



American Academy of Maxillofacial Prosthetics
69th Annual Meeting: October 30 – November 1, 2022
Omni Austin Downtown, Austin, Texas

Program Speaker – Blake M. Warner

Title

Gene Transfer Therapy to Correct Salivary Hypofunction and Improve Quality of Life

Abstract

Xerostomia is a common clinical complaint in the United States. A spectrum of clinical conditions and medications can lead to both reversible and irreversible salivary hypofunction. However, for irreversible types of salivary hypofunction, including ionizing radiation (IR) and autoimmune diseases (e.g., Sjogren's Disease), there is a lack of effective long-term therapies. Untreated salivary hypofunction and resultant xerostomia reduce oral function, quality-of-life, and overall health and remain major unmet medical needs. Our groups' long-term work has been focused on understanding the physiology of salivary gland function and the identification and testing of novel therapeutic approaches to reverse salivary dysfunction. First, our work has shown that both IR and Sjögren's Disease glands exhibit reduced water permeability in the secretory epithelia. To correct these defects, Dr. Bruce Baum (NIDCR) originally hypothesized that gene transfer of aquaporin-1 would reverse water permeability defects and was confirmed extensively in vitro and in vivo models. Subsequently, safety studies in humans demonstrated the safety and effectiveness of adenovirus vector gene transfer of human aquaporin-1 (hAQP1) to the parotid gland to correct salivary hypofunction and the perception of a dry mouth. However these effects were generally short-lived. To improve the stability of gene transfer, Dr. John Chiorini developed an adeno-associated virus serotype-2 (AAV2) vector with low immunogenicity to achieve long-term salivary gland transduction. The objective of this open and enrolling study is to test the safety of AAV2hAQP1 in adult subjects with established IR-induced parotid gland hypofunction. Future studies are in planning phases to apply these, and other novel strategies to a wider variety of clinical conditions (i.e., Sjogren's Disease, immunotherapy-related sicca) to improve salivary hypofunction and quality of life long term.

In this talk I will discuss:

- Salivary gland damage and salivary hypofunction post ionizing radiation.
- Hypothesis and proof-of-concept for hAQP1 gene transfer
- Early pre-clinical studies
- Early Ad-hAQP1 clinical studies early and late results
- Open and enrolling trials and reported data for AAV2-hAQP1
- Future Directions, pre-clinical and proof-of-concept for SjD

Biography

Dr. Blake M. Warner completed his Bachelors of Science in Biochemistry the Miami University. After working for 2 years as a research assistant at the University of Cincinnati College of Medicine, he went on to complete a Masters of Public Health, Doctorate of Dental Surgery (*Cum Laude*), and a Doctorate of Philosophy at The Ohio State University. He then completed hospital-based residency training at the University of Pittsburgh Medical Center and went on to complete a post-doctoral clinical research fellowship at the National Institute of Dental and Craniofacial Research (NIDCR) in the Laboratory of Dr. John Chiorini. He then earned an Assistant Clinical Investigator position in the NIDCR and serves as the Chief of the Sjögren's Disease Clinic and the Salivary Disorders Unit laboratory.

Dr. Warner is a board-certified oral and maxillofacial pathologist-scientist. He investigates disorders affecting the salivary glands including: autoimmune diseases (i.e., Sjögrens Disease [SjD]), viruses (e.g., HCV, SARS-CoV-2), and iatrogenic salivary damage by oncologic therapies (e.g., ionizing radiation). The modalities used to treat salivary disorders, beyond supportive care, are poorly effective. My integrated research program capitalizes on a dedicated multispecialty clinical research team (oral pathology/dentistry, rheumatology, and ophthalmology) and associated vibrant and collaborative laboratory focused on interrogating the clinical phenotypes, genetics, and immunopathology of salivary dysfunction.

**Has disclosed Affiliation/Financial Interest with the following companies: Pfizer, Inc., Mitobridge, Inc. (Subsidiary of Astellas Bio)*