Preclinical assessment of an anti-SARS-CoV-2 antibody

Gregorio Carballo-Uicab[1,3], Edith González-González[1,3], Luis Valencia-Flores[1,3], Ilselena Cortez-Paniagua[1,3], Juana Salinas-Trujano[1,3], Blanca Sánchez-Morales[2,3] , Luis Vallejo-Castillo[1,3], Sonia M. Pérez-Tapia[1,3], Juan C. Almagro[1,2,3]

[1] **UDIBI, Instituto Politécnico Nacional**, Mexico City, Mexico
[2] **GlobalBio, Inc**. Cambridge, MA 02138
[3]Laboratorio Nacional para Servicios Especializados de Investigación, Desarrollo e Innovación (I+D+i) para Farmoquímicos y Biotecnológicos, **LANSEIDI-FarBiotec-CONACyT**, Mexico City 11340, Mexico

Abstract

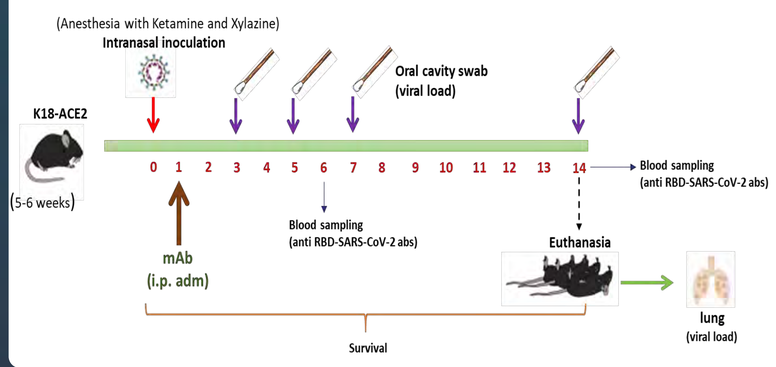
Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the virus responsible for COVID-19 (coronavirus disease). This virus emerged in China (December 2019) and since then has caused over 6 million fatalities incalculable financial problems. The mechanism of infection of SARS-CoV-2 involves the recognition of the human Angiotensin-Converting Enzyme 2 (ACE-2) through its Receptor Binding Domain (RBD) of the S1 protein.

The international scientific community, the WHO, and Drug Agencies have strongly suggested developing prophylactic (vaccines) and therapeutic (neutralizing antibodies or NAb) treatments. Nabs are intended for immunosuppressed people and those that cannot be vaccinated. Although Nabs are developed faster than vaccines (the first approved treatment for the COVID-19 pandemic was an antibody cocktail Casirivimab + imdevimab, 21/Nov/2020), they have also to accomplish with safety, efficacy, and quality. A crucial aspect of Nab development is the preclinical evaluation, which includes efficacy in relevant models, tissue cross-reactivity (TCR) assay, toxicity, pharmacological safety, and determination of the toxicokinetics and pharmacokinetics.

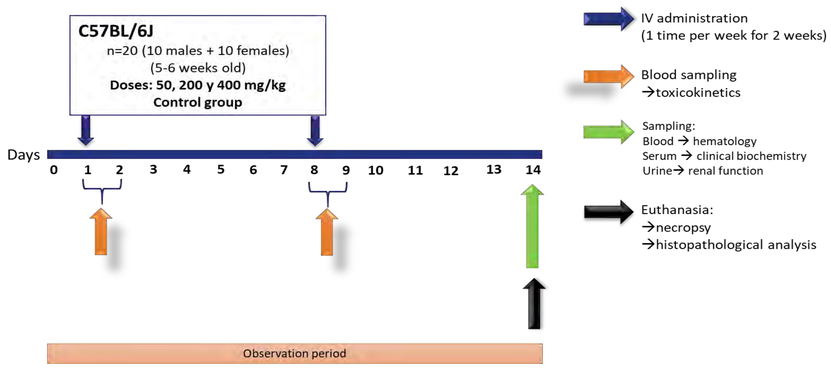
Our working group has extensive experience in discovering treatments based on monoclonal antibodies (mAbs) using phage display technology and semi-immune libraries. In this sense, a Nab against the SARS-CoV-2 has been obtained. This work aims to describe the non-clinical strategy to determine the efficacy of the D1H antibody (efficacy, toxicity, and pharmacokinetics), and to show results from efficacy studies.

