Efficient replication of the novel human betacoronavirus EMC on primary human epithelium highlights its zoonotic potential

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The recent emergence of a novel human coronavirus (HCoV-EMC) in the Middle East raised considerable concerns, as it is associated with severe acute pneumonia, renal failure, and fatal outcome and thus resembles the clinical presentation of severe acute respiratory syndrome (SARS) observed in 2002 and 2003. Like SARS-CoV, HCoV-EMC is of zoonotic origin and closely related to bat coronaviruses. The human airway epithelium (HAE) represents the entry point and primary target tissue for respiratory viruses and is highly relevant for assessing the zoonotic potential of emerging respiratory viruses, such as HCoV-EMC. Here, we show that pseudostratified HAE cultures derived from different donors are highly permissive to HCoV-EMC infection, and by using reverse transcription (RT)-PCR and RNAseq data, we experimentally determined the identity of seven HCoV-EMC subgenomic mRNAs. Although the HAE cells were readily responsive to type I and type III interferon (IFN), we observed neither a pronounced inflammatory cytokine nor any detectable IFN responses following HCoV-EMC, SARS-CoV, or HCoV-229E infection, suggesting that innate immune evasion mechanisms and putative IFN antagonists of HCoV-EMC are operational in the new host. Importantly, however, we demonstrate that both type I and type III IFN can efficiently reduce HCoV-EMC replication in HAE cultures, providing a possible treatment option in cases of suspected HCoV-EMC infection. IMPORTANCE A novel human coronavirus, HCoV-EMC, has recently been described to be associated with severe respiratory tract infection and fatalities, similar to severe acute respiratory syndrome (SARS) observed during the 2002-2003 epidemic. Closely related coronaviruses replicate in bats, suggesting that, like SARS-CoV, HCoV-EMC is of zoonotic origin. Since the animal reservoir and circumstances of zoonotic transmission are yet elusive, it is critically important to assess potential species barriers of HCoV-EMC infection. An important first barrier against invading respiratory pathogens is the epithelium, representing the entry point and primary target tissue of respiratory viruses. We show that human bronchial epithelia are highly susceptible to HCoV-EMC infection. Furthermore, HCoV-EMC, like other coronaviruses, evades innate immune recognition, reflected by the lack of interferon and minimal inflammatory cytokine expression following infection.
Importantly, type I and type III interferon treatment can efficiently reduce HCoV-EMC replication in the human airway epithelium, providing a possible avenue for treatment of emerging virus infections.

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