Digital ventilated cage (DVC®) in Covid19 Research: immediate mice sickness detection

Introduction

Since the Pandemic start, a global effort raised to identify the mechanisms of action of the SARS-CoV-2 (Covid19) virus and find a cure. In preclinical research, several animal models have been proposed ranging from Syrian Hamsters up to Non-Human Primates. Unfortunately, the most used animal model, namely the mouse, does not properly show signs of infections because of lacking the receptor by which the virus can enter the murine cells. In February 2020, Jackson Lab thawed the **K18-hACE2 mice**, initially created for studying the SARS Virus (McCray et al., 2007), that are carrying the human ACE2 receptor, which is "lock" by which the virus enters the cell with its "key" the spike protein. This mouse model has been presented in several articles as one of the most wanted by several journals (scientific or more for the general audience, two are mentioned below).

https://www.nytimes.com/2020/03/14/science/animals-coronavirus-vaccine.html

https://www.nature.com/articles/d41586-020-00698-x

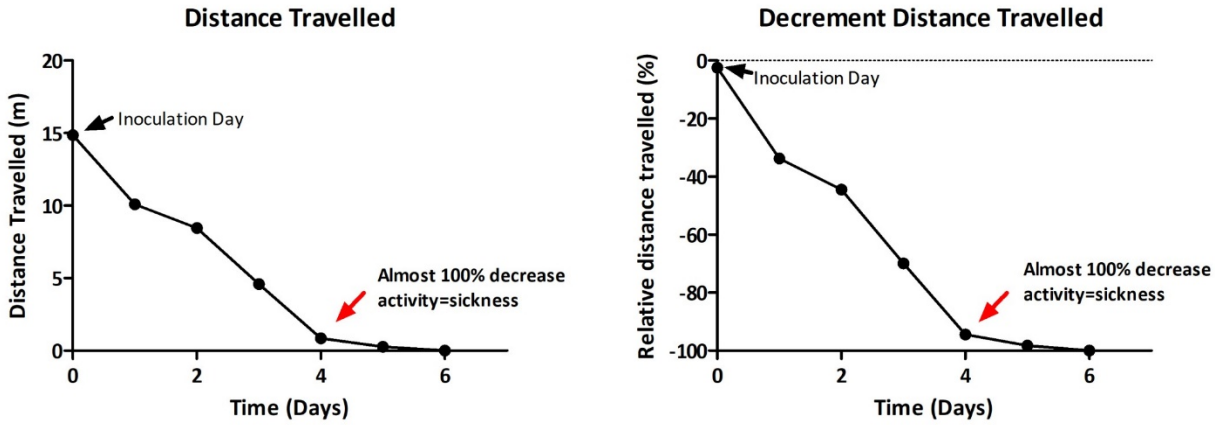
As the mice have become only available in early summer 2020, the most prominent centres in the world have started to work with those mice to evaluate the viral response and its cures (drugs or vaccines). Most of publications about infectious disease, including *in-vivo* laboratory animals' experiments, use body weight as output for animal welfare. Two recent publications indicate that body weight loss, as indicator for clinical sign, is visible only from day 4 onwards (Jiang et al., 2020; Winkler et al., 2020). However, we tested the hypothesis of whether the Home Cage Monitoring System namely the Digital Ventilated Cages (DVC®) identifies sickness induced by Covid19 via measuring locomotion as measured of clinical sign. As control we incorporated body weight loss as gold standard measure.

Methods

At Tecniplast S.p.A., in collaboration with RI-MUHC BSL3 Facility at McGill University, Montreal, we evaluated through our non-intrusive and outside of the cage technology directly in the home rack

called Digital Ventilated Cage (DVC®) (Iannello, 2019; Pernold et al., 2019) the clinical signs of those mice upon SARS-CoV2. To this end, Eight K18-hACE2 (C57Bl/6J background) mice were exposed to the SARS-COV-2 virus, and the locomotion was assessed for six days. Body weight was taken daily as reference.

Results & Brief Discussion



The graphs show that there was a significant decrease in distance travelled of about 50% after two days and a full decline of 98% decrease after four days following inoculation. Noteworthy, after six days, the animals were completely immobile. These results indicate sickness of the animal, and it is the first data of its kind showing that SARS-CoV-2 impacts in such a dramatic way the animal locomotion. Instead, mice started to have body weight loss only after 4 days and decline by 15-20% after 6-7 days following inoculation (Data not shown). These findings are in line to what was recently published (Jiang et al., 2020; Winkler et al., 2020).

Noteworthy, the locomotion results are in line with what was reported before by other studies, namely that after seven days of SARS inoculation, the hACE2 mouse model become very sick up and eventually died after seven days (McCray et al., 2007).

Conclusion

The DVC® system demonstrated its potential to identify the viral effect (immediate sickness). Current research is underway to understand what the effects are via different vaccines. Additionally, because the technology can be applied in BSL-3 and 4 environments, the same system could also be

used for automated, high-throughput, and unbiased data collection to support neurological diseases such as rabies or other zoonotic models.

Acknowledgments

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