NIH-Funded Research Develops Promising Gene Therapy for Cancer Treatment Side Effect

Allegheny Health Network researchers used a pioneering ultrasound-assisted gene transfer technique to treat xerostomia, a devastating side effect of radