B6-SSS

Strain Name： C57BL/6JGpt-*Fbn1*$^{em1Cin(W1572C)}$/Gpt
Strain Type： Knock-in
Strain Number： T054130
Background： C57BL/6JGpt

Description

Stiff skin syndrome (SSS) is a rare, autosomal dominant cutaneous disorder with progressive, symmetric, sclerotic skin changes of the shoulders, hips, and thighs. Other stiff skin syndrome signs and symptoms may include excessive hair growth (hypertrichosis), loss of body fat (lipodystrophy), scoliosis, muscle weakness, slow growth, and short stature. SSS is caused by heterozygous missense mutations in the Arg-Gly-Asp (RGD) integrin-binding domain of the *FBN1* (fibrillin 1) gene. Mutations in the *FBN1* gene that cause stiff skin syndrome affect the fibrillin-1 protein, which is thought to cause abnormal associations between fibrillin and another protein called elastin. When these two proteins interact abnormally in the extracellular matrix, this leads to the development of features of stiff skin syndrome[1].

SSS mouse models carrying a W1572C mutation (equivalent to the human W1570C mutation) in the mouse *Fbn1* gene well simulate human SSS. Mice heterozygous for W1572C mutation are phenocopy SSS with increased deposition of collagen by 1 month of age and reduction of subcutaneous fat by three months of age, disorganized and excessive microfibrillar aggregates in the dermis, and circulating anti-nuclear and anti-topoisomerase I antibodies by three months of age. In addition, The dermis of SSS mice also show infiltration with plasmacytoid dendritic cells (pDCs) and pro-inflammatory T helper (Th) cell[2]. In keeping with Th2, Th9, and/or Th17-skewing, there is also increased expression of IL-9, IL-13, and IL-22 by dermal cells.

Gempharmatech uses gene editing technology to obtain a mouse model of *Fbn1* gene mutation. This strain showed pathological changes such as microabscesses, epidermal thickening, subcutaneous tissue myofiber degeneration and necrosis, inflammatory cell infiltration and fibrous tissue proliferation in the skin of 1-month-old and 3-month-old. B6-SSS mice can be used to screen the therapeutic drugs for stiff skin syndrome and the study of pathophysiology of stiff skin syndrome.

Strategy

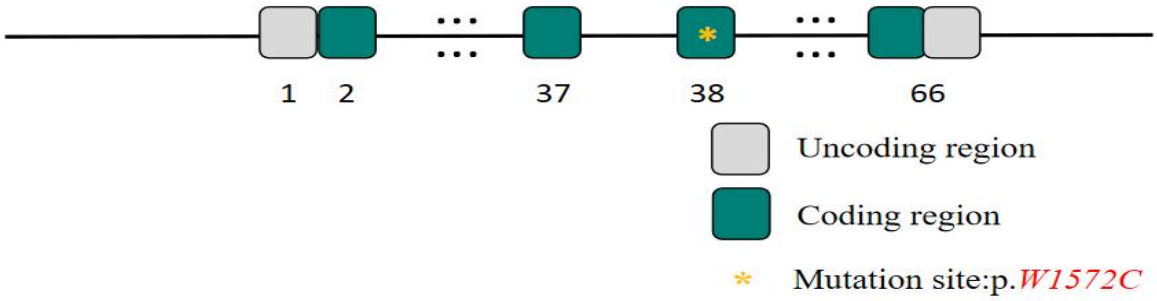

Fig 1. Schematic diagram of B6-SSS model strategy.

