B6-*Dmd* Del50

Strain Name： C57BL/6JGpt-*Dmd*^{em21Cd701E50}/Gpt

Strain type： Knock-out

Strain number： T056003

Background： C57BL/6JGpt

Description

Duchenne muscular dystrophy (DMD) belongs to the X-linked recessive genetic disease. The disease is characterized by progressive atrophy of proximal skeletal muscles of the extremities and pseudo hypertrophy of the calf gastrocnemius [1], which also involves the myocarid and respiratory muscles, leading to early death [2]. This disease also affects the development of central nervous systems and organs. The DMD gene encodes a large rod-shaped cytoskeleton protein (Dystrophin), the protein is mainly distributed in the inner surface of the bone and myocardial muscle fibers, which helps muscle fibers maintain their integrity and elasticity during contraction. It is also a vital component of the muscular dystrophin complex and acts as a very important bridge to maintain the cytoskeleton[3].

The main cause of DMD disease is the truncation of the Dystrophin caused by DMD gene mutation or deletion, which lead to the functional loss of Dystrophin. There are many kinds of DMD gene mutation and deletion, mainly occurring in the exon 45-55 region. At present, there is no effective cure for the disease, several gene therapise are in progress, among them, and exon skipping therapy is one of the most popular treatment[4]. Based on the high-frequency deletion region of DMD gene in patients, GemPharmatech constructed a B6-*Dmd* Del50 mouse model of by deleting exon 50 of the mouse *Dmd* gene. B6-*Dmd* Del50 mice can be used to exon skipping therapy screening and optimization. and the study of the pathogenesis of DMD disease.

