SARS-CoV-2 infection induces greater disease severity in the Physiogenex free-choice diet-induced obese NASH hamster

a metabolic comorbidities model of Covid-19

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Golden Syrian hamster: a preclinical model of human SARS-Cov-2 infection

- As in humans, hamster ACE2 functions as a receptor for SARS-CoV-2.
- Pathogenesis and transmissibility of the SARS-CoV-2 has been demonstrated in Golden Syrian hamsters
- With the absence of comorbidities, animals recover from mild infection.

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Spike protein recognition of mammalian ACE2 predicts the host range and an optimized ACE2 for SARS-CoV-2 infection

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ABSTRACT

SARS-CoV-2 causes the recent global COVID-19 public health emergency. ACE2 is the receptor for both SARS-CoV-2 and SARS-CoV. To predict the potential host range of SARS-CoV-2, we analyzed the key residues of ACE2 for recognizing S protein. We found that most of the selected mammals including pets (dog and cat), pangolin and *Circetidae* mammals remained the most of key residues for association with S protein from SARS-CoV and SARS-CoV-2. The interaction interface between cat/dog/pangolin/Chinese hamster ACE2 and SARS-CoV/SARS-CoV-2 S protein was simulated through homology modeling. We identified that N82 in ACE2 showed a closer contact with SARS-CoV-2 S protein than M82 in human ACE2. Our finding will provide important insights into the host range of SARS-CoV-2 and a new strategy to design an optimized ACE2 for SARS-CoV-2 infection.

Article

Pathogenesis and transmission of SARS-CoV-2 in golden hamsters

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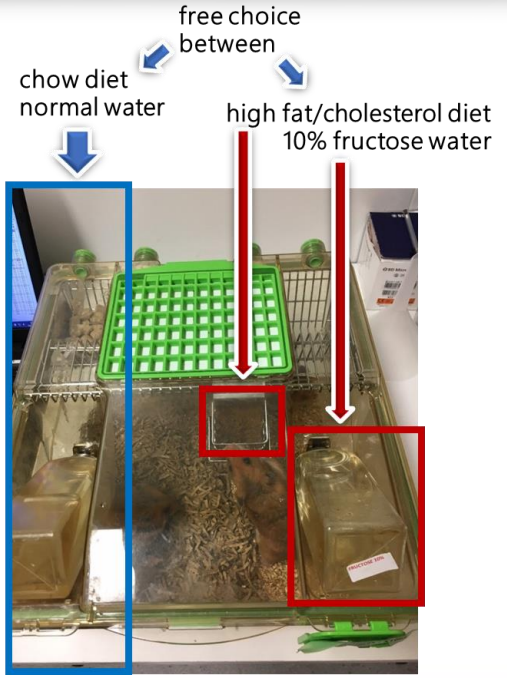
Sin Fun Sia[1,3], Li-Meng Yan[1,3], Alex W. H. Chin[1,3], Kevin Fung[2], Ka-Tim Choy[1], Alvina Y. L. Wong[1], Prathanporn Kaewpreedee[1], Ranawaka A. P. M. Perera[1], Leo L. M. Poon[1], John M. Nicholls[2], Malik Peiris[1] & Hui-Ling Yen[1]✉

SARS-CoV-2, a novel coronavirus with high nucleotide identity to SARS-CoV and SARS-related coronaviruses detected in horseshoe bats, has spread across the world and impacted global healthcare systems and economy[1,2]. A suitable small animal model is needed to support vaccine and therapy development. We report the pathogenesis and transmissibility of the SARS-CoV-2 in golden Syrian hamsters. Immunohistochemistry demonstrated viral antigens in nasal mucosa, bronchial epithelial cells, and in areas of lung consolidation on days 2 and 5 post-inoculation (dpi), followed by rapid viral clearance and pneumocyte hyperplasia on 7 dpi. Viral antigen was also found in the duodenum epithelial cells with viral RNA detected in feces. Notably, SARS-CoV-2 transmitted efficiently from inoculated hamsters to naïve hamsters by direct contact and via aerosols. Transmission via fomites in soiled cages was less efficient. Although viral RNA was continuously detected in the nasal washes of inoculated hamsters for 14 days, the communicable period was short and correlated with the detection of infectious virus but not viral RNA. Inoculated and naturally-infected hamsters showed apparent weight loss, and all animals recovered with the detection of neutralizing antibodies. Our results suggest that SARS-CoV-2 infection in golden Syrian hamsters resemble features found in humans with mild infections.

