Basophils Play an Essential Role in Protective Immunity Against Ticks

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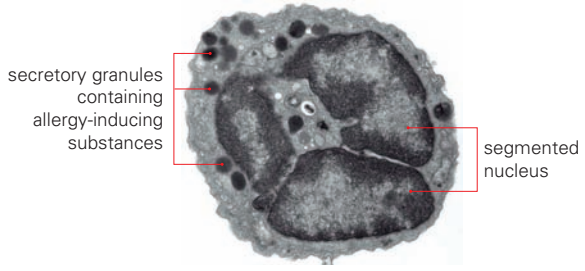
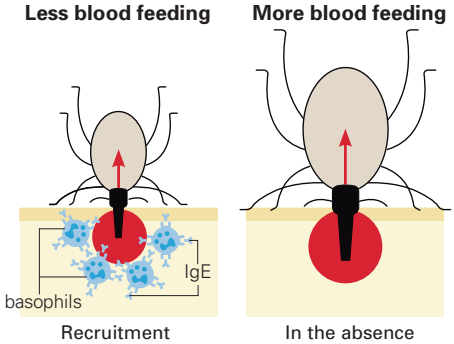
BASOPHILS ACCOUNT FOR less than 1% of white blood cells in circulating blood. Although the existence of basophils was first documented 120 years ago, the functional significance of this minor population has long been an enigma. Recently, we demonstrated that basophils are critically involved in the development of allergic reactions, such as chronic allergic inflammation in the skin and systemic anaphylaxis, through mechanisms distinct from those by mast cells. However, it is unlikely that many animal species, including humans, evolutionarily conserve basophils to only elicit allergic responses without any host-beneficial function. In the present study, we uncovered that basophils play an important role in protective immunity against ticks.

Ticks are blood-feeding parasites, and can transmit microorganisms, which can cause several serious infectious diseases in human and animals. Lyme disease with arthritis and neurological abnormalities is a representative of tick-borne diseases, and its incidence has increased recently both in Europe and the U.S.A. Of note, many animal species develop resistance to tick feeding after a single or multiple tick infestations. Importantly, this acquired tick resistance contributes to reducing the pathogen transmission from infected ticks to host animals. However, the cellular and molecular mechanisms underlying acquired protective immunity against ticks remained ill defined. We first demonstrated that basophils are recruited to tick feeding sites during the second but not first infestation in the mouse model of tick infestation. To examine the functional significance of this basophil recruitment, we have established for the first time engineered mice that are deficient only in basophils. In these mice, diphtheria toxin receptor is selectively expressed by basophils, and therefore only basophils are depleted when diphtheria toxin is administered into mice. When the engineered mice received diphtheria toxin injection before the second infestation, they failed to manifest tick resistance during the second infestation, indicating that basophils are important for acquisition of tick resistance. Mice develop antibodies, particularly of IgE class, against tick antigens in the first infestation. Basophils express IgE receptors that capture circulating IgE. In the second infestation, IgE-armed basophils are recruited to the tick feeding sites, and activated when tick antigens bind to anti-tick IgE on their surface. Activated basophils in turn release a variety of mediators, including proteases, which interfere with tick feeding. We also found that basophils are involved in the protective immunity against intestinal helminth infections. Taken together, our findings strongly suggested that the primary function of basophils is to protect hosts from parasitic infections.

On a global basis, ticks are second to mosquitoes as vectors of pathogens that cause various human infectious diseases. Helminths are common infectious agents of humans in developing countries. The number of patients suffering from such parasitic infections has drastically reduced, while the incidence of allergic disorders has increased. Allergic responses and inflammatory responses associated with protective immunity against parasitic infections appear to be the opposite sides of the same coin. We believe that studies on the role of basophils in allergic and anti-parasitic responses would cast new light on the development of novel strategies for treatment and prevention of allergic disorders and parasitic infections.

Electron microscopic view of mouse basophils





(Left) In the second tick infestation, IgE-armed basophils are recruited to tick feeding sites to inhibit blood feeding by ticks.
(Right) When basophils are depleted, mice lose the tick resistance, resulting in more blood feeding by ticks.
(The figure was taken and modified from reference #3)

References
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