Tumor-Suppressor Protein p53 binds to RSV RNA and Increases RSV Replication by Enhancement of Viral Transcriptional

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Respiratory syncytial virus (RSV) infection is the major cause of childhood lower respiratory illness and has been associated with the induction and exacerbation of asthma. Previously, we reported that RSV infection induced TGF-b expression that caused cell cycle arrest and subsequently enhanced RSV replication. In the current study, we demonstrate that a downstream target of TGF-b signaling, namely P53, is a pivotal transcription factor for RSV replication. Over-expression of p53 protein in H1299 and A549 human epithelial cells enhanced RSV replication by 9 folds. Accordingly, knockdown of p53 using siRNA significantly reduced RSV replication in both cell lines. Stabilization of p53 with nutlin-3 enhanced RSV replication by 8 folds in primary human lung epithelial (PHBE) cells. We hypothesized that a plausible mechanism of enhanced RSV replication by p53 was through direct binding of p53 to RSV RNA. A search of RSV genome revealed several putative p53-responsive elements. The direct interaction of p53 and RSV RNA was shown by EMSA analysis using RSV-specific RNA oligonucleotides. Taken together, we have identified a novel role for p53 as a cis-acting enhancer in regulation of RSV replication. These findings suggest that enhanced p53 expression through lung injury, smoking or air pollution could facilitate a significant increase in RSV replication leading to more severe respiratory pathologies.