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The expanding universe of the basophil

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In this issue of Blood, Ohnmacht and Voehringer expand our view of the murine basophil, implicating these cells in eosinophilia and intestinal helminth rejection as well as determining the lifespan of basophils in both basal and inflammatory states.

Interest in the role of basophils in immune responses has been rejuvenated recently. Demonstration of their ability to promote humoral memory responses, drive IgE-dependent dermatitis, and shift an immune response toward Th2–dominated inflammation are some of the many biologic activities described. In this issue, Ohnmacht and Voehringer address the development and lifespan of basophils and further investigate their role in helminth infections. In addressing these issues, they first identified the expression of the Thy1 antigen on the surface of IL-4–expressing cells, which were defined by expression of green fluorescent protein in the transgenic mouse. The basophils were distinguished from the other IL-4, FcεRI− cell type, the mast cell, by the lack of the mast cell marker c-kit. They then used the Thy-1 antigen to deplete these cells in mice by the injection of an anti-Thy1 antibody. Other labs have previously used antibody directed to FcεRI or CD200R3. The depletion of basophils by anti-Thy1 represents a novel approach, albeit limited by the fact that due to the expression of this antigen by T cells, it was only useful in lymphocyte-deficient RAG−/− mice that lack T and B cells and are used to study only innate immune responses. Nonetheless, basophil-depleted RAG−/− mice clearly showed a diminished capacity to reject Nippostrongylus worms from the small intestine and decreased eosinophilia in both the lung and spleen. Further, using passive sensitization followed by antigen activation, they noted increased numbers of eosinophils in blood, spleen, and lung, and an increase in IL-5 message in the lung. As both of these effects were Thy-1 sensitive, this suggests IL-5 production by the activated basophils is important in promoting and maintaining the attendant eosinophilia in these tissues which in turn likely mediated the helminth expulsion.

Unfortunately, all of these strategies to deplete basophils suffer from the possibility of off-target effects which have not been fully addressed. In all 3 instances, the markers used for depletion are also expressed on the mast cell, the committed mast cell progenitor, and/or the common basophil-mast cell progenitor identified in the spleen of C57BL/6 mice by Ariyohbu et al. Although none of the authors noted a decrease in the mature mast cell number identified in the peritoneal cavity of mice, these cells represent a mature end-stage cell that may not be affected in the limited time frame of these treatments. Nonetheless, this consideration does not diminish other aspects of the study, which demonstrated a life span of basophiles of only about 60 hours and the increased production of these cells in the bone marrow following helminth infection. This latter finding is consistent with those of Ariyohbu et al who, following infection with the helminth, Trichinella spiralis, also noted increased basophil production by the bone marrow and increased numbers of the common basophil–mast cell progenitor in the spleen. Importantly, Ohnmacht and Voehringer then addressed whether the increased numbers associated with TH2 inflammation was the result of increased production, increased survival, or both. The increased survival as a consequence of the cytokines generated by TH2 inflammation, particularly IL-3, has been shown in vitro using human basophils and was recently further studied by Didichenko et al, who found this is mediated by IL-3 activation of PIM-1. To test whether the basophil lifespan in vivo was increased in association with inflammation provoked by the Nippostrongylus infection, the authors transferred labeled basophils and noted the rate of loss of these cells in normal versus infected mice. No difference in clearance of the cells was noted between the 2 groups of animals, indicating that the increase in basophil number is likely due to the increased production of these cells in the bone marrow. In lieu of the availability of a basophil–deficient mouse to confirm the findings, these studies represent the best approach and provide a significant increase in our understanding of the development and expanding role of these cells in inflammation.

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REFERENCES

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