LUPUS NEPHRITIS

Activated basophils exacerbate lupus nephritis by amplifying production of autoreactive IgE

Lupus nephritis in patients with systemic lupus erythematosus (SLE) is characterized by the deposition of immune complexes containing autoantibodies reactive to nuclear components and double-stranded DNA (dsDNA) in the glomeruli of the kidneys. The mechanisms of B-cell activation—and thus autoantibody production—in SLE are not well understood. Evidence suggests that type 1 T helper (T_H1) cells, T_H17 cells and regulatory T cells are involved, but several studies have suggested that T_H2 cells might also have a role in the disease. In a paper published in *Nature Medicine*, Charles *et al.* used a mouse model of SLE-like disease to explore the role of the T_H2 response in lupus nephritis.

In *Lyn*$^{-/-}$ mice, the production of T_H2 cytokines, such as interleukin (IL)-4, is increased, and in later life they develop an SLE-like autoimmune disease with lupus-like nephritis. The authors found that nephritis in these mice was dependent on IL-4 and autoreactive IgE, and that basophils—granulocytes that are generally associated with allergic reactions but have recently been shown to have other roles, including T_H2 cell activation and antigen presentation—support plasma cells that produce autoreactive antibodies. They went on to show that circulating self-reactive IgE immune complexes activate basophils, leading to increased expression of MHC class II molecules (involved in antigen presentation) and CD62 ligand, and to homing of activated basophils to the spleen and lymph nodes. Here, they were shown to secrete IL-4, which drives the T_H2-type immune response and leads to increased production of cytokines and autoantibodies (particularly IgE).

> “...basophils and a T_H2 environment affect the production of autoreactive antibodies...”

In a sample of patients with SLE, the authors found that levels of antinuclear and anti-dsDNA IgE antibodies were directly associated with disease activity and lupus nephritis. Also, their basophils showed increased expression of CD62 ligand and HLA-DR, and were found in the spleen and lymph nodes.

The authors conclude that basophils and a T_H2 environment affect the production of the autoreactive antibodies that lead to kidney damage. Activated basophils seem to amplify or enhance autoimmune responses in patients with SLE, which suggests that interventions capable of decreasing the levels of circulating self-reactive IgE, or reducing the activity of basophils, might be effective in patients with this disease.

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Original article Charles, N. *et al.* Basophils and the T helper 2 environment can promote the development of lupus nephritis. *Nat. Med.* **16**, 701–707 (2010)