A lesson from the wild: The natural state of eosinophils is Ly6Ghi.

Abstract

With a long history of promoting pathological inflammation, eosinophils are now emerging as important regulatory cells. Yet, findings from controlled laboratory experiments so far lack translation to animals, including humans, in their natural environment. In order to appreciate the breadth of eosinophil phenotype under non-laboratory, uncontrolled conditions, we exploit a free-living population of the model organism Mus musculus domesticus. Eosinophils were present at significantly higher proportions in the spleen and bone marrow of wild mice compared with laboratory mice. Strikingly, the majority of eosinophils of wild mice exhibited a unique Ly6Ghi phenotype seldom described in laboratory literature. Ly6G expression correlated with activation status in spleen and bone marrow, but not peritoneal exudate cells, and is therefore likely not an activation marker per se. Intermediate Ly6G expression was transiently induced in a small proportion of eosinophils from C57BL/6 laboratory mice during acute infection with the whipworm Trichuris muris, but not during low-dose chronic infection, which better represents parasite exposure in the wild. We conclude that the natural state of the eosinophil is not adequately reflected in the standard laboratory mouse, which compromises our attempts to dissect their functional relevance. Our findings emphasize the importance of studying the immune system in its natural context – alongside more mechanistic laboratory experiments – in order to capture the entirety of immune phenotypes and functions.Eosinophils have long been considered destructive end-stage effector cells. They promote allergic inflammation, and whilst helminth infections in humans are typically associated with eosinophilia, their role in the anti-helminth responses is controversial. Eosinophil-deficient mouse models have been studied for over 20 years and have largely failed to show any overt signs of ill health .The absence of adverse effects unambiguously caused by depletion of eosinophils following the growing trend of anti-IL-5 treatment in humans suffering from severe asthma paves the way for the conclusion that this immune cell type is redundant in humans .Nevertheless, eosinophils or eosinophil-like cells are conserved across all vertebrate species, meaning that over the past 450 million years since the diversification of vertebrates, no vertebrate species has lost this cell type along its evolutionary path. Yet, an important concept in ecological theory is the trade-off between immune investment and fitness, termed ‘immune trade-off’, that is that immune responses are energetically costly and that a higher investment in the immune system can lead to a lower reproductive success. It is therefore highly likely that the eosinophil plays as yet unappreciated roles under naturally occurring circumstances, to justify its ubiquitous presence in the phylum Chordata.

BIOGRAPHY

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