

# a unique series of humanized-ACE2 and Ace2-KO mouse models available for your COVID-19 research needs

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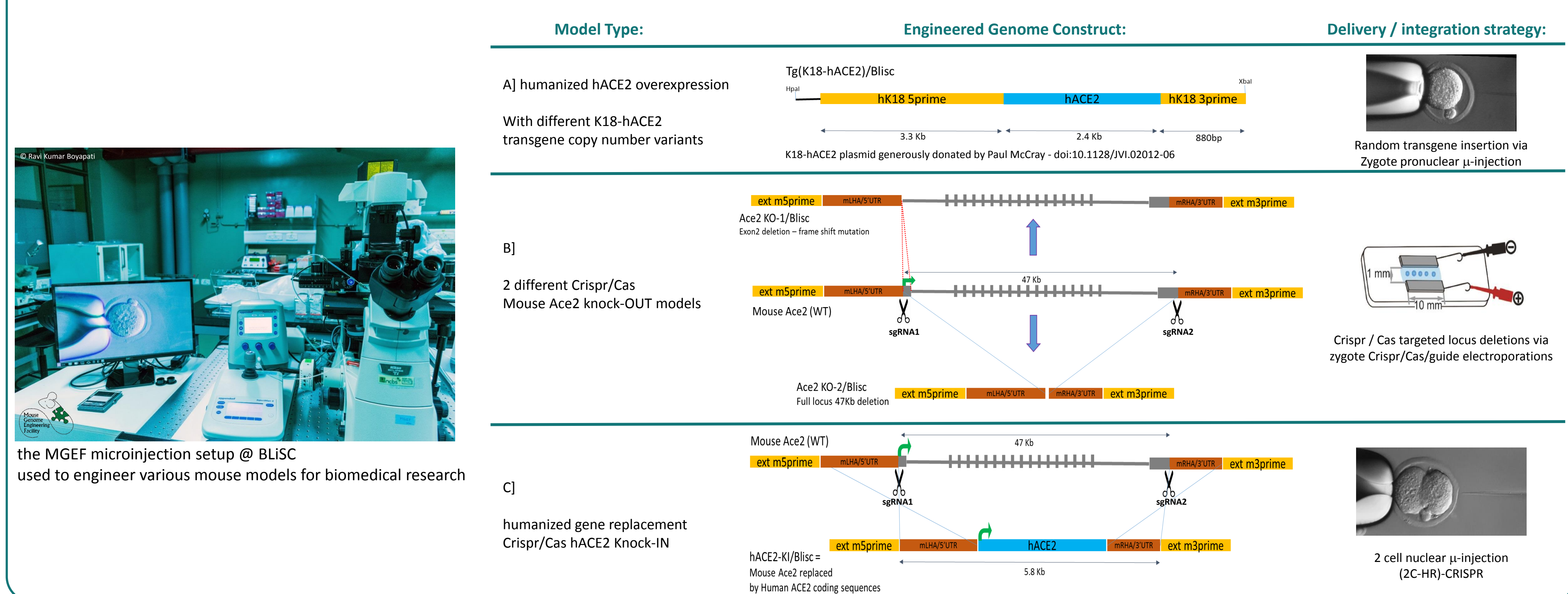
## ABSTRACT:

In response to the immediate needs of researchers nationwide, the Mouse Genome Engineering Facility (MGEF) of the Bangalore Life Science Cluster (BLiSC) has leveraged its expertise and infrastructure to address this public health crisis. By August 2020, MGEF designed a series of unique ACE2 mouse models to facilitate SARS-CoV2 /COVID-19 related research and therapeutics projects.

The first set of models are the Transgenic: Tg(K18-hACE2)/Blisc mice. These are humanized models over-expressing the human ACE2 gene under the regulatory sequences of the human keratin 18 (KRT18) promoter. 3 different Tg(K18-hACE2)/Blisc founder lines were established and characterized. Each line expressing different levels of the K18-hACE2 transgene leading to different levels of SARS-CoV2 infection responses recapitulating the different severity levels of COVID-19 symptoms.

These Tg(K18-hACE2)/Blisc lines are currently being redistributed across the country for various COVID-19 vaccine and therapeutic assays. Two different mAce2 Knock OUT (KO) mice also have been generated and we have generated constructs to engineer Targeted Knock-IN hACE2-KI/Blisc models in which the mouse Ace2 locus is replaced by the human ACE2 coding sequences. These KI models are being designed in a NSG background and can be customized as unique tools for translational approaches to personalized or population based precision medicine. We will present here our results characterizing the different ACE2 mouse models generated at MGEF/BLiSC and our future plans to enhance vaccine and therapeutic research and screening capacities in India.

