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Regulated expression of IL-13 receptor by T cell cytokines modulates conjunctival goblet cell density

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Lay Abstract:

The most potentially blinding ocular diseases have extensive goblet cell loss, such as in Sjögren's Syndrome. The importance of goblet cells in homeostasis also applies to mucosal surfaces other than the ocular surface such as the lung, GI tract, urinary tract, etc. Research has shown that Sjogren's syndrome is the result of the loss of goblet cells. Our research will aim at better understanding the regulation of goblet cell differentiation and the production of goblet cell mucin, helping to elucidate the pathogenesis of Sjogren's syndrome which has been shown to have some association with anomalous goblet cell development.

Scientific Abstract:

Soluble mucins that are secreted by the goblet cells play an integral role in stabilizing the precorneal tear layer. While the Th2 cytokine IL-13's effect on goblet cell hyperplasia has been extensively studied in the GI and respiratory tracts, its effect on regulating conjunctival goblet cell density has not been explored to the same extent. Several studies have shown that the cytokine IFN- γ counter regulates IL-13 in several tissues. We have previously observed that the Th1 cytokine IFN- γ inhibits goblet cell development, since IFN- γ KO mice are resistant to desiccating stress-induced goblet cell decrease. Therefore, we hypothesize that the balance of the Th1 and Th2 cytokines IFN- γ and IL-13 may regulate goblet cell differentiation on the surface of the eye and this occurs through their regulation of IL-13R expression.

We aim to: 1) evaluate the expression of IL-13 receptors in the normal ocular surface of C57BL/6, IL-13KO and IFN- γ KO mice and 2) evaluate the effect of IL-13 on conjunctival goblet cell density in the IL-13KO mice. We will accomplish aim 1 by evaluating expression of IL-13 receptors in cornea and conjunctiva sections of normal C57BL/6, IL-13 and IFN- γ KO mice by immunostaining. To accomplish aim 2, IL-13KO mice will receive subconjunctival injections of IL-13 and its goblet cell density will be compared to a distinct group of IL-13KO that will receive injections of saline. The data collected will help us to better understand the regulation of goblet cell differentiation and production of goblet cell mucin.