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**Host Pathogen Interactions Are Critical In The Outcome Of H5N1 Infections In Chickens And Ducks**

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Avian H5N1 influenza viruses are increasingly widespread in poultry. These viruses are often linked with a high rate of mortality, resulting in death in a matter of hours. However, the mechanisms of disease pathogenesis are still somewhat poorly understood. Intriguingly, however, ducks often appear asymptomatic, with only a few strains of H5N1 AI causing pathogenesis. Moreover, the infection in ducks appears to progress gradually in comparison to the hyperinflammatory response observed in other poultry, such as chickens. It is not clear how this varying virulence comes about, but it is thought that the differing immune responses in chickens and ducks during infection are critical in determining the severity of infection. We investigated the expression of several key proinflammatory molecules during H5N1 AI infection of chickens and ducks. Two H5N1 strains, one from Vietnam, A/Muscovy duck/Vietnam/453/2004 (Vt453) and the second from Indonesia, A/Duck/Indramayu/BBVW/109/2006 (Ind109) were compared. We used QPCR, IHC and bioassays to observe a range of chicken and duck genes, such as interleukins, interferons and reactive nitrogen intermediates. In the chicken these viruses caused severe infection, with a high viral load and increased production of proinflammatory molecules. In chickens, Interleukin 6 (IL6), Interferon  $\gamma$  (IFN $\gamma$ ), inducible Nitric Oxide Synthase (iNOS) and the acute phase protein Serum Amyloid A (SAA) showed the greatest changes in gene expression during infection by H5N1 AI. Contrastingly, ducks displayed only small changes in their cytokine profile and only at later time-points. These observations support the association of high virulence and hypercytokinemia with the response in chickens, whilst the lower cytokine response in ducks may explain the decrease in mortality observed in these birds. A better understanding of these host-pathogen interactions during viral infection will lead to the development of new therapeutics aimed at modulating the immune response.

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