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Cell lineage analysis in lacrimal gland maintenance and repair

LAY ABSTRACT

The Lay Abstract is for publicity purposes and should use simple language summarizing the proposed research and its significance.

Repair of the lacrimal gland would be a major triumph for therapeutic treatment of dry eye disease. But to do this, there are basic questions that need to be answered: How are cells in healthy lacrimal glands normally maintained? Does it depend on stem cells? How do lacrimal glands regenerate after injury? In a recently completed study, we have established how secretory cells are normally replaced in the salivary glands. Our results challenge the current dogma, and indicate that stem cells do not play a major role in maintaining a healthy gland. Based on the similarities between salivary and lacrimal glands, we propose that lacrimal glands may rely on the same mechanisms. We propose to use genetic models to directly follow secretory acinar cell replacement and regeneration in the lacrimal glands. The outcome of this study will provide a framework on which cell based therapy can be modeled.

SCIENTIFIC ABSTRACT

The Scientific Abstract is written for SSF reviewers and a professional audience.

The autoimmune disease Sjögren's syndrome has a detrimental effect on lacrimal glands (LG) with severe and irreversible loss of secretory cells leading to dry eyes. Recently, proof of principle was shown by generating fully functional bioengineered LG from embryonic germs. Although this holds great promise for replacement therapy to permanently treat patients with dry eye diseases, an optimal non-embryonic source of therapeutic cells is still needed. Understanding cell lineage relationships during maintenance and regeneration is therefore critical. We have recently established a revised model for salivary gland homeostasis based predominantly on self-duplication of secretory cells, rather than on differentiation of stem cells. Our preliminary analysis suggests that the lacrimal glands may use the same means of secretory cell replacement. We propose to test this hypothesis by using genetic models to trace the origin of newly formed acinar cells to determine the *in vivo* source for secretory cells in maintenance and regeneration.