Also Known As: K18-hACE2

K18-hACE2 transgenic mice express human ACE2, the receptor used by severe acute respiratory syndrome coronavirus (SARS-CoV) to gain cellular entry. The human keratin 18 promoter directs expression to epithelia, including airway epithelia where infections typically begin. Because K18-hACE2 are susceptible to SARS-CoV-2 and SARS-CoV viruses, they are useful for studying antiviral therapies to COVID-19 and SARS.

These mice should be handled in a manner consistent with CDC/ABSA/WHO guidelines for prevention of human infection with the SARS-CoV-2 virus. Proper PPE and handling methods should be used at all times when working with these mice. Additional important guidelines for using SARS-CoV-2 susceptible mouse lines.

View in Mandarin.

Of note, humanized ACE2 knock-in lines are also available, such as hACE2-KI (Stock No. 035000) and ACE2-GR (Stock No. 035800).

Donating Investigator

Dr. Stanley Perlman, University of Iowa

Dr. Paul B McCray, University of Iowa
**Tg(K18-ACE2)2Prlmn**

**Allele Type**
Transgenic (Inserted expressed sequence)

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**RESEARCH APPLICATIONS**

Internal/Organ Research  
Mouse/Human Gene Homologs  
Immunology, Inflammation and Autoimmunity Research  
Virology Research  
Research Tools  
Developmental Biology Research

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**BASE PRICE**

Starting at:

$106.00 Domestic price for female 4-week

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**Details**

The Jackson Laboratory has been informed by multiple independent investigators testing these K18-hACE2 mice that, similar to SARS-CoV infection, intranasal infection with SARS-CoV-2 virus results in K18-hACE2 mice with severe illness - reaching criteria for euthanasia ~5-8 days post-challenge [Zheng et al. bioRxiv August 2020; 1x10^5 PFU] [June 2020 data from Drs. Perlman and McCray]. This was evidenced by body weight loss, rapid breathing, hunched posture and inactivity as
result of infection. Virus titers were reportedly detected in the lungs, brain, kidney, liver and spleen (see additional organs below). Gross pathology of the lungs indicates lesions as a result of infection. Vehicle or untreated control mice showed no signs of illness - gaining weight with a normal appearance.

In addition, K18-hACE2 mice infected with SARS-CoV-2 may replicate the chemokine/cytokine storm traits observed in humans [Oladunni et al. bioRxiv July 2020; 1x10^5 PFU], and may exhibit viral replication in gut [Rathnasinghe et al. 2020 Emerg Microbes Infect; 1x10^4 PFU] and heart [Winkler et al. 2020 Nat Immunol 21:1327; 2.5x10^4 PFU]. Importantly, some K18-hACE2 animals given lower dose SARS-CoV-2 (2x10^3 PFU) survived despite significant weight loss [Golden et al. 2020 JCI Insight 5:e142032].

K18-hACE2 transgenic mice express the receptor for severe acute respiratory syndrome (SARS), caused by a coronavirus (SARS-CoV) in airway and other epithelia under control of the human keratin 18 (KRT18) promoter. Specifically, these mice contain 2.5 kb of the KRT18 genomic sequence, including the promoter, and the first intron (with a mutation in the 3’ splice acceptor site to reduce exon skipping) and a translational enhancer (TE) sequence from alfalfa mosaic virus, upstream of the human angiotensin I converting enzyme (peptidyl-dipeptidase A) 2 coding sequence (hACE2), followed by exons 6-7 and the poly(A) signal of the human K18 gene. These elements have been found to be necessary for high-level expression and epithelial cell specificity of hACE2, the primary host cell receptor for SARS-CoV. In these mice, from founder line 2, K18-hACE2 transgene expression is evident in airway epithelial cells (but not in alveolar epithelia), as well as in epithelia of other internal organs, including the liver, kidney, and gastrointestinal tract. Recent research indicates that this line may also be useful in studies related to the study of 2019 novel coronavirus (SARS-CoV-2) pathogenesis.

Homozygous mice are viable and fertile.

These K18-hACE2 mice develop a rapidly lethal infection after intranasal inoculation with a human strain of SARS-CoV. Infection begins in airway epithelia, with subsequent alveolar involvement and extrapulmonary virus spread to the brain. Infection results in macrophage and lymphocyte infiltration in the lungs and upregulation of proinflammatory cytokines and chemokines in both the lung and the brain. By days 3 to 5 postinfection, K18-hACE2 mice begin to lose weight and become lethargic with labored breathing. Mice from this founder line are moribund 4 days after inoculation, and all mice are dead 7 days after inoculation. Transgenic expression of hACE2 in epithelia converts a mild SARS-CoV infection into a rapidly fatal disease. [McCray et al. 2007 J Virol. 81:813 (PMID:17079315)]

Please note, these K18-hACE2 mice should be handled in a manner consistent with CDC/ABSA/WHO guidelines for prevention of human infection with the SARS-CoV-2 virus. Proper PPE and handling methods should be used at all times when working with these mice. Additional important guidelines for using SARS-CoV-2 susceptible mouse lines.

October 2020 - Note on Distribution: To best meet researcher demand for the K18-hACE2 mouse model, we currently distribute offspring from either of the following breeding units:

[i] hemizygous x C57BL/6J breeding units - the resulting offspring are affixed with a RapID Ear Tag, genotyped to determine if hemizygous or non-carrier, and then distributed retaining the ear tag [learn more about RapID Ear Tag].

[ii] homozygous x C57BL/6J breeding units - the resulting offspring are 'obligate hemizygous' and therefore are not genotyped or affixed with RapID Ear Tags prior to distribution.

As with any mutant/transgenic mouse line, researchers are strongly encouraged to genotype the mice they receive to confirm expected zygosity and to confirm the genotyping assay works in their laboratory.

Development
Control Suggestions
Selected References
Genetics

Tg(K18-ACE2)2Prlmn
Genotyping Protocols
Probe: Tg(K18-ACE2)2Prlnn QPCR
Probe: Tg(K18-ACE2)2Prlnn QPCR
Sanger sequencing: Chr2_rs13476660-SEQ
Separated PCR: Tg(K18-ACE2)2Prlnn-Chr2
Genotyping resources and troubleshooting

Breeding Considerations
When maintaining a live colony, investigators may breed hemizygous mice to wildtype (non-carrier) mice from the colony, or to C57BL/6J inbred mice (Stock No. 000664). Homozygous mice are viable and fertile (August 2020).

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As with any mutant/transgenic mouse line, researchers are strongly encouraged to genotype the mice they receive to confirm expected zygosity and to confirm the genotyping assay works in their laboratory.

Additional Breeding and Husbandry Support
Mating System
Hemizygous x C57BL/6J (000664)
C57BL/6J (000664) x Homozygote

Citation
When using the K18-hACE2 mouse strain in a publication, please cite the originating article(s) and include JAX stock #034860 in your Materials and Methods section.
### Pricing & Availability

- **Readily Available**
  - Readily available in any quantity needed.

### Domestic Pricing for
- **Commercial & For-Profit**
- **Not-For-Profit & Academic**

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