Strategy

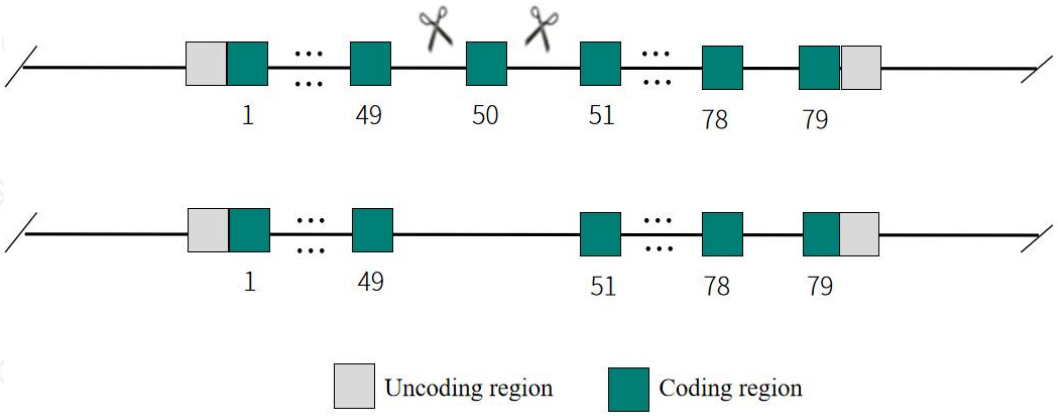

Fig 1. Schematic diagram of B6-*Dmd* Del50 model stratery

Application

1. Screening of drugs for muscular dystrophy
2. Pathophysiological study on muscular dystrophy

Data support

1. Expression of Dystrophin

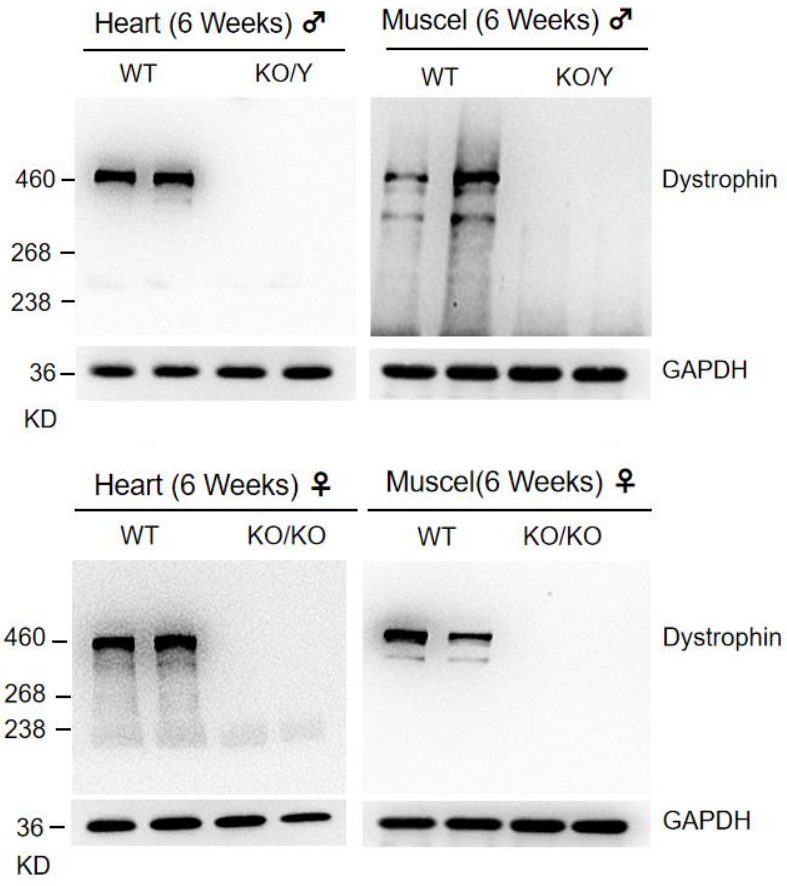

Fig 2. The expression of Dystrophin protein in B6-*Dmd* Del50 mice is deficient

The expression of DMD protein in heart and muscle of 6-week-old WT mice and B6-*Dmd* Del50 mice were detected by western blot analysis. As shown in Figure 2, B6-*Dmd* Del50 mice did not express DMD protein in the heart and muscle.

2. Pathological detection of B6-*Dmd* Del50 muscle

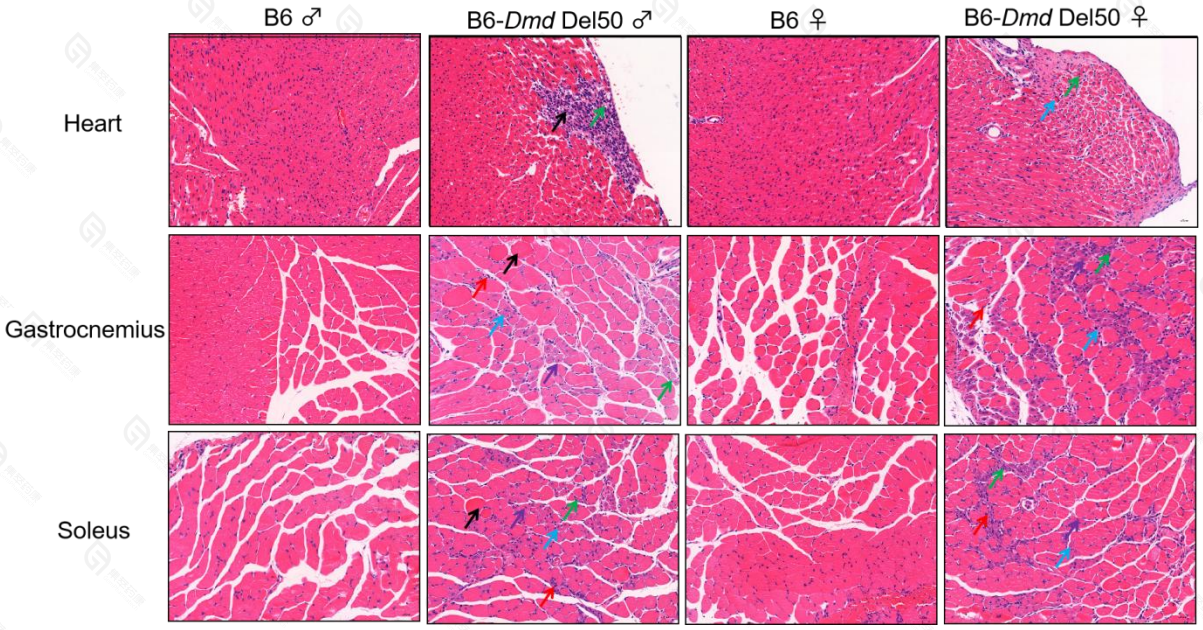

Fig 3. B6-*Dmd* Del50 mice showed obvious pathological changes in heart and muscle tissue

