

Functional characterization of NS1 phosphorylation in pandemic H1N1 influenza A virus (pdm09) reveals site specific modulation of virus–host interactions

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The non-structural protein 1 (NS1) of pandemic H1N1 influenza A virus (pdm09) is a multifunctional virulence factor that antagonizes innate immunity and regulates multiple virus-host cell interactions. Despite its central role during infection, the contribution of site-specific phosphorylation remains poorly understood. We analyzed phospho-ablative and phospho-mimetic NS1 mutants using recombinant viruses and viral minigenome, IFN- β promoter, and transcriptional read-through reporter assays together with a six-site NS1 variant associated with restored CPSF30 binding. Replication kinetics of phosphorylation mutants were comparable to wild type. The phospho-mimetic S83D+T86D mutant markedly reduced viral polymerase activity, whereas the corresponding phospho-ablative mutant showed only minor effects, supporting a regulatory role of phosphorylation at these residues. All mutants retained robust IFN- β antagonistic activity, with S213E showing the strongest inhibition. The six-site NS1 variant increased transcriptional read-through, while viral polymerase activity and IFN- β antagonism remained largely unchanged. Together, these findings demonstrate that NS1 phosphorylation selectively modulates distinct viral functions without substantially affecting viral replication, whereas naturally occurring sequence variation primarily alters transcriptional read-through, providing new insights into the functional regulation of pdm09 NS1.

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Yes, I am a junior scientist.

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