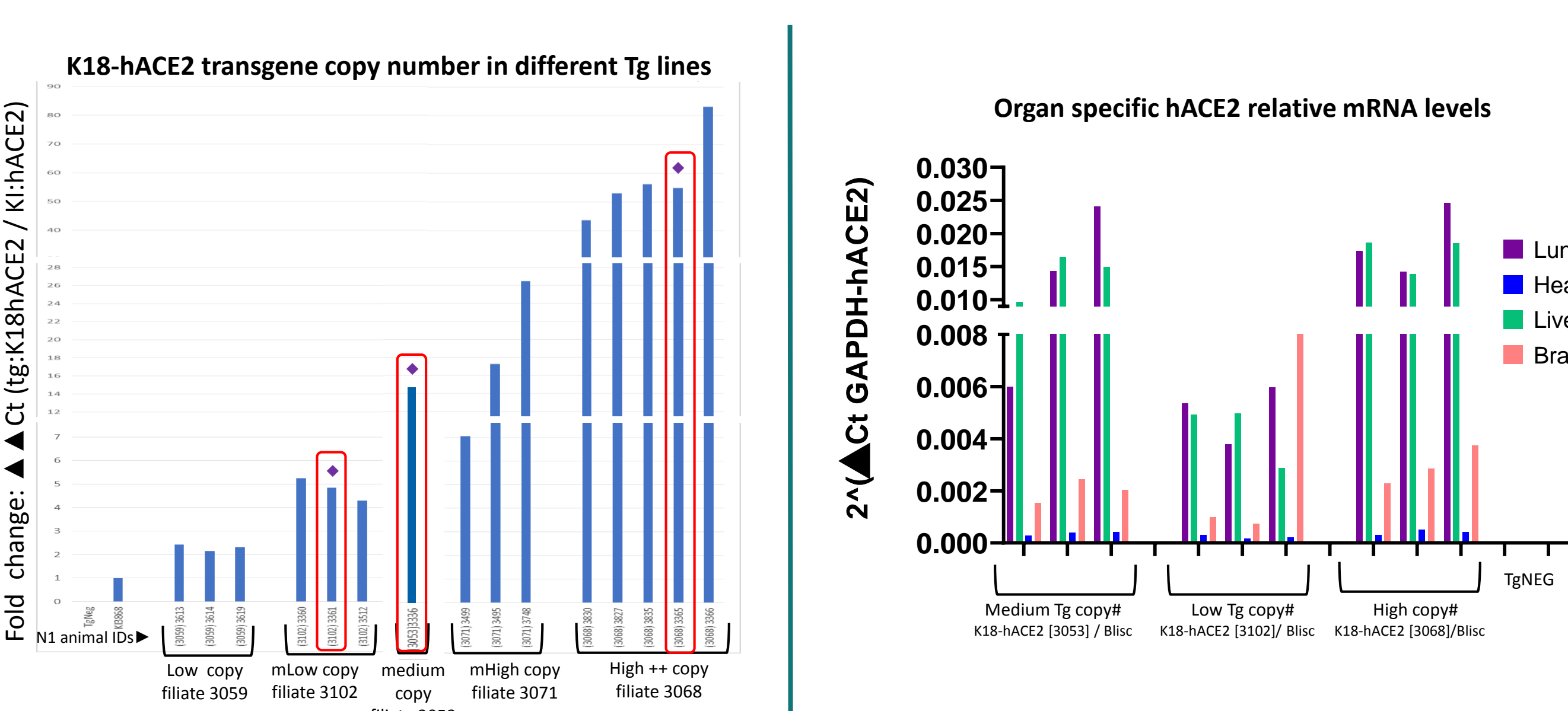
## 1) Different ACE2 alleles designed to answer different biomedical questions