Representative images of HE staining in the heart and muscle of B6-*Dmd* Del50 mice at 4-week- old. Compared with B6 mice, the muscle tissue of B6-*Dmd* Del50 mice (heart, gastrocnemius and soleus) showed fiber atrophy or degeneration necrosis, with the reduced area, lymphocyte infiltration in the necrotic area, fibrous tissue hyperplasia in the necrotic area and interstitium.

Muscle fiber necrosis green arrow), Lymphocytes (red arrow), Atrophy of muscle fibers (blue arrows), Eosinophilic degeneration (blue arrow), Nuclear translocation (purple arrow), Scale Bar=50 μm.

3. Creatine kinase content of B6-*Dmd* Del50 mice

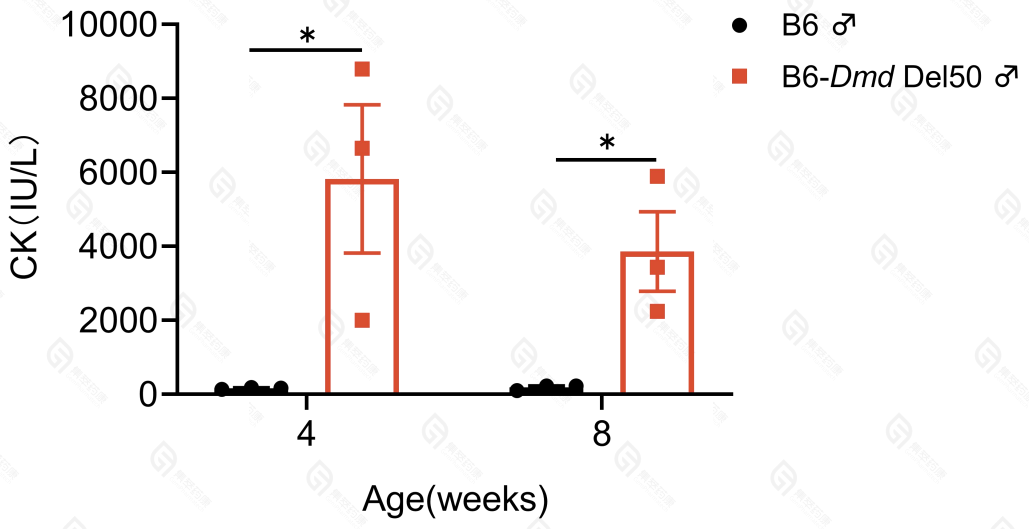

Fig 4. The creatine kinase content was significantly increased in B6-*Dmd* Del50 mice

The level of creatine kinase (CK) in B6-*Dmd* Del50 mice was significantly higher than that in B6 control mice at 4-week- old and 8-week- old. The result showed that the damage of myocardium and skeletal muscle of B6-*Dmd* Del50 mice, and muscle tissue necrosis and dissolution. (n=3, MEAN ± SEM, *p<0.05, T test)

Reference：

1. Sacco, Alessandra, et al. "Short telomeres and stem cell exhaustion model Duchenne muscular dystrophy in mdx/mTR mice." Cell 143.7 (2010): 1059-1071.
2. Mourkioti, Foteini, et al. "Role of telomere dysfunction in cardiac failure in Duchenne muscular dystrophy." Nature cell biology 15.8 (2013): 895-904.
3. Elangkovan, Nertiyan, and George Dickson. "Gene therapy for Duchenne muscular dystrophy." Journal of Neuromuscular Diseases 8.s2 (2021): S303-S316.
4. Sheikh, Omar, and Toshifumi Yokota. "Developing DMD therapeutics: a review of the effectiveness of small molecules, stop-codon readthrough, dystrophin gene replacement, and exon-skipping therapies." Expert opinion on investigational drugs 30.2 (2021): 167-176.