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Anti-IL5 mepolizumab minimally influences residual blood eosinophils in severe asthma

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Shareable abstract (@ERSpublications)
Asthma patients receiving anti-IL5 therapies retain residual blood eosinophils, of which potential alterations remain unknown. This study shows that these residual eosinophils harbour largely unaltered quiescent and activated gene expression programmes. https://bit.ly/37od6QN

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Abstract

Neutralising antibodies against the cytokine interleukin (IL)5 have become widely used for the control of severe eosinophilic asthma. Remarkably, patients receiving neutralising anti-IL5 biological therapies retain a very stable population of residual blood eosinophils. Whether these residual eosinophils are endowed with particular biological activity has not yet been studied, but is of importance in predicting potential long-term effects of IL5 neutralisation in patients. To tackle the effect of IL5 depletion on residual eosinophils, we used a comparative RNA-sequencing approach and compared the gene expression programme of eosinophils arising in IL5-depleted or IL5-replete human or murine hosts, at steady-state *in vivo* and following *in vitro* stimulation with the eosinophil-activating alarmin IL33. We compared blood eosinophils from patients with severe allergic eosinophilic asthma treated with anti-IL5 mepolizumab therapy to those of healthy controls and matched asthma patients receiving anti-IgE omalizumab therapy. We made similar comparisons on bone marrow eosinophils from mice genetically deficient or not for IL5. We report that restriction of IL5 availability did not elicit any detectable transcriptional response in steady-state residual eosinophils in mepolizumab-treated patients or IL5-deficient mice, and influenced only a handful of genes in their response to IL33. Together, these results support the notion that treatment with IL5 neutralising antibodies spares a pool of circulating residual eosinophils largely resembling those of healthy individuals.