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## Letter to the Editor

**Co-infection of MERS-CoV and SARS-CoV-2 in the same host: A silent threat**

Dear Editor,

The novel coronavirus, SARS-CoV-2, emerged in late 2019 in Wuhan City, Hubei Province, China. Travelers carried the virus to many countries, sparking memories of previous coronavirus epidemics such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). As of 1 June 2020, SARS-CoV-2 has infected 6,057,853 people and taken 371,166 lives across the globe [1].

Recombination has been a powerful tool for emerging viruses to get innovative genetic configuration that supports host adaptations and facilitate the course of cross-species diffusion. Numerous recently emerged RNA viruses which were involved in human diseases exhibited active recombination or reassortment events. In coronaviruses (CoVs), a high recombination rate has been reported which can be attributed to the large genome size, discontinuous transcription, and sub- or fully transcriptionally active genomic length of RNA. Under experimental conditions, the recombination frequency of CoVs can be as high as 25% for the entire genome. In comparison with other single-stranded RNA viruses, the estimated mutation rates in CoV are moderate to high with average substitution rates reported as  $\sim 10^{-4}$  substitutions per year per site [2].

CoVs have in the past demonstrated a marked capacity to employ homologous recombination, a process by which viruses exchange genetic material in the context of a coinfection. Indeed, studies have generated substantial evidence that SARS-CoV genome exhibited signs of a mosaic ancestry, and showed that there are at least seven potential regions of recombination in the SARS-CoV genome in the replicase- and spike-coding regions [3]. Further investigation of SARS-CoV origin suggested that SARS-CoV emerged following a recombination event of bat SARS-related coronaviruses (SARSr-CoVs) [4]. Similarly, the epidemic MERS-CoV experienced recombination events between the different lineages, which occurred in dromedary camels in Saudi Arabia [5]. Unsurprisingly, SARS-CoV-2 was also shown to use recombination as a crucial strategy in different genomic regions including the envelope, membrane, nucleocapsid, and spike glycoproteins to become a novel infectious agent, impacting virus reproductive adaptability, allowing for genotype adjustment [6]. Single-nucleotide variation analysis of 84 SARS-CoV-2 genomes have revealed that SARS-CoV-2 has been undergoing active recombination [7]. Moreover, latest reports on SARS-CoV-2 evolution provide compelling evidence that SARS-CoV-2's entire receptor binding motif (RBM) was introduced through recombination with CoVs from pangolins [8].

MERS-CoV seasonal outbreaks still occur in the Middle East (peaks observed in spring season), particularly in the Kingdom

of Saudi Arabia (KSA), concurrently to SARS-CoV-2 outbreaks. Between 1 December 2019 and 31 January 2020, 19 new cases of MERS-CoV have been reported in KSA [9], while monthly number of cases were 18 and 15 for February and March 2020 [10], respectively, indicative of ongoing circulation. WHO reports on 1 June 2020 show 85,261 total cases of SARS-CoV-2 in KSA alone [1]. Although SARS-CoV-2 has appeared more transmissible, it is less deadly than MERS-CoV which has a fatality rate of 34%. Considering the evolutionary trajectories of CoVs, the current co-circulation of SARS-CoV-2 and MERS-CoV represents a threat to public health where a possible co-infection in a human host may result in the emergence of a both highly transmissible and highly fatal new CoV. Emergence of such recombinant CoV would require development of diagnostic assays for continuous surveillance in endemic areas, and would have implications for treatment and immunity as neutralizing antibodies in CoV-infected individuals are raised against the spike protein and would not provide protection against re-infection with a novel recombinant CoV.

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