

## **Phenotypic High-Throughput Screening of MMV COVID Box for discovery of protective compounds against St. Louis encephalitis virus infection.**

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Arthropod-borne viruses are organisms of great clinical importance that have caused significant impacts on human health in the last decades. The Flavivirus genus stands out among them for comprising important human pathogens such as Dengue, Yellow fever, and Zika virus. Furthermore, there are others with the potential to emerge, such as St. Louis encephalitis virus (SLEV), which is present in the Americas and may cause neuropathologies that lead to death or sequelae. There is no specific treatment or vaccine against SLEV. The High-Throughput Screening (HTS) assay is a method that allows a large number of compounds to be tested in an automated way, which makes it a viable model for drug discovery. However, drug discovery is an expensive and overlong process that can take several years to be completed. Considering that, drug repurposing can be a viable strategy in the development of new treatments for diseases once the compounds have already been tested and approved for human use, requiring less time and money than the discovery of an entirely new drug. From this, a phenotypic *High-Throughput Screening* was developed and validated through the MMV Covid-Box library. Of the eighty compounds screened at three different concentrations, nine of them showed a protective effect against infection at different levels. Since they belong to distinct pharmacological classes, the study suggests there may be different relevant molecular pathways in viral infection and, thus different targets against it. Therefore, we seek to better understand the mechanisms of infection for the future development of treatment strategies for this and other related arboviruses.

Key-words: Drug repurposing; *High-Throughput Screening*; St. Louis encephalitis virus

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