Sex differences in lung resident and inflammatory dendritic cells during influenza virus infection

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Abstract

Differential gene expression between male and female immune cell subsets significantly contributes to the observed sex disparity in immune cell function. Bridging innate and adaptive immunity, dendritic cells (DC) are sentinels in peripheral tissues that respond to pathogens and initiate immune responses. Sex hormones and their receptors, specifically estrogen receptor alpha (ERa, *Esr1*), play important roles in DC differentiation and function. Prior research has established that ERa regulates the development of DCs in vitro, specifically a subset of DCs that expands in response to inflammatory signals. We hypothesized that wild-type (WT) mice would show sex differences in pulmonary DC subsets during homeostasis or following an in vivo influenza A virus (IAV) infection, and mice with DCs deficient in *Esr1* would fail to expand specific DC subsets. To test this, we infected female and male WT mice with a sublethal dose of influenza A virus (IAV) and used flow cytometry to determine conventional DC type 1 and 2 (cDC1 and cDC2), inflammatory cDC2 (inf cDC2), and monocyte-derived DC (Mo-DC) numbers in the lung in homeostasis or early post-infection. Our analyses revealed no significant difference in numbers of male and female cDC1s, cDC2s, and Mo-DCs in homeostasis. However, on day 5 after IAV infection, WT females harbored greater numbers of inf cDC2s. Future experiments will identify the impact of *Esr1* in DCs, using mice in which *Esr1* was selectively knocked out in CD11c+ DCs. In sum, our data show that females have more inf cDC2s early after IAV infection, suggesting that female-specific factors promote the expansion of the inflammatory cDC2 subset in vivo during respiratory infection.