

ABSTRACT

Persisting as a risk to public health worldwide, the COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has prompted extensive global research efforts to unravel the dynamic of virus-host interplay contributing to disease severity. One of the SARS-CoV-2 accessory proteins, ORF9b, is recognized for its role in the alteration of host antiviral type I interferon pathways. Currently, there has been worldwide SARS-CoV-2 variants harboring multiple mutations within the ORF9b genome. Thus, this research examined the anti-type I interferon activity of different SARS-CoV-2 ORF9b proteins from Wuhan Hu-1 (WH1) and Omicron subvariants, including XBB.1.5, XBB.1.16, and EG.5.1. Through plasmid construction, western blot, and luciferase-based type I interferon assay in HEK293 cells, it was revealed that WH1 ORF9b had lower protein expression levels and anti-type I interferon activity in comparison to WH1 ORF6, another protein with well-characterized type I interferon antagonistic activity. Amino acid mutations within the ORF9b protein, particularly I5T, did not markedly affect the anti-type I interferon activity.

Keywords: SARS-CoV-2, ORF9b, type I interferon