 150 kDa as published in the previous report due to complicated post-translational modification[8] .The predicted band size of commercial anit-mouse SEMA4D antibody used in this validation is around 96 kDa and the anti-human SEMA4D antibody is approximately 150 kDa.

References

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