hACE2（Extracellular humanization）

Stain Name：B6JGpt-*Ace2*$^{em1Cin(hACE2\text{-}stop)}$/Gpt

Strain Type：Knock-in

Strain ID：T037630

Background：C57BL/6JGpt

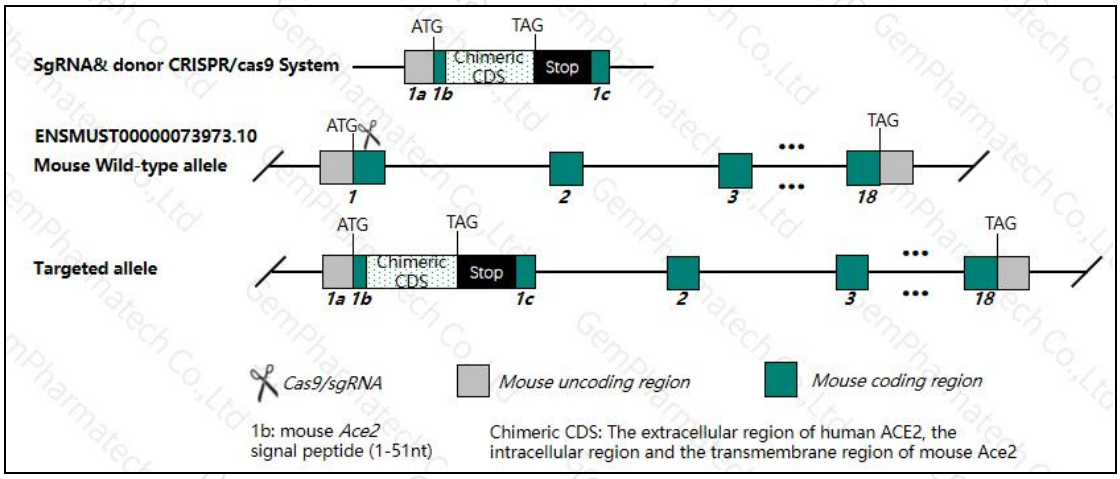
Description

SARS-CoV-2 binds to the ACE2 receptor on the surface of human cells through the spike protein (S protein), thereby entering the cell body for replication and infection, causing a cascade of immune responses and cytokine storms. Angiotensin-converting enzyme (ACE)2, also known as ACeh, is a Zn metalloprotease, which belongs to type 1 transmembrane protein. The structure includes a signal peptide, a transmembrane domain and a metalloprotease containing HEXXH zinc binding domain Active site.

The gene *ACE2* is located on the X chromosome and is mainly expressed in the gastrointestinal tract, heart, kidney, lung, testis and brain. There are key differences between human ACE2 and mouse ACE2 sequences. SARS-CoV-2, which can infect humans, may not infect mice. Therefore, wild-type mice are not suitable for virus research and vaccine development.

GemPharmatech uses gene editing technology to develop a humanized mouse model of ACE2, which simulates the clinical manifestation of human infection with the new coronavirus. We insert the mouse-derived Ace2 signal peptide into the human-mouse chimeric CDS on the C57BL/6JGpt background. The human-mouse chimeric CDS will be expressed under the transcriptional regulation of the mouse endogenous Ace2 gene to simulate severe human COVID- 19 phenotype.