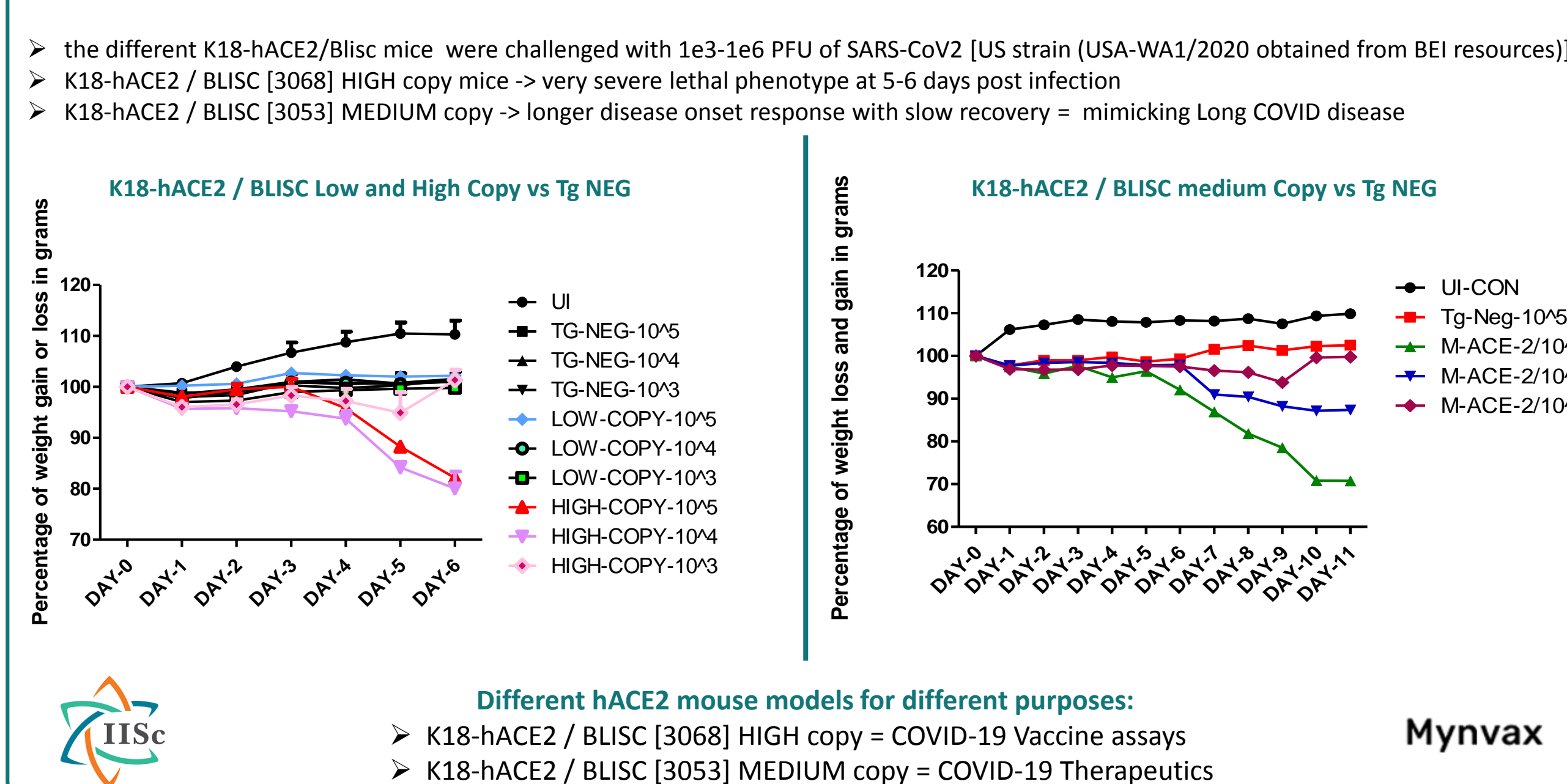
## 2) hACE2 and mAce2 KO / BLiSC animal colonies maintained in High Barrier SPF facility



