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Ultrasound-assisted gene transfer of IL17R:Fc to the salivary glands as a gene therapy for Sjögren's Syndrome
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LAY ABSTRACT

This research project builds upon several promising prior studies which have utilized gene therapy as a therapeutic strategy for Sjögren's Syndrome. Gene therapy is a particularly exciting approach to this difficult disease because it can directly target the salivary gland with a gene drug, avoiding the systemic toxicity often seen with traditional pharmaceuticals. The major innovation embodied in this project is the application of a new ultrasound-assisted method of gene drug delivery. Prior instances of salivary gland gene therapy, including the first-in-man human clinical trial, have used viral vector as the gene delivery vehicle. These vectors are ideal for proof-of-principle studies, but are not practical for long-term therapy. Our ultrasound approach overcomes the drawbacks of viral vectors, and it is hoped that this project will provide a strong rationale for translating this promising technology to higher mammals and ultimately humans.

SCIENTIFIC ABSTRACT

Adenoviral-mediated gene therapy has shown proof-of-principle efficacy in several animal models of SS, notable a recent study that showed functional and immunological improvement of SS-prone C57BL/6.NOD-Aec1Aec2 mice using an IL-17R:Fc fusion protein as the therapeutic transgene. In order to make these promising demonstrations practical for SS therapy, a gene delivery method that allow repeated serial re-dosing over the lifetime of the individual is absolutely essential, and currently-available viral vectors (Adeno and AAV) cannot meet this critical criterion. This project proposes to apply ultrasound-assisted gene therapy to deliver the IL-17R:Fc transgene C57BL/6.NOD-Aec1Aec2 and precisely mimic the therapeutic metrics of Nguygen et al (attached). UAGT meets all of the criteria for a practicable, re-dosable gene delivery strategy for chronic salivary gland gene therapy. The studied outlined in this proposal, if successful, will provide a strong rationale for translating this enabling technology to higher mammals and eventually human SS patients.