

Animal models for BSL-3 virus

SARS-CoV-2

Animal: K18ACE2 or hACE2-KI mice, or another suitable model.

Virus: SARS-CoV-2

Experimental design: The animals are divided in the adequate number of groups with a statistically meaningful number of animals per group. For example, 6 groups of 11 mice per group (n=11) are infected with an inoculum of SARS-CoV-2. After an adequate interval of time (8h, 16h, 24h, etc.) the animals are treated with the test-compound intranasally under an appropriate anesthetic/sedation protocol. For example, mice and hamster are typically anesthetized via intraperitoneal (IP) injection of ketamine/xylazine (50/5 mg/kg) for each intranasal administration (50µL per nostril, for example) of the test-compounds or vehicle. Groups with different doses of the elected test-compounds follow this protocol for the duration of time established for the experiment (2 to 6 days, for example). A mock group that received the exact same manipulation and is given only vehicle (PBS or 0.9% saline for example) is also included. Groups receiving positive controls with clinically accepted pharmaceuticals at the dosing regimen established in the literature will also be included in the study if there are such compounds available. For example, SARS-CoV-2 can use as positive control compounds such as Molnupiravir or Paxlovid, following the accepted use in the literature adequate for the animal model. The body weight of each animal is recorded daily beginning on the day of virus challenge. The animals are observed daily for survival and signals of morbidity relevant to the study. The animals are euthanized at an adequate timepoint for the experiment, for example 6dpi. Measurables such as viral loads in the lungs and upper respiratory tract are measured. Harvesting of organs and tissues for histopathological analysis to be considered according to need.

Example of a study plan in the table below. More than one test compound can be envisioned.

No./group	Group No.	Compound	Dose	Treatment Route & schedule	Observations/testing
3	1	Untreated			Daily body weight measurement and mortality observation. Mice will be sacrificed at 6dpi, and viral loads in the lungs and nose will be measured. Histopathological analysis according to need.
11	2	Vehicle placebo		Intranasal administration (50ul in both nostrils) daily for 2 to 5 days, beginning at an established time post-infection (8h, 12h, 16h, etc.)	
11	3	Compound(s)	Dose 1		
11	4		Dose 2		
11	5		Dose 3		
11	6	Positive control(s) Molnupiravir Paxlovid	Dose accepted in the literature	Optimal administration accepted in the literature	