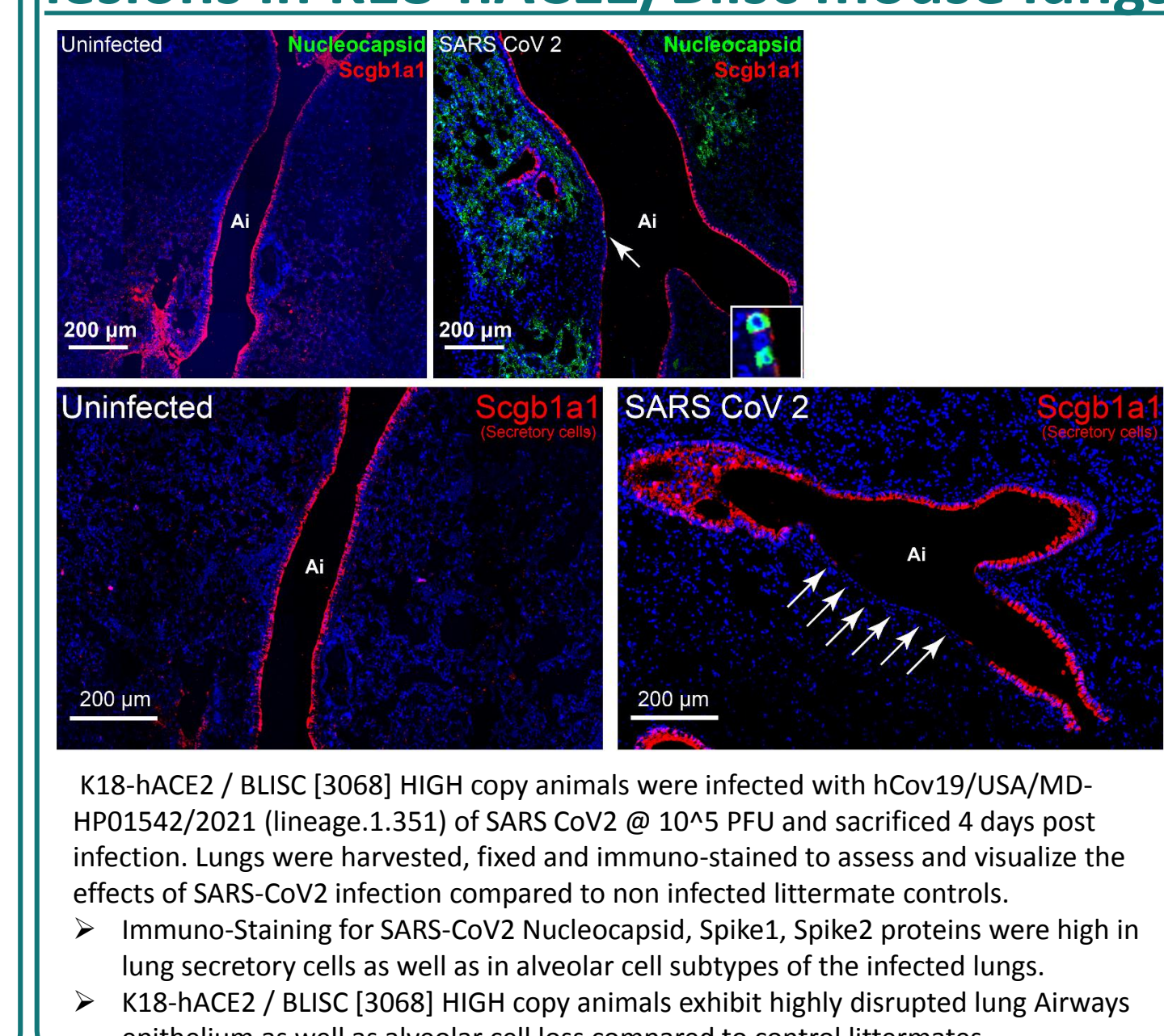
## 3) different K18-hACE2 transgene copy number mouse lines drive different levels of hACE2 expression in different organs



