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Nipah virus (NiV) is a deadly zoonotic agent of the family Paramyxoviridae that has the ability to cause severe pneumonia and/or encephalitis in humans. NiV-induced respiratory disease results from an acute lung injury and inflammation of the small airways. It has been reported that Reactive Oxygen Species (ROS) produced by airway epithelial cells in response to infection with the paramyxovirus Respiratory Syncytial Virus, contribute to the pathogenesis of lung inflammation by inducing proinflammatory gene expression and oxidative stress. However, the biological factors involved in the NiV-induced airway disease are still unknown. Here, we investigated whether NiV infected human airway epithelial cells undergo oxidative stress and its potential role in immune response modulation. We identified the Nrf2-mediated oxidative stress response as one of the top canonical pathways affected during NiV infection of primary human airway epithelial cells. Oxidative stress was confirmed in infected cells as indicated by a significant increase of a lipid oxidation marker and a decrease of the GSH/GSSG ratio, which correlated well with the reduction of critical antioxidant enzyme gene/protein expression. In addition, infected cells treated by PDTC or BHA antioxidant resulted in a significant decrease of a lipid oxidation marker and inflammatory response in a dose dependent manner. BHA and the Heme Oxygenase 1 inducer CoPP also lowered virus replication. These results suggest that oxidative stress in NiV infected respiratory epithelium is the result of inefficient ROS decomposition due to a lack of antioxidant enzymes. Understanding the role of oxidative stress in NiV pathogenesis is crucial for the development of therapeutics modulating ROS and the inflammatory response associated with NiV infection of the lung.

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