Title: Long-term derangement of antigen presenting cells in the respiratory tract of mice following influenza virus infection

Body: Inhaled agents pose a major challenge to immunological homeostasis in the respiratory tract (RT), requiring constant screening for their risk to the host. This requires a balanced network of antigen presenting cells (APC) that can initiate tolerance or immunity as required. Respiratory viruses such as Influenza pose a serious threat of disruption of this balance via their potent inflammatory and cytotoxic activities, potentially increasing the risk of allergy or secondary infections. In this study, we used a mouse model of A/PR8/34 H1N1 Influenza Type A Virus (IAV) infection to examine its long-term effects on APC in airway mucosal (AM) and parenchymal lung (PL) tissue following IAV infection. In adult mice, we found marked differences in the kinetics of dendritic cell (DC) subsets in the AM and PL environments, with a generally more acute responses in AMDC that resolved by day 7 after infection, but with persistent depletion of CD11b^lo PLDC for up to 3 weeks following infection. Similarly, transient upregulation of CD40 and CD80 was observed on AMDC at day 7, but this was delayed until day 14 in PLDC. A marked depletion in tissue-resident PL macrophages was observed at day 14 post-infection, with these cells showing a persistent activation state. In mice infected at 3 weeks of age or younger, DC and macrophages showed persistent changes for up to 5 weeks following infection. These data demonstrate that IAV has differential effects on APC populations in compartments of the RT, leading to long-term derangement in the numbers and activation states of these cells, that may persistently disrupt the regulation of immunological homeostasis at this site.