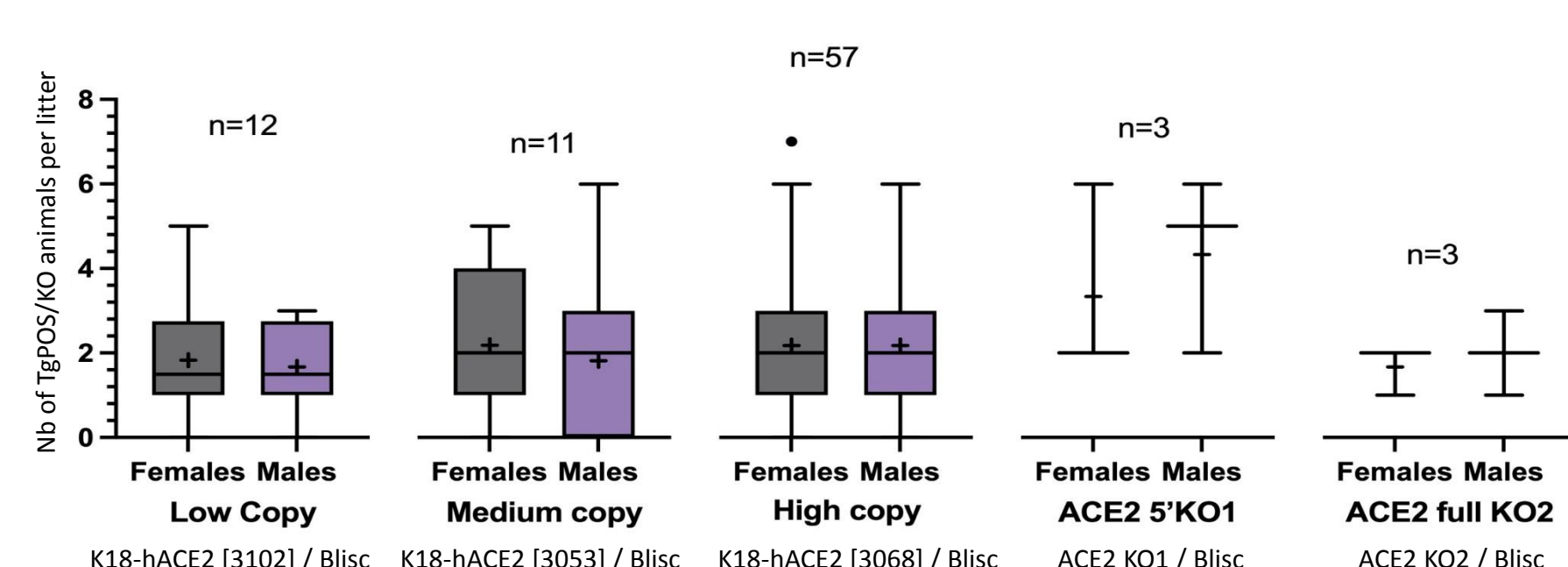
## 4) K18-hACE2/Blisc mice respond to SARS-CoV2 infection



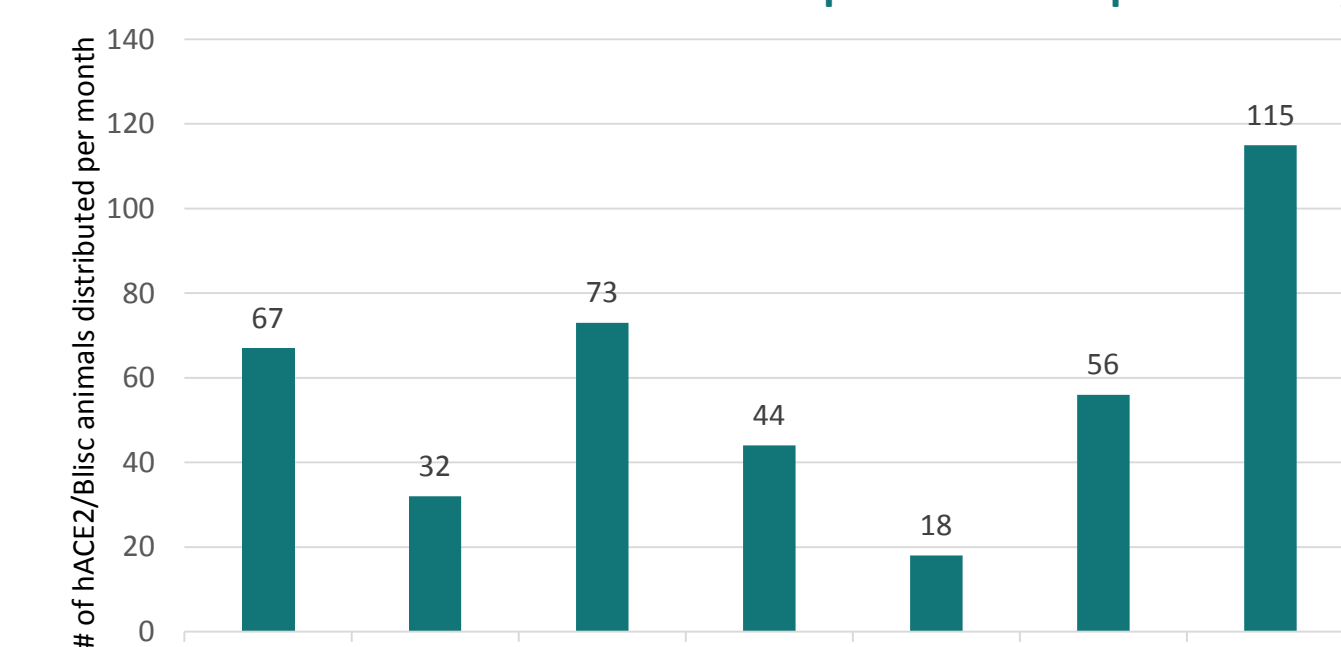
## 5) SARS-CoV2 infection induces acute lesions in K18-hACE2/Blisc mouse lungs



