

# First gene therapy study in human salivary gland shows promise

November 5 2012

---

Gene therapy can be performed safely in the human salivary gland, according to scientists at the National Institute of Dental and Craniofacial Research (NIDCR), part of the National Institutes of Health.

This finding comes from the first-ever safety, or Phase I, clinical study of [gene therapy](#) in a human salivary gland. Its results, published this week in the [Proceedings of the National Academy of Sciences](#), also show that the transferred gene, Aquaporin-1, has great potential to help head and neck cancer survivors who battle with chronic dry mouth. Aquaporin-1 encodes a protein that naturally forms pore-like water channels in the membranes of cells to help move fluid, such as occurs when salivary gland cells secrete saliva into the mouth.

These initial results clear the way for additional gene therapy studies in the salivary glands. Although sometimes overlooked, salivary glands present an ideal target for gene therapy. They are easily accessible and, once a gene is introduced, it has no obvious escape route into the bloodstream, where it can have unintended consequences.

"You cannot imagine how fulfilling it is to jot down an idea on a napkin in 1991 and then see it enter a clinical trial and help people.," said Bruce Baum, D.M.D., Ph.D., lead author on the study and recently retired NIDCR scientist who spent the last 21 years moving gene therapy in the salivary glands from the research bench to the clinic. "Can a scientist ask for anything better?"

Baum's interest in helping head and neck [cancer survivors](#) dates to the early 1980s. While attending to patients in the NIDCR's Dry Mouth Clinic, Baum encountered numerous people with head and [neck cancer](#) who had received [radiation therapy](#) to shrink their tumors. The radiation, while effective in treating cancer, had inadvertently damaged nearby salivary glands, compromising their ability to secrete saliva into the mouth.

Baum said he was thoroughly frustrated at the time because he had no effective moisture-restoring treatments to offer most patients. They had beaten cancer, but the radiation had left them with a permanent parched sensation in their mouths that diminished their quality of life and often led to chronic oral problems, such as difficulty swallowing, inflammation, infection, bad breath, and pain.

In the early 1990s, as the first gene-therapy studies entered research clinics, Baum saw an opportunity to make a difference. An initial napkin sketch of the procedure and 15 years of research later, Baum and his colleagues had assembled a compelling scientific case in animal studies that the transferred Aquaporin-1 gene, once expressed, will create new water channels in the impermeable salivary gland cells and allow water to flow through them. After rigorous reviews by NIH and the U. S. Food and Drug Administration, the Phase I protocol was launched and the first patients treated in 2008.

The scientists gave 11 [head and neck cancer](#) survivors a single-dose injection of the Aquaporin-1 gene directly into one of their two parotid salivary glands, the largest of the major salivary glands. The gene was packaged in a disabled, non-replicating adenovirus, the cause of the common cold when intact but incapable of causing a cold in this case. As is standard in gene therapy studies, the virus served as the vector, or Trojan horse, to deliver the gene into the cells lining the salivary gland.

The scientists found that five participants had increased levels of saliva secretion, as well as a renewed sense of moisture and lubrication in their mouths, within the study's first 42 days, the period covered in this report. Of the six who didn't benefit from gene therapy, none had serious side effects. The most common side effect was a transient and relatively minor immune response against the disabled adenovirus.

"It is time to evaluate a different vector to deliver the Aquaporin-1 gene, one that will cause only a minimal immune response," said Baum. "But these data will serve as stepping stones for other scientists to improve on this first attempt in the years ahead. The future for applications of gene therapy in the [salivary gland](#) is bright. "

Provided by National Institutes of Health

Citation: First gene therapy study in human salivary gland shows promise (2012, November 5) retrieved 25 April 2024 from

<https://medicalxpress.com/news/2012-11-gene-therapy-human-salivary-gland.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------