A Gammaherpesvirus Affects Lung Resident Group 2 Innate Lymphoid Cells in the Context of HDM-Induced Asthma

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The “hygiene hypothesis” postulates that allergic diseases could be prevented by some infections in early childhood. Gammaherpesviruses (γ-HVs) are among the most prevalent human viruses and profoundly impact on the immune system of their hosts. While infection by these viruses generally occurs during childhood, an increased age of seroconversion to these viruses has been observed in westernized countries suggesting that delayed γ-HV infection could contribute to the increased burden of allergic diseases. Using Murid gammaherpesvirus 4 (MuHV-4), a mouse model of human γ-HV infections, we recently showed that γ-HV infection inhibits the development of House Dust Mites (HDM)-induced airway allergy (Machiels et al. Nature Immunology, 18(12):1310-1320 (2017). Group 2 innate lymphoid cells (ILC2s) play a major role in the initiation, maintenance and memory of type 2 immune responses. As activation of these cells can be modulated by viruses associated with asthma exacerbation, we investigated whether MuHV-4 infection affects the lung ILC2s compartment.

1. Gammaherpesvirus infection induces persisting changes in the alveolar niche that protect against airway allergy

MuHV-4 infection induces persisting changes in macrophage populations that could be blocked by the infection while proliferation and recruitment of ILC2s were unchanged. Single-cell RNA sequencing revealed shared general strategies in the infiltrating monocytes and resident AMs in the context of HDM-induced allergy. Adapted from Bérengère de Laval & Michael H Stowasser, Nature Immunology, May and June, 2017:1879-1886 (2017).

2. MuHV-4 infection affects the function of lung ILC2s after HDM sensitization

MuHV-4 infection does not modify lung ILC2s expansion after HDM sensitization. MuHV-4 infection affects the function of lung ILC2s after HDM sensitization. MuHV-4 infection impacts the function of ILC2s after HDM sensitization. Adapted from Bérengère de Laval & Michael H Stowasser, Nature Immunology, May and June, 2017:1879-1886 (2017).

3. MuHV-4 infection affects activation of ILC2s as revealed by lower expression of PD-1/KLRG1 after HDM sensitization


4. MuHV-4 infection does not modify lung ILC2s expansion after HDM sensitization


5. HDM sensitization initiates recruitment of ILC2s that is not impacted by MuHV-4 infection

5. HDM sensitization initiates recruitment of ILC2s that is not impacted by MuHV-4 infection. Our results showed that MuHV-4 respiratory infection impacts the function of ILC2s following HDM treatment and reduces their capacity to produce type 2 cytokines IL-13 and IL-5. The increased expression of ILC2s activation markers PD-1 and KLRG1 following HDM treatment was blocked by the infection while proliferation and recruitment of ILC2s were unchanged. Single-cell RNA sequencing revealed shared general pattern upon HDM sensitization between mock and MuHV-4 infected groups and highlighted the presence of a sub-population of ILC2s expressing higher MHC-II, ICOS and Ly6a in MuHV-4 HDM mice compared to their mock HDM counterparts. These differences may have a determining role in the subsequent development of immune responses against respiratory allergens.