Strategy



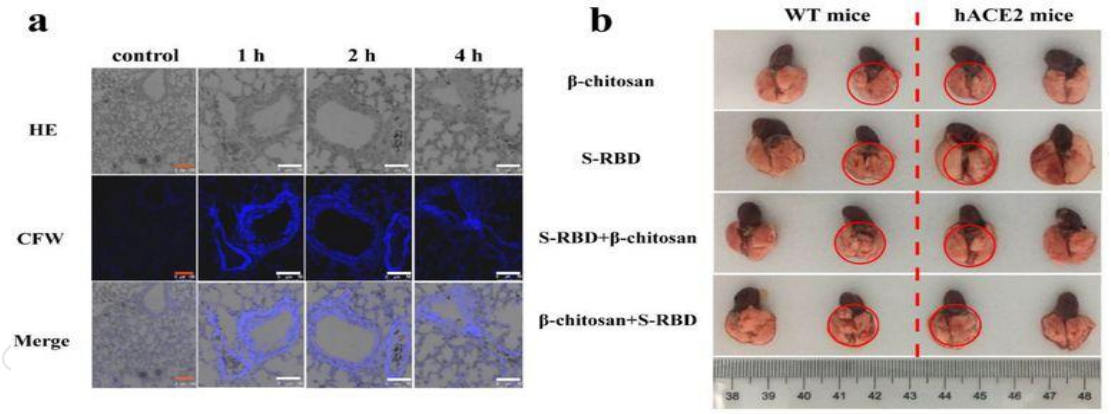
Applications

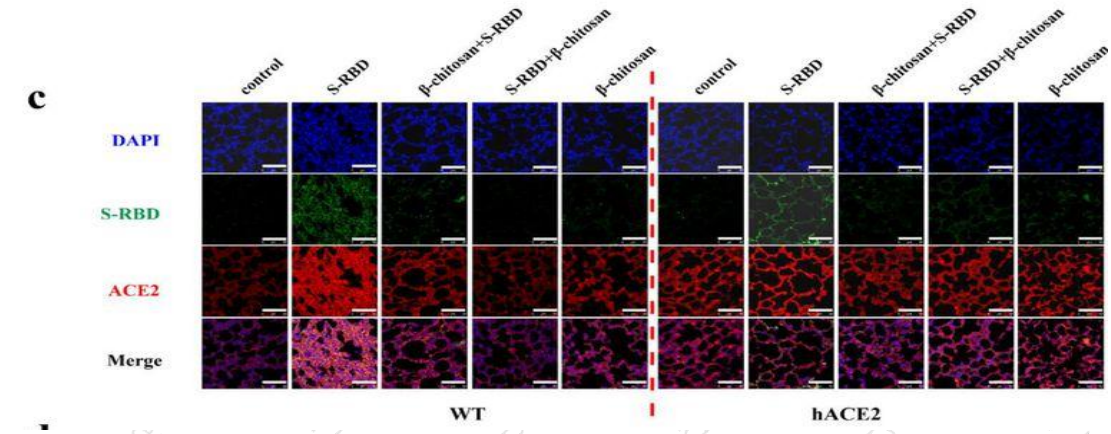
1. Study on the mechanism of SARS-CoV-2；
2. Evaluation of the efficacy and safety of SARS-CoV-2 vaccines or inhibitors；
3. Autoimmune disease research;

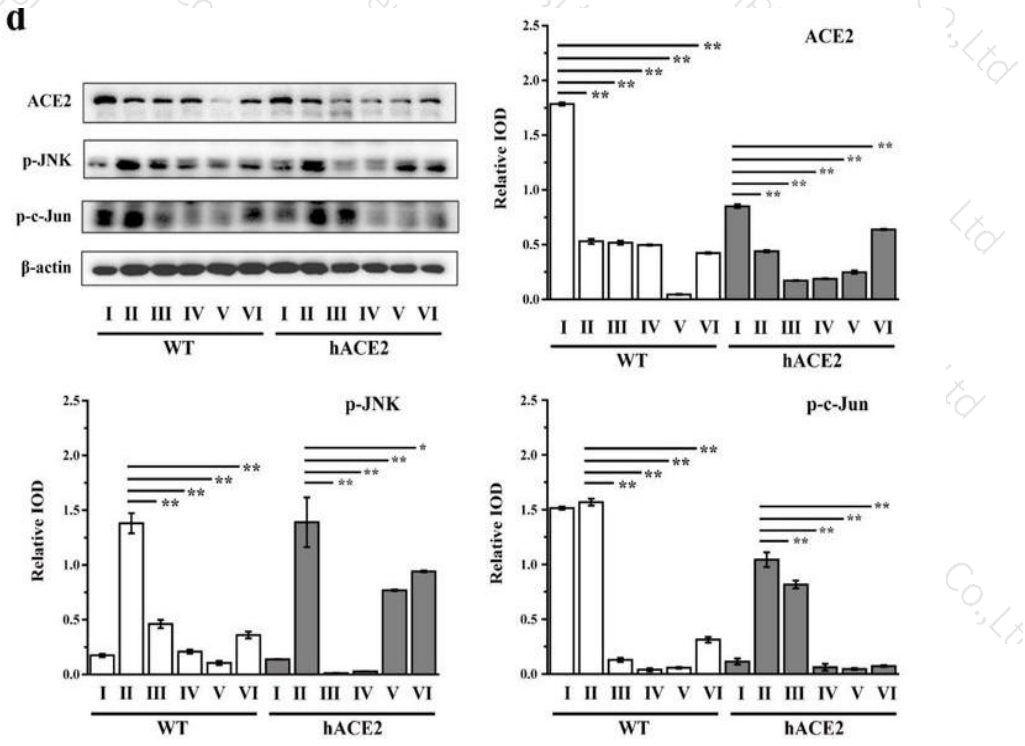
Identification

1) Mouse Age：3W-4W
2) Genotype：KI/Y，homozygote, sex-linked inheritance
3) Genetic Locus：*Ace2*

Data support


a
control
1 h
2 h
4 h
HE
CFW
Merge
b
WT mice
hACE2 mice
β-chitosan
S-RBD
S-RBD+β-chitosan
β-chitosan+S-RBD


c
control
S-RBD
β-chitosan+S-RBD
S-RBD+β-chitosan
β-chitosan
DAPI
S-RBD
ACE2
Merge
WT
hACE2


d
ACE2
p-JNK
p-c-Jun
β-actin
I II III IV V VI I II III IV V VI
WT
hACE2
Relative IOD
p-JNK
p-c-Jun

Gulimiran Alitongbieke, Xiu-min Li. et al. Effect of β-chitosan on the binding interaction between SARS-CoV-2 S-RBD and ACE2. BioRxiv. 2020.10.14.335893. doi: https://doi.org/10.1101/2020.07.31.229781.

The distribution, histopathology and immunofluorescence of β-chitosan in the lungs of hACE2 mice, and its effect on inflammation-related proteins

Publications

1. L Bai, Y Zhao, J Dong. et al. Co-infection of influenza A virus enhances SARS-CoV-2 infectivity. ACS Energy Letters. 2020, 14. doi. org/10. 1101/2020. 10. 14. 335893. 【K18 hACE2. T037657】

2. S Zhang, Y Liu, X Wang, L Yang. et al. SARS-CoV-2 binds platelet ACE2 to enhance thrombosis in COVID-19. J Hematol Oncol. 2020, 10. DOI:10. 21203/rs. 2. 20606/v1. 【K18-hACE2. T037657】

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