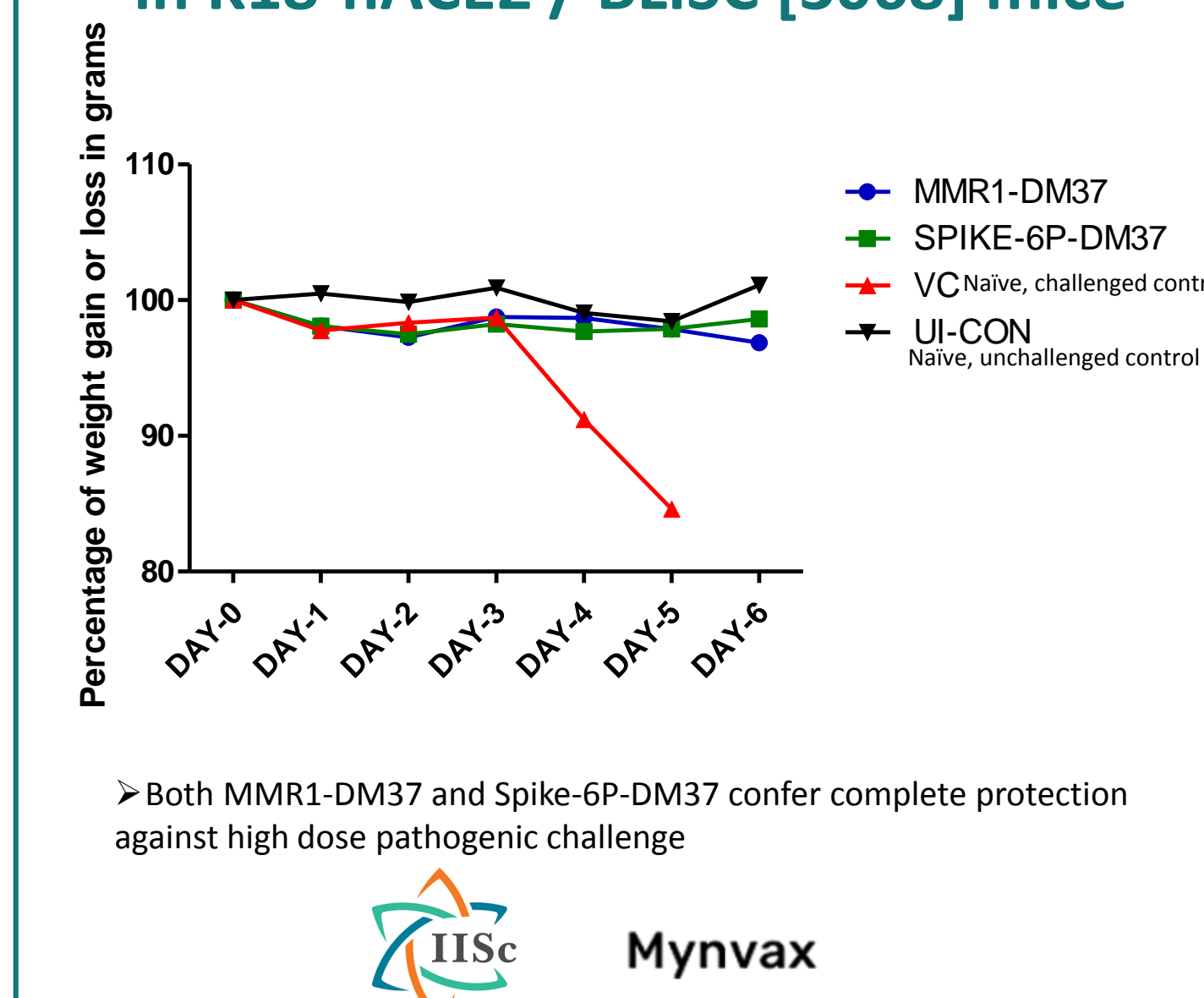
## 6) MGEF now setup to provide age matched cohorts of up to 50tg Positive animals per cohort



➤ Over 400 K18-hACE2/Blisc mice have been redistributed across India For various COVID-19 vaccine & Therapeutics development assays.



## 7) Protective efficacy of designed vaccine formulations against SARS-CoV2 in K18-hACE2 / BLiSC [3068] mice



## 8) Future Directions: Establishing Patient & Population Humanized Mouse models for Precision Medicine screening assays

