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Differential beta-coronavirus infection dynamics in human bronchial epithelial organoids

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Our study investigates the interactions between various beta-coronaviruses (beta-CoVs) and the lower respiratory system using human bronchial epithelial (HBE) organoids. The focus is on HCoV-OC43, SARS-CoV, MERS-CoV, and SARS-CoV-2, with an emphasis on their replication patterns and impacts on the organoids. All beta-CoVs exhibited robust replication, with SARS-CoV-2 achieving peak viral RNA levels at 72 hours post-infection. The infections induced significant alterations in cell populations, characterized by an increase in goblet cells and a decrease in ciliated cells. Distinct cell tropisms were observed for each virus: HCoV-OC43 predominantly infected club cells, SARS-CoV targeted both goblet and ciliated cells, SARS-CoV-2 primarily infected ciliated cells, and MERS-CoV exhibited a strong preference for goblet cells. We revealed an upregulation of genes associated with viral receptors and proteases. Notably, HCoV-OC43 activated the unfolded protein response pathway, potentially facilitating its replication. Furthermore, a complex interplay between inflammatory pathways and the suppression of interferon responses during beta-CoV infections was identified. These findings enhance our understanding of how beta-CoVs interact with host cells and elucidate the antiviral defense mechanisms within the respiratory system.