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Aberrant anti-viral response of natural killer cells in severe asthma

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NK cells from severe asthma patients exhibit decreased activation, cytotoxic capacity and IFN- γ production after *in vitro* stimulation with rhinovirus RV-A9, in comparison to healthy donors. Exhausted phenotype is associated to increased Tim-3 expression. <http://bit.ly/2UFjtdc>

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ABSTRACT Rhinovirus infections are the main cause of asthma exacerbations. As natural killer (NK) cells are important actors of the antiviral innate response, we aimed at evaluating the functions of NK cells from severe asthma patients in response to rhinovirus-like molecules or rhinoviruses.

Peripheral blood mononuclear cells from patients with severe asthma and healthy donors were stimulated with pathogen-like molecules or with the rhinoviruses (RV)-A9 and RV-2. NK cell activation, degranulation and interferon (IFN)- γ expression were analysed.

NK cells from severe asthma patients were less cytotoxic than those from healthy donors in response to toll-like receptor (TLR)3, TLR7/8 or RV-A9 but not in response to RV-2 stimulation. Furthermore, when cultured with interleukin (IL)-12+IL-15, cytokines which are produced during viral infections, NK cells from patients with severe asthma were less cytotoxic and expressed less IFN- γ than NK cells from healthy donors. NK cells from severe asthmatics exhibited an exhausted phenotype, with an increased expression of the checkpoint molecule Tim-3.

Together, our findings indicate that the activation of NK cells from patients with severe asthma may be insufficient during some but not all respiratory infections. The exhausted phenotype may participate in NK cell impairment and aggravation of viral-induced asthma exacerbation in these patients.