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A high-throughput drug screening assay to identify competent replication inhibitors against the Equine Viral Arteritis (EAV) virus and other related viruses, A ONE HEALTH approach study.

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Introduction
The high mutation rate of RNA viruses can make of them more inter-species transmissible and represent a significant global health issue. One Health approaches are important because they can help better understand viral infections regarding the problem from different angles to develop the most interesting and global therapeutic solutions. In our laboratory, we study the Equine Arteritis Virus (EAV), a virus from the Nidovirus order, which has a worldwide distribution and a major health and economic impact on the equine industry. Currently, therapeutic EAV tools are limited to two efficient vaccines and only one authorized in some EU countries. Unfortunately, these control measures are not enough to control this disease, and each year EAV outbreaks impact the equine population worldwide. Our work aims to explore the use of antiviral molecules to treat EAV-infected animals during the acute phase of the viral infection and be used as a complementary tool in the programs of control of EAV disease.
Material and Methods
We have set up an in-vitro EAV infection model on equine cells [1]. We have upgraded this infection model to a high-throughput screening system by optimizing the culture and detection conditions, to be able to screen 1250 molecules used in the human pharmacopeia. A cytotoxic and cytoprotection assays were performed and the supernatant of the most promising molecules were collected after 72hpi for viral quantification by RT-qPCR analysis.
Results
We have developed a High-throughput drug screening model for lytic viruses and screened 1250 molecules. We have identified 75 candidates with better or similar performances regarding our internal control Ribavirin. From those 75 molecules, after studying their capacity to impair viral replication, we selected a list of 45 promising molecules that could decrease the viral replication more than 10 times and some of them 10000 times, without cytotoxic effect. Interestingly, 7/45 molecules never showed before antiviral activity. Our in-vitro results contribute today to enlarging their therapeutic spectrum, inhibiting the replication of a nidovirus. In addition to that, 3 of this 10 new antiviral molecules are today included in the equine pharmacopeia which could accelerate the steps for developing an EVA antiviral treatment. These exciting results encourage us also to explore these molecules from a one-health perspective, and we tested some of these molecules as a potential therapy against nidovirus infecting humans and other animals. We tested 2 molecules in an in-vitro model of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), also a member of the Nidovirales order, like the EAV virus. Despite belonging to different families, they share many molecular properties, including genomic organization and replication strategy. Our results were a success and we got a viral replication inhibition of more than 95%.
Conclusion
Our experimental results allow us to conclude that we have identified potential antiviral candidates to control EAV diffusion during EVA outbreaks. We have also identified new antiviral properties of therapeutic molecules that enlarge their therapeutic spectrum impairing Nidovirus replications, and that could contribute today and maybe in the future to control emerging viral diseases.