Rapid identification of coronavirus replicase inhibitors using a selectable replicon RNA

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A previously unknown coronavirus (CoV) is the aetiological agent causing severe acute respiratory syndrome (SARS), for which an effective antiviral treatment is urgently needed. To enable the rapid and biosafe identification of coronavirus replicase inhibitors, we have generated a non-cytopathic, selectable replicon RNA (based on human CoV 229E) that can be stably maintained in eukaryotic cells. Most importantly, the replicon RNA mediates reporter gene expression as a marker for coronavirus replication. We have used a replicon RNA-containing cell line to test the inhibitory effect of several compounds that are currently being assessed for SARS treatment. Amongst those, interferon-alpha displayed the strongest inhibitory activity. Our results demonstrate that coronavirus replicon cell lines provide a versatile and safe assay for the identification of coronavirus replicase inhibitors. Once this technology is adapted to SARS-CoV replicon RNAs, it will allow high throughput screening for SARS-CoV replicase inhibitors without the need to grow infectious SARS-CoV.