Interferon-gamma influences the pathogenesis after H5N1 influenza A virus infection in mice

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The highly pathogenic avian influenza (HPAI) H5N1 virus is a major challenge to animal and human health. Since pandemic influenza virus has its origin in avian influenza viruses, the HPAI H5N1 virus has to be considered as a potential strain for a pandemic threat. Cytokines and chemokines are markedly elevated during H5N1 influenza virus infection leading to hypercytokinemia or "cytokine storm". The contribution of this cytokine storm to H5N1 pathogenesis is controversially discussed. Since it is known that type I and type II interferons (IFN) play a major role in the antiviral immune response, we investigated the pathogenesis of IFN-typ I and typ II receptor knockout mice after infection with H5N1 influenza virus. To assess the cytokine/chemokine-level of the different IFN knockout mice during the H5N1 infection, we used quantitative RT-PCR and the Multiplex-Cytokine-Assay. We found that there are differences in the mortality and in the expression of various cytokines and chemokines in the lung of mice three and six days after H5N1 infection. Mice without any IFN receptor or mice without IFN-gamma receptor were more suitable to infection with H5N1. Nevertheless the cytokine profile was not altered except a 3-fold increase of IP10 (interferon-gamma-induced protein) in the IFN –gamma receptor-/- mice. From our results we conclude: (1) hypercytokinemia might not be a major player in H5N1 pathogenesis or hypercytokinemia is dominated by IP10. (2) IP10 is not exclusively regulated by IFN-gamma since IP10 is upregulated in IFN-gamma receptor-/- mice.

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