Strategy for the preclinical assessment of the anti SARS-CoV-2 Nab

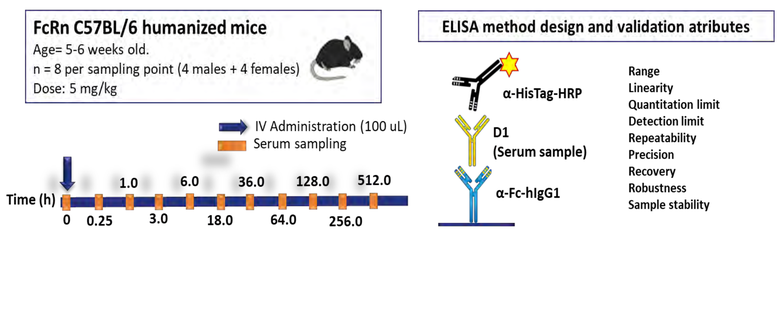
Pharmacodynamics (PD)



Toxicicity/ toxicokinetics (TK)



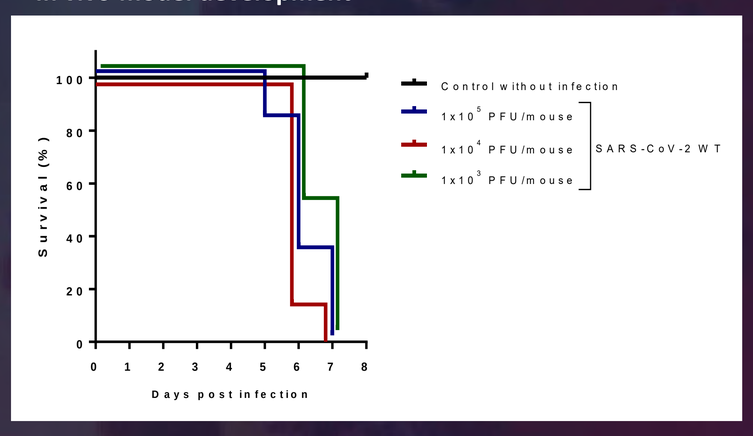
Pharmacokinetics (PK)



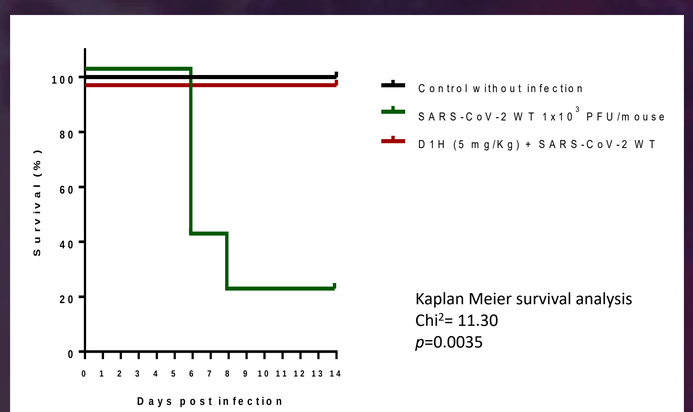
Results: PD

Survival

In vivo model development

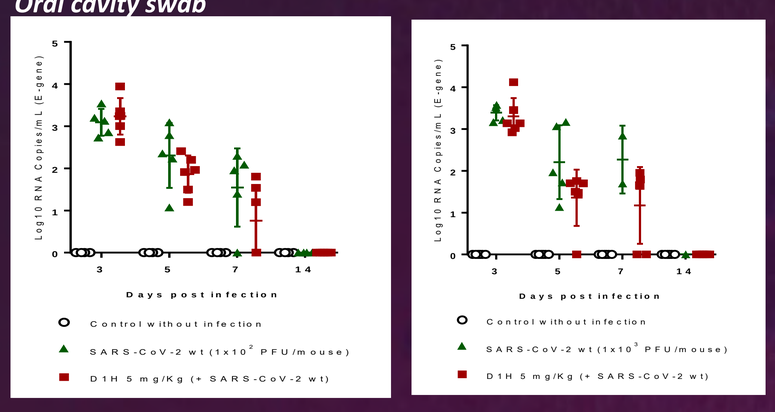


Evaluation of therapeutic effect

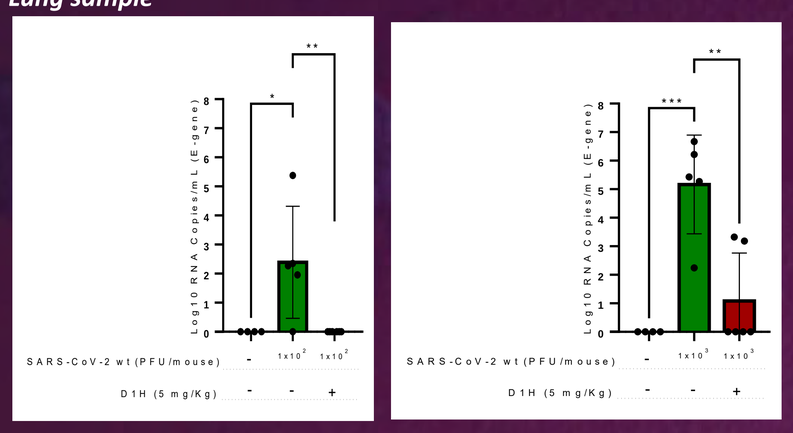


Viral load

Oral cavity swab



Lung sample

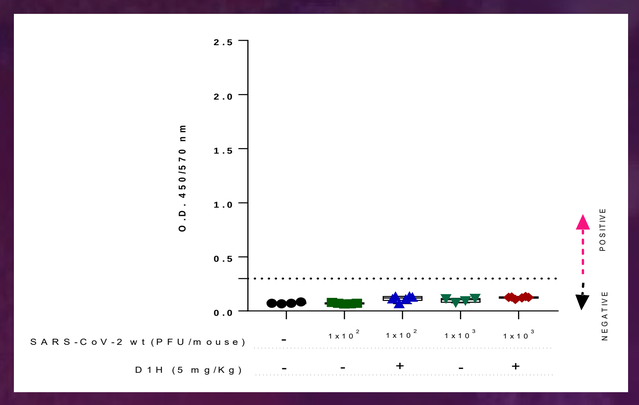


ANOVA de una vía + *post hoc* de Dunnet
F(3, 17)= 6.65; p=0.0036

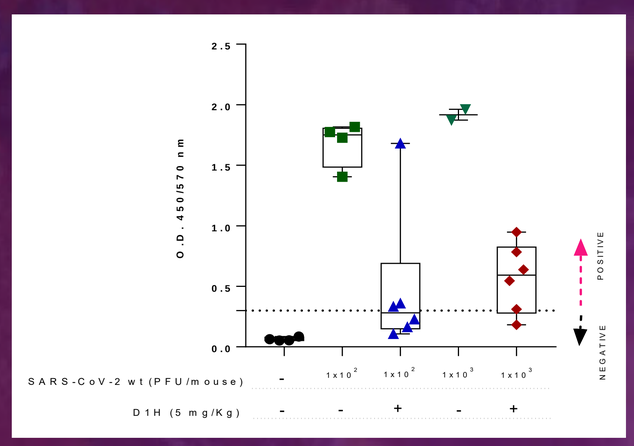
ANOVA de una vía + *post hoc* de Dunnet
F(2, 12)= 16.27; p=0.0004

Production of anti RBD-SARS-CoV-2 antibodies

Day 6 post infection



Day 14 post infection



For Information, please contact:

Juan C. Almagro, Ph.D.
juan.c.almagro@globalbioinc.com
Tel: +1.617.710.4487
www.globalbioinc.com

Sonia Mayra Perez Tapia, Ph.D.
mayra.perez@udibi.com.mx
Tel: +55.52.55.5498.6682
57296000 EXT 62543
www.udidi.com.mx

Gregorio Carballo Uicab, MSc.
gregorio.carballo@udibi.com.mx
57296000 EXT 62543
www.udidi.com.mx

Conclusion

- **The anti-SARS-CoV-2 monoclonal antibody called D1H has a protective effect at a dose of 5 mg/Kg in the Wuhan variant SARS-CoV-2 infection model, showing 100% survival and a significant decrease in viral load in the lung.**