Applications

1. Screening drugs for stiff skin syndrome treatment
2. Pathophysiology of stiff skin syndrome

Supporting data

1. Pathological examination of 1-month- old B6-SSS mice

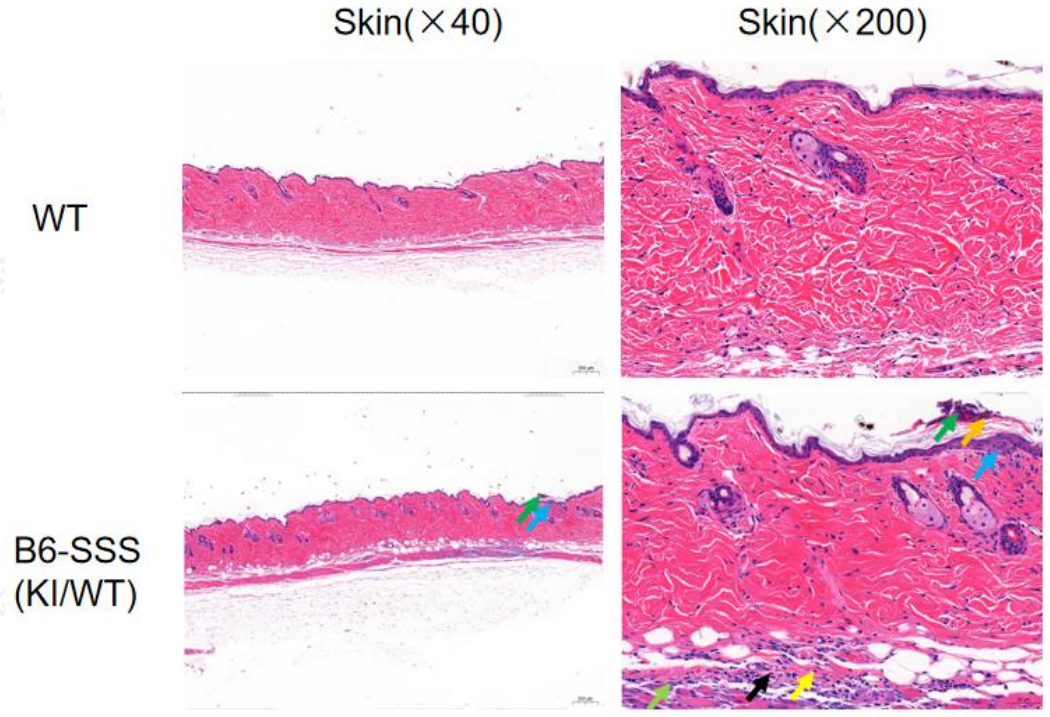

Fig 2. Pathological examination of 1-month- old B6-SSS mice.
Representative images of HE staining in the skin of 1-month- old heterozygous (KI/WT) B6-SSS. Compared with WT, the skin tissue of B6-SSS showed microabscess, epidermal thickening, subcutaneous muscle fiber degeneration and necrosis, inflammatory cells infiltration and fibrous tissue hyperplasia.

Note: Microabscess (↑) Epidermal thickening (↑) Fibrodegenerative necrosis (↑) Neutrophils (↑) Lymphocytes (↑) Fibroblasts (↑).

2. **Pathological examination of 3-month- old B6-SSS mice**

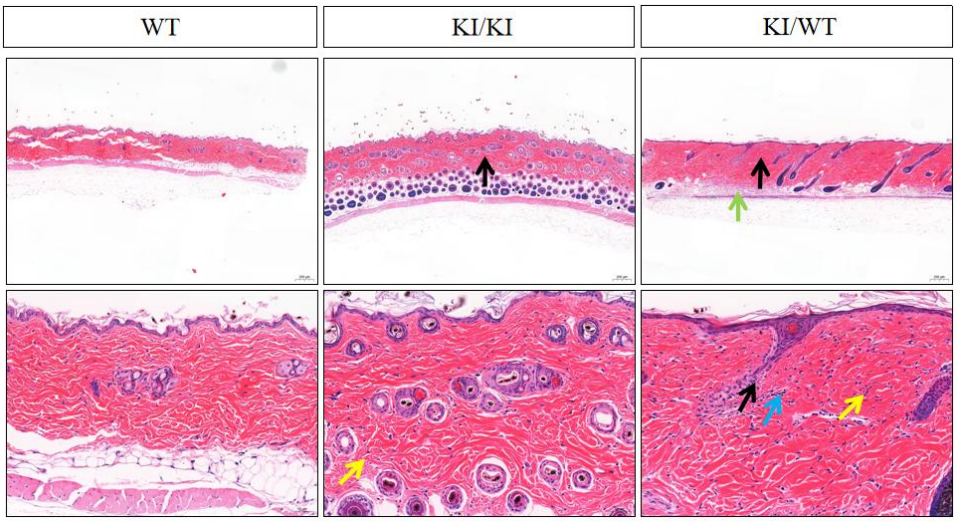

Fig 3. Pathological examination of 3-month- old B6-SSS mice.
Representative images of HE staining in the skin of 3-month- old heterozygous(KI/WT) and homozygous(KI/KI) B6-SSS. Compared with WT, the skin tissue of B6-SSS showed epidermal thickening, collagen fiber hyperplasia and inflammatory cells infiltration.
Note: Epidermal thickening (↑) Collagen fiber hyperplasia (↑) Inflammatory cells infiltration (↑) Lymphocytes (↑)

3. The dermal thickness of 3-month- old B6-SSS mice

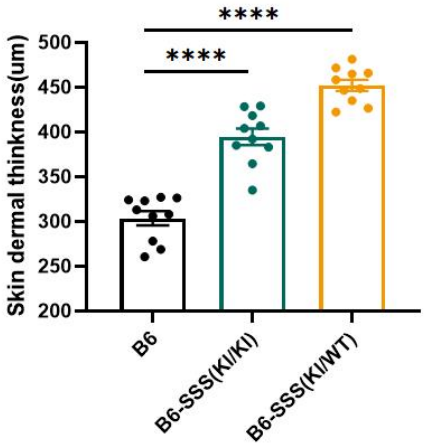

Fig 4. The dermal thickness of 3-month- old B6-SSS mice.
The dermal thickness was measured on the images of HE staining in the skin of 3-month-old heterozygote (KI/WT) and homozygote (KI/KI) B6-SSS. Compared with WT, the dermal thickness of 3-month-old heterozygote (KI/WT) and homozygote (KI/KI) B6-SSS mice increased significantly.

References

1. Loeys BL, Gerber EE, Riegert-Johnson D, Iqbal S, Whiteman P, McConnell V, Chillakuri CR, Macaya D, Coucke PJ, De Paepe A, Judge DP, Wigley F, Davis EC, Mardon HJ, Handford P, Keene DR, Sakai LY, Dietz HC. Mutations in fibrillin-1 cause congenital scleroderma: stiff skin syndrome. Sci Transl Med. 2010 Mar 17;2(23):23ra20.
2. Gerber EE, Gallo EM, Fontana SC, Davis EC, Wigley FM, Huso DL, Dietz HC. Integrin-modulating therapy prevents fibrosis and autoimmunity in mouse models of scleroderma. Nature. 2013 Nov 7;503(7474):126-30.