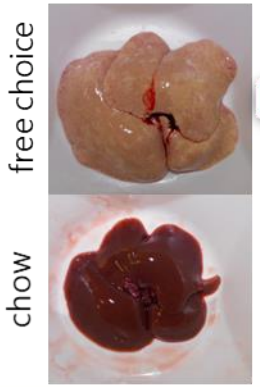
Physiogenex free choice diet-induced obese NASH hamster: A model of metabolic comorbidities

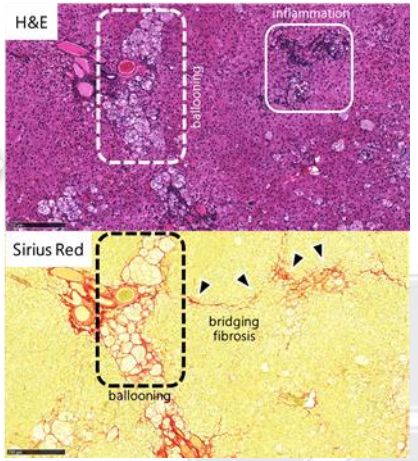
Up to 20-week free choice diet induction
(cohort of hamsters already on diet available)



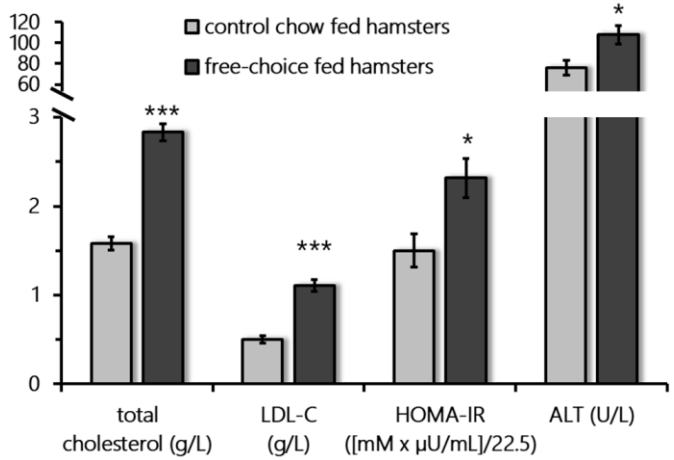
obesity

NASH +
liver fibrosis





dyslipidemia/insulin resistance



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Briand et al., *Eur J Pharmacol* 2018; Briand et al. *Metabolism*, 2021

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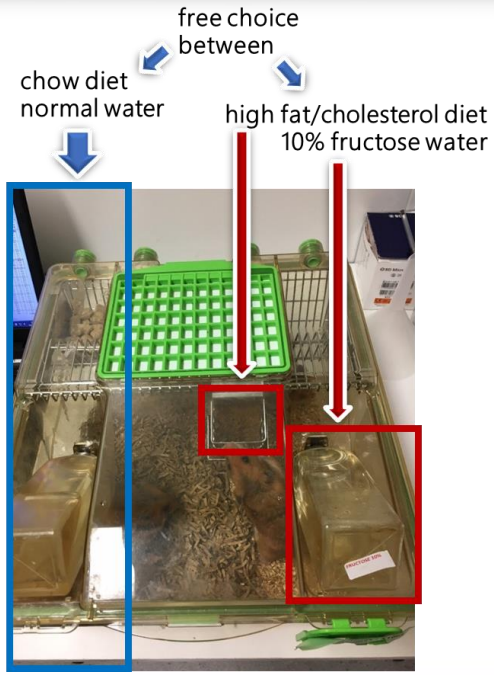
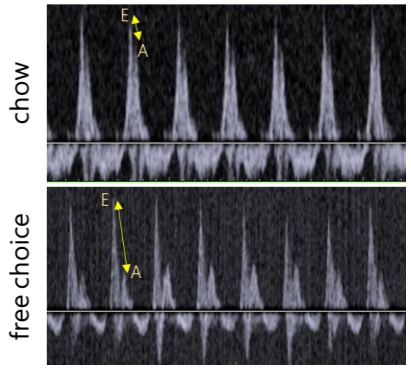
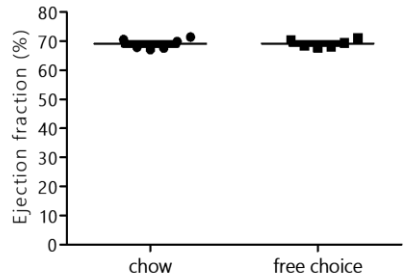
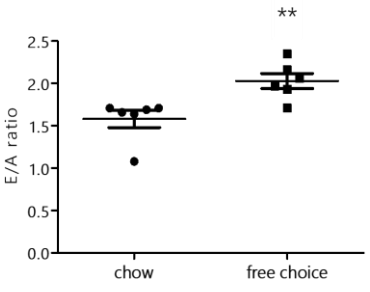


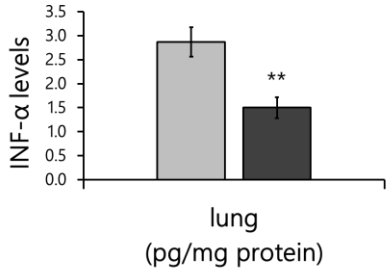
heart failure with preserved ejection fraction

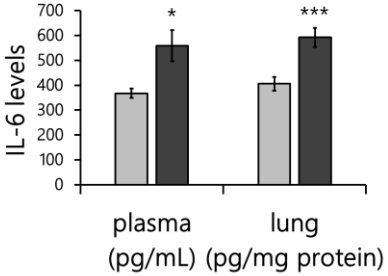




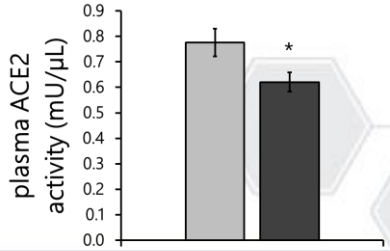


low Inf-α / high IL-6 lung pro-inflammatory profile





lower plasma ACE2 activity



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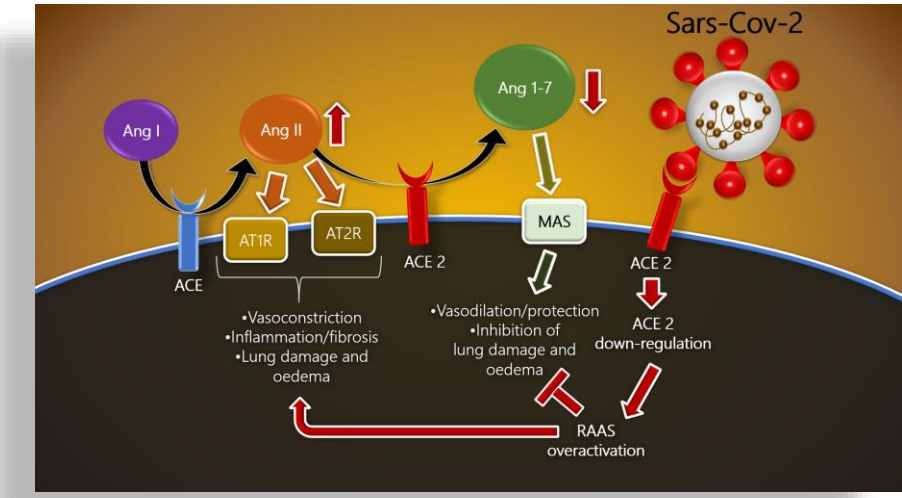
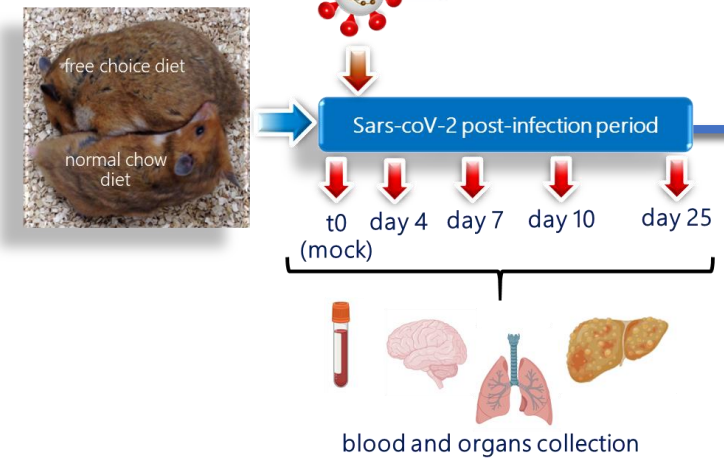
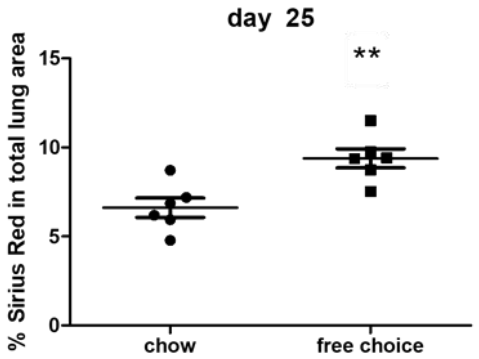
SARS-CoV-2 infection induces greater disease severity in free choice diet fed hamsters vs. chow diet fed controls

Free choice diet
increases serum AngII levels
and reduces serum Ang1-7 levels

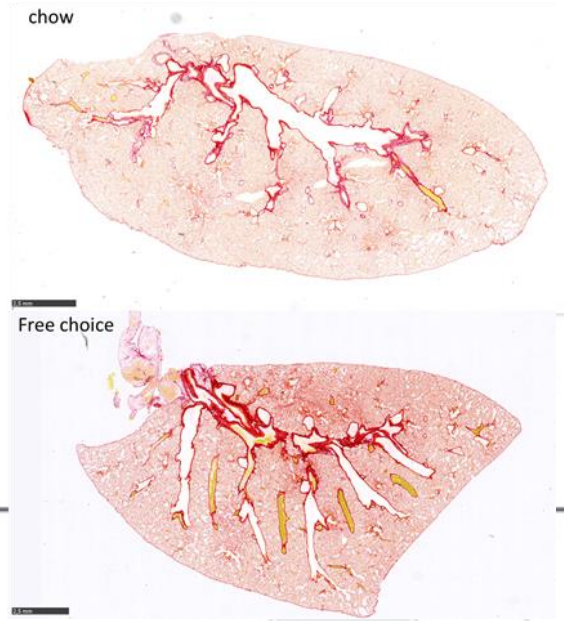




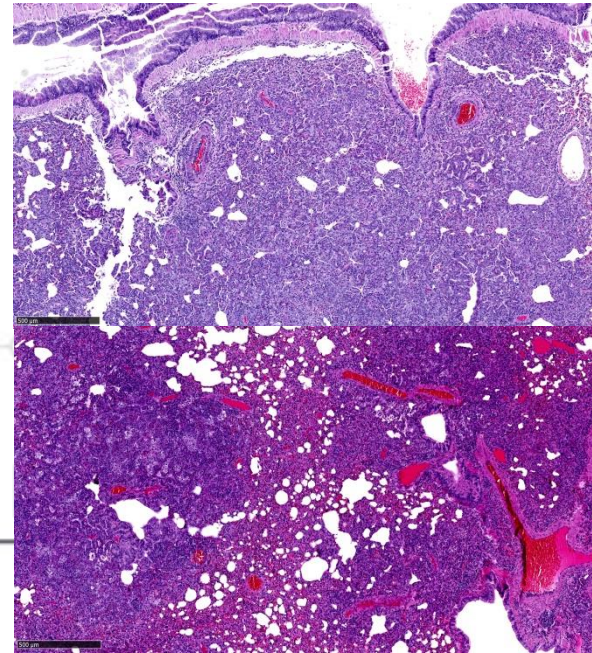
Free choice diet
induces more severe lung damages
and results in higher lung fibrosis



lung Sirius Red staining (day 25)



lung H&E staining (day 10)



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