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Genetically engineered models **(GEMS)**

Humanized ACE2/Tmprss2 (hACE2/hTmprss2) Double Knockin Mouse

MODEL	Humanized Tmprss2 Knockin Mouse
STRAIN	C57BL/6Hsd-*ACE*$^{em1(ACE2)Env}$*Tmprss2*$^{em1(TMPRSS2)Env}$
LOCATION	U.S.
AVAILABILITY	Live colony

GENETICS BACKGROUND

- Background strain: C57BL/6

ZYGOSITY GENOTYPE

- Homozygous/Homozygous *(ACE2/TMPRSS2)* Females
- Hemizygous/Homozygous *(ACE2/TMPRSS2)* Males

RESEARCH USE

- Infectious disease
- COVID-19
- SARS

ORIGIN

The humanized ACE2/Tmprss2 (hACE2/hTmprss2) double knockin (KI) mouse model was created at the Inotiv St. Louis, MO, model creation facility in 2020 and is maintained and distributed by Inotiv.

DESCRIPTION

Cellular infection by coronaviruses, including SARS-CoV and SARS-CoV-2, is a two-step process that utilizes the host proteins ACE2 and Tmprss2. Angiotensin-converting enzyme 2 (ACE2), a key enzyme in the renin-angiotensin system that regulates blood volume and arterial tone, is the entry receptor for SARS-CoV and SARS-CoV-2. The S1 subunit of the coronavirus spike (S) protein contains a receptor binding domain (RBD) that recognizes and binds to ACE2. Upon receptor binding, Tmprss2, a transmembrane serine protease, cleaves the S protein at the junction of the S1 and S2 subunits, allowing fusion of the cellular and viral membranes and the subsequent entry of SARS-CoV-2 into the cell. As such, ACE2 and Tmprss2 are being investigated as potential targets for anti-viral drugs.

The hACE2/hTmprss2 double KI mouse was created through the crossing of the hACE2 and hTmprss2 single KI mouse models. The hACE2 and hTmprss2 single KI models were generated by integrating a codon optimized human *ACE2* or *TMPRSS2* cDNA expression cassette into the respective mouse gene through CRISPR-based technology. This results in the mouse gene promoter and other regulatory elements driving the expression of the human ACE2 or Tmprss2 protein while terminating expression of the respective mouse gene.