Different Mechanisms of Apoptosis by Influenza A and B Virus

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Abstract:

Background and Aims: The ability of Influenza A (infA) viruses to counteract and manipulate the host response to infection is well acknowledged. In addition, the activation of the PI3K/Akt survival pathway by the infA NS1 protein has been described as one of the strategies to delay the apoptotic response of the infected cell. As influenza B (infB) viruses differ genetically and phenotypically from infA viruses, namely at the NS protein level, we aimed to compare general apoptosis and survival pathways induced by each influenza type.

Methods: MDCK-SIAT1 cells were infected with infA(H1N1)pdm09 virus A/Portugal/82/2009 (APT82) and infB virus B/Lisboa/08/2006 (BLx08). Activities of caspase-3 -7 -8 and -9 were measured at several time points post-infection (hpi). Total levels of Akt, pAkt, NF-κB, IκB, p53 and β-actin were also examined by Western blot.

Results: Our results indicate that the apoptosis process induced by BLx08 was associated with activation of both intrinsic, caspase-9-dependent and extrinsic, caspase-8-dependent pathways as early as at 8hpi. In contrast, APT82-induced apoptosis only involved the activation of the intrinsic pathway, and occurred at 32hpi.

Surprisingly, our data show that the activation of the survival pathway PI3K/Akt was significantly increased upon BLx08 infection when compared with APT82 infection. In fact, increased levels of pAkt were observed at the same time of caspase activation in the early phase of BLx08 infection. This, however, did not result in increased downstream NFκB activation, since its inhibitor IκB was also markedly upregulated.

Increased p53 levels associated with APT82 infection may also explain the delayed apoptosis response in infA, assessed by caspase activity, as it may require transcriptional activation that it is deregulated and directed to viral replication.

Conclusion: InfB and infA infection differs in time and levels of activation of apoptosis and survival signaling pathways. PI3K/Akt activation in infB is not sufficient to inhibit apoptosis. Further studies will clarify this difference and shed light into the use of cellular mechanisms as new ways to fight influenza.

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