Human ACE2 Transgenic Mice:
hACE2 AC70 & hACE2 AC22

Complementary models for COVID-19 vaccine and therapeutic evaluation and pathogenesis research.

Preclinical animal models susceptible to SARS-CoV-2 are urgently needed for research on COVID-19, including development of vaccines and therapeutics. Mice expressing human ACE2 are susceptible to infection by SARS-CoV-2, the virus that causes COVID-19. Taconic Biosciences offers a set of two human ACE2 mouse strains with options for lethal and lethality-resistant models of SARS-CoV-2 infection to study the full range of COVID-19 disease outcomes. Unlike ferrets or hamsters, hACE2 mice allow researchers to leverage the full power of the mouse as a model organism, including additional genetic and other manipulations to study the role of co-morbidities in COVID-19.

PRODUCT SPECIFICS

- The hACE2 AC70 and hACE2 AC22 strains ubiquitously express human ACE2 cDNA under the control of the CAG promoter.

- ACE2 is the receptor bound by SARS-CoV-2 and SARS-CoV spike proteins during viral entry into host cells; these spike proteins have much higher binding affinity to human ACE2 compared to mouse ACE2.

- Lethal SARS-CoV-2 infection model: hACE2 AC70 mice rapidly lose weight and die following infection with SARS-CoV-2. Lethal dose is <10 virions.

- Lethality-resistant SARS-CoV-2 infection model: hACE2 AC22 mice uniformly lose weight and ~30-40% of mice die by 7 dpi following intranasal infection with 10^5 $TCID_{50}$.

- These strains are also susceptible to SARS-CoV, the virus which causes SARS. Following intranasal infection with SARS-CoV, hACE2 AC70 mice rapidly lose weight and die within days, whereas hACE2 AC22 mice lose significant bodyweight, but recover from infection without mortality.

BIOSECURITY ALERT
Due to the susceptibility of these strains to SARS-CoV-2 and the current prevalence of this virus in the human population, special biosecurity precautions are required for housing and husbandry for hACE2 mice — both naïve mice and mice used in infection studies.

ORDERING INFORMATION

hACE2 AC70

Model #	Genotype	Nomenclature
18222-F	tg/wt	B6;C3-Tg(CAG-ACE2)70Ctkt
18222-M	tg/y	B6;C3-Tg(CAG-ACE2)70Ctkt
18222-F	wt/wt	B6;C3-Tg(CAG-ACE2)70Ctkt
18222-M	wt/y	B6;C3-Tg(CAG-ACE2)70Ctkt

hACE2 AC22

Model #	Genotype	Nomenclature
18225-F	tg/wt	B6;C3(C)-Tg(CAG-ACE2)22Ctkt
18225-M	tg/wt	B6;C3(C)-Tg(CAG-ACE2)22Ctkt
18225-F	wt/wt	B6;C3(C)-Tg(CAG-ACE2)22Ctkt
18225-M	wt/wt	B6;C3(C)-Tg(CAG-ACE2)22Ctkt

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THE COMPLETE SOLUTION

MODELS TO DRIVE DRUG DISCOVERY
Taconic Biosciences is uniquely positioned to enable drug discovery through animal models by being the only company that partners with customers to provide expertise, quality, and availability, along with downstream services:

▶ Expertise at every step

▶ Highest quality standards in the industry

▶ Availability and access to drive global research

MODEL GENERATION SOLUTIONS
Taconic's Model Generation Solutions empower our customers with a unique combination of capabilities, specifically tailored to each individual discovery program:

▶ Most experienced model generation and breeding company

▶ Most comprehensive toolkit

▶ Exclusive programs

▶ Concierge approach to partnering with customers

COLONY MANAGEMENT SOLUTIONS
Taconic's fully-integrated colony management solutions bring innovative models from design to study-ready cohorts with unprecedented speed and transparency:

▶ Most experienced model generation and colony management company

▶ The complete toolkit

▶ Colony management solution process

▶ Partnering with our customers

▶ Expanded applications and opportunities

YOUR PARTNER

WHAT WE DO
Taconic Biosciences is a fully-licensed, global leader in genetically engineered rodent models and services. Founded in 1952, Taconic provides the best animal solutions so that customers can acquire, custom-generate, breed, precondition, test, and distribute valuable research models worldwide.

WHO WE ARE
Taconic has created a unique ecosystem of experts to provide our customers with the best animal model solutions. Whether it is choosing the right model for your study, designing a custom model, creating an efficient breeding plan, or providing expertise in critical support functions like veterinary science, genetics, and embryology; Taconic is ready to help you drive your research from idea to cure.

CONTACT US
To get started, contact one of our customer service team members. Contact us at **info@taconic.com**.

VISIT TACONIC.COM
There is so much more to learn. Visit taconic.com to see our full breadth of animal model solutions and valuable resources.

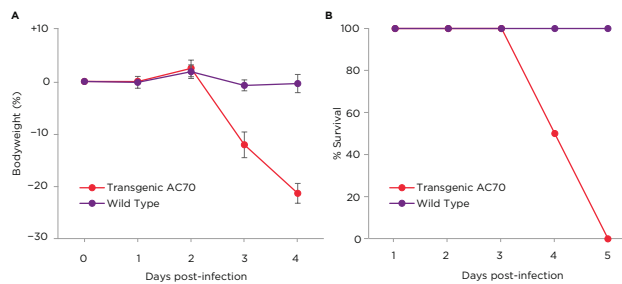### hACE2 AC70 is a Model of Lethal SARS-CoV-2 Infection

Figure 1 hACE2 AC70 mice (Transgenic AC70) and age- and sex-matched wild type littermates (Wild Type) were challenged intranasally with 10^6 $TCID_{50}$ of SARS-CoV-2 (US_WA-1/2020). Challenged mice were monitored daily for morbidity (weight loss) and mortality. Average percentage of weight loss with SEM values is shown in panel A. Percent survival as shown in panel B indicates infected transgenic mice uniformly succumbed to infection with 100% mortality by day 5.

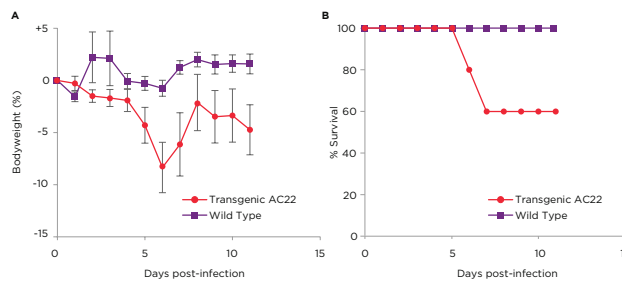### hACE2 AC22 is a Lethality-Resistant Model of SARS-CoV-2 Infection

Figure 2 Female hACE2 AC22 mice (Transgenic AC22) and wild type littermates (Wild Type) were challenged intranasally with 10^5 $TCID_{50}$ of SARS-CoV-2 (US_WA-1/2020). Challenged mice were monitored daily for morbidity (weight loss) and mortality. Average percentage of weight loss with SEM values is shown in panel A. Percent survival as shown in panel B indicates that while this dose resulted in 40% mortality by 7 days post-infection, most mice recovered.*

TACONIC'S CORONAVIRUS TOOLKIT

Taconic offers a wide range of products and services for COVID-19 research.

COVID-19 DISEASE MODELS

▶ Humanized and knockout models for many relevant genes, including Ace2, Tmprss2, Dpp4, Apoe and more

▶ Aged inbred mice available for study of age-related disease outcomes

ANTIBODY DEVELOPMENT AND PRODUCTION

▶ Strains for polyclonal and monoclonal antibody development and scale up

VACCINE RESEARCH AND DEVELOPMENT

▶ Transgenic human HLA mice for validation of human immune response to vaccine epitopes

▶ Humanized immune system mice to study human immune response to infection and/or vaccines

COLONY MANAGEMENT AND MODEL GENERATION SOLUTIONS

▶ Leverage the most comprehensive, fully licensed gene modification toolkit in the industry to make your own coronavirus model

▶ Our colony management solutions can offer relief to labs and vivaria across the world that are faced with social distancing restrictions, staff reductions, or temporary closures

See the entire Coronavirus toolkit at **taconic.com** or schedule a call with us to learn more.

* Personal communication, Kent Tseng, UTMB.

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