Persistent viruses, such as gammaherpesviruses, profoundly imprint on the immune system of their hosts. Accordingly, we recently showed that infection by Murid herpesvirus 4 (MuHV-4), a gammaherpesvirus infecting mice, inhibits the development of House Dust Mites (HDM)-induced airway allergy. Group 2 innate lymphoid cells (ILC2s) play a major role in the initiation, maintenance and memory of type 2 immune responses. Activation of these cells can be triggered by allergens but also by viruses such as influenza, rhinovirus and respiratory syncytial virus. Here, we therefore investigated whether, and by which potential mechanisms, MuHV-4 infection affects the lung ILC2 compartment.

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

2. Identification of lung NK and ILC subpopulations by flow cytometry strategy

3. MuHV-4 infection affects number and function of lung ILC2s after HDM treatment

4. MuHV-4 infection does not induce ILC2 plasticity towards an ILC1 phenotype

5. MuHV-4 infection affects ILC2s activation at early time points

6. MuHV-4 infection blocks the increase of PD1/KLRG1 expression in ILC2s after HDM sensitization

Our results showed that MuHV-4 respiratory infection profoundly imprints the number and function of ILC2s following HDM treatment:

- by reducing their capacity to produce type 2 cytokines IL-13 and IL-5 after HDM sensitization or challenge
- by decreasing their PD-1 and KLRG1 surface expression which have been associated with ILC2 activation
- as early as 8 days post-infection

Overall, these results show that MuHV-4 infection significantly and sustainably affects the lung ILC2 population. This may have a determining role in the subsequent development of immune responses against respiratory allergens.

In the future, we want to test the effect of MuHV-4 infection on both resident and inflammatory ILC2s and to identify the mechanisms triggering these differences.

**References**

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