A gammaherpesvirus infection blocks the functionality of type 2 innate lymphoid cells in the context of HDM-induced airway allergy

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The “Hygiene hypothesis” postulates that allergies could be prevented by some infections in early childhood. Gammaherpesviruses (γHVs) are among the most prevalent human viruses, they infect in early age and profoundly imprint the immune system of their hosts. Using Murid herpesvirus 4 (MuHV-4), a mouse model of human γHV infections, our laboratory recently showed that γHV infection inhibits the development of allergic asthma trough the replacement of resident alveolar macrophages by regulatory monocytes. However, the mechanisms by which airway allergy is controlled in that context are still ill-defined. Here, we showed that group 2 innate lymphoid cells (ILC2s) are massively affected by MuHV-4 infection. In particular, the number of pulmonary ILC2s was decreased for the long term and these cells displayed reduced capacity to respond to type 2 stimuli. These modifications appeared to be related to the microenvironment and especially to IFNγ. However, in contrast with reports from other viral infections, ILC2s from MuHV-4 infected mice did not exhibit any characteristic of plasticity towards an ILC1 phenotype but displayed decreased expression of the canonical Th2 transcription factor GATA-3. Finally, single cell transcriptome analysis revealed the presence of a specific ILC2s sub-population overexpressing MHC-II in MuHV-4 infected mice. Altogether, our results show that persistent γHV infections profoundly impact the functionality and composition of lung ILC2s in a potential dialogue with monocytes/macrophages.

Keywords : ILC2/gammaherpesvirus/airway allergy
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