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Mechanism and Functional Relevance of Corneal Lymphangiogenesis in Dry Eye Disease
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Lay Abstract

Sjögren's syndrome is a chronic autoimmune disorder in which the body's immune system attacks its own tear- and saliva-secreting glands. Autoimmune attack of tear-secreting glands and ocular surface leads to dry eye disease (DED) – a hallmark of Sjögren's syndrome, which in severe cases can lead to significant discomfort, visual impairment and blindness. The precise mechanism of dry eye development is poorly understood. We propose that dry eye induces growth of corneal lymphatic vessels which facilitate migration of corneal immune cells to the lymphoid tissues where they activate autoimmunity. We plan to delineate the mechanism of the formation of lymphatic vessels in DED corneas and propose that blockage of these lymphatics could prove a powerful means of suppressing generation of autoreactive immune cells and ocular surface inflammation in Sjögren's syndrome.

Scientific Abstract

We have recently demonstrated that the draining lymphoid tissues are the primary site for generation of autoreactive-T cells in dry eye diseases (DED). However, the mechanisms by which corneal antigen presenting cells (APC) migrate to the lymphoid compartment and prime autoreactive naïve T cells, primary steps for induction of autoimmunity, are still not well understood. We thus hypothesize and provide preliminary data that immunopathogenesis of DED is associated with the selective induction of corneal neo-lymphatic vessels which facilitate trafficking of mature corneal APC toward the draining lymph nodes. To validate our hypothesis, we propose three specific aims – Specific Aims 1 and 2 involve confirmation and determination of cellular and molecular factors that contribute to lymphangiogenesis in DED cornea; and Specific Aim 3 will test the efficacy of in-vivo blockade of select pro-lymphangiogenic molecules on DED. These studies will assist in identifying potentially important therapeutic targets in the ocular surface disease associated with Sjögren's syndrome.