Influenza A Virus Enhances Its Replication Through The Regulation Of Annexin-A1 Dependent Trafficking And Apoptosis

Abstract
The influenza virus infects millions of people each year and can result in severe or even fatal complications including pneumonia and respiratory distress syndrome. Understanding virus recognition and host responses to flu infection will enable the future development of more effective anti-viral therapies. Previous research has revealed diverse yet important roles for Annexin (ANX) family proteins in modulating the course of influenza A virus (IAV) infection. However, the role of Annexin-A1 (ANXA1) in IAV infection has not been addressed. We have recently shown a key involvement of immune-modulatory ANXA1 in innate viral receptor pathways (1). Here, we show that ANXA1- deficient (-/-) mice exhibit a survival advantage, and this correlates with lower viral titers and higher leukocyte infiltration into the lungs. Furthermore, the presence of ANXA1 enhances viral replication in vitro and IAV-mediated apoptosis is enhanced by ANXA1. We also show that ANXA1 is involved in virus attachment and replication early in the virus life cycle and is regulated and cleaved during IAV infection. Overall, our study demonstrates that ANXA1 plays an important role in virus life cycle and that the regulation of ANXA1 expression during IAV infection appears to be a viral strategy to enhance its infectivity.

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Selected Publications
