THE ROLE OF OXIDATIVE STRESS IN NIPAH VIRUS INFECTED HUMAN RESPIRATORY EPITHELIUM

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Nipah virus (NiV) is a deadly zoonotic agent of the family Paramyxoviridae, genus Henipavirus. NiV can cause severe respiratory disease and/or encephalitis and there is no licensed vaccine or therapeutic available for humans. NiV-induced respiratory disease results from acute lung injury of the small airways that can progress to acute respiratory distress syndrome (ARDS). Reactive Oxygen Species (ROS) are molecules produced by airway epithelial cells and play an important role in the pathogenesis of several lung inflammatory diseases, including ARDS, by inducing proinflammatory gene expression and oxidative stress. ROS are produced during Respiratory Syncytial Virus (RSV) infection (family Paramyxoviridae) and play a fundamental role in the pathogenesis of RSV-associated lung inflammatory disease. However, the biological factors involved in the NiV-induced airway disease are still unknown. Here, we investigated whether NiV infected human respiratory epithelial cells undergo oxidative stress and its potential role in the induction of immune response. We performed a global transcriptomic analysis on primary human respiratory epithelial cells infected by NiV and identified the Nrf2-mediated oxidative stress response as one of the top 5 canonical pathways induced during infection. A decrease in expression of antioxidant enzymes including catalase was confirmed by real-time PCR. The state of oxidative stress was confirmed in infected cells as indicated by an increase in isoprostane, a marker of lipid peroxidation. Finally, anti-oxidant treatment of cells during NiV infection resulted in significant decrease of oxidative stress but not virus replication. These results suggest that oxidative stress in NiV infected respiratory epithelium might be the result of inefficient decomposition of ROS due to a lack of antioxidant enzymes. Understanding the molecular mechanisms of oxidative stress in henipavirus pathogenesis is crucial for the development of novel therapeutic intervention strategies to treat and prevent lethal disease, as well as advance the fundamental understanding of virus-host interactions.