**ABSTRACT**

The SARS-CoV-2 outbreak has so far not been confined due to the unpreparedness and unsuccessful development of antiviral drugs against SARS-CoV-2. The development of a SARS-CoV-2 replicon system will enable us to work with this pathogen in low-level of biosafety laboratory (level-2) and importantly will allow us to introduce targeted mutations in the viral genome. This will lay foundation to the investigation into its biology and underlying disease etiology. Furthermore, the replicon system can serve as a platform to develop reporter viruses essential for rapid screening of antivirals. Truncated versions of the genomes, where key structural proteins are substituted with various reporter genes and/or antibiotic resistance gene(s) will further be developed to preclude the necessity of BSL3 facility and facilitate research projects in the BSL2 laboratories. The coronaviruses encode the largest genomes among RNA viruses and have raised some unique challenges in developing a molecular clone in the past and present. In current study, we are trying to overcome these problems by adopting two distinct approaches i) use of bacterial artificial chromosomes (BACs) and ii) in vitro ligation of cDNA fragments followed by generation of full-length RNA by in vitro transcription.

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**Advantages & Disadvantages of Replicon system**

1. **Deletion of the structural genes will render the replicon defective in producing progeny virions, thereby enabling safe handling under BSL-2 conditions.**
2. **Replicon RNA can be introduced to a variety of cell lines, allowing for assessment of viral replication under more physiologically relevant conditions.**
3. **A high-throughput antiviral assay will be developed using the described replicon system. Under those assay conditions, the sensitivity of viral replication to SARS-CoV-2 inhibitors will be tested.**
4. **Additionally, our replicon lacks the structural genes including S, E, and M. Thus, this system cannot be used for the compounds acting on receptor binding, virus entry, uncoating, and virus release. These targets could be covered by using a single-round infectious pseudo-type reporter virus used in the BSL-2 laboratory.**

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