To be perfectly frank, there is no proper therapy for Sjögren’s syndrome. Of course, there are therapies to treat the symptoms, but none that treats the underlying immunological pathology of the disease prevents directed therapy. Interleukin-21 (IL-21) is elevated in the serum of patients with this disease and is expressed by the lymphocytes infiltrating the salivary glands. The known functions of IL-21 in facilitating differentiation, proliferation, and survival of both B and T cells mesh well with the findings in Sjögren’s syndrome. Demonstration of IL-21 as a fundamental aspect of the pathophysiology of Sjögren’s syndrome could lead to the development of anti-IL-21 therapy for this disease.

The known functions of IL-21 fit well with the findings in patients with Sjögren’s syndrome. The disease is characterized by lymphocytic infiltrates in the salivary and lacrimal glands that contain both B and T cells that in many patients demonstrate ectopic germinal center formation. Kang and colleagues found that the degree of lymphocytic infiltration was correlated with IL-21 levels. Proliferation of both naïve and memory CD8+ T cells as well as activation, proliferation, and survival of CD4+ T cells are supported by IL-21. B cells and CD4+ T cells are prominent in Sjögren’s infiltrates. Furthermore, Kang and colleagues found expression of IL-21 in the infiltrating cells. There are, of course, high levels of autoantibodies in the form of concentrations (in milligram per...
deciliter) of anti-Ro (or SSA) and anti-La (or SSB), along with consequent hypergammaglobulinemia, especially IgG1. The data are clear that B cells are hyperactivated in patients with Sjögren’s syndrome. IL-21 promotes the proliferation of B cells, resulting in differentiation into plasma cells, which produce immunoglobulin, especially IgG1.

IL-21 is involved in the differentiation of T helper 17 (Th17) cells that IL-21 acts to facilitate IL-23-induced expansion of these cells. As noted above, an IL-23 monoclonal antibody is available clinically, but the involvement of Th17 cells in the pathogenesis of Sjögren’s syndrome is unknown. If Th17 cells are, in fact, players in Sjögren’s syndrome, then perhaps the available anti-IL-23 monoclonal antibodies would be beneficial in the disease. This, of course, remains to be determined.

Certainly, the findings reported by Kang and colleagues [1] as well as others in regard to IL-21 in Sjögren’s syndrome [8] and other inflammatory rheumatic illnesses [9,10] suggest that therapy directed at IL-21 may be useful in human autoimmune disease. These findings need to be confirmed and advanced but perhaps will underpin the development of therapy directed at the underlying pathophysiology of Sjögren’s syndrome.

Abbreviations
IL, interleukin; Th17, T helper 17; TNF, tumor necrosis factor.

Competing interests
The author declares that he has no competing interests.

Author details
1Departments of Medicine and Pathology, University of Oklahoma Health Sciences Center, 1000 North Lincoln Blvd, Oklahoma City, OK 73104, USA.
2Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, 825 NE 13th Street, MS 53, Oklahoma City, OK 73104, USA.
3Medical Service, Oklahoma City VA Medical Center, 921 NE 13th Street, Oklahoma City, OK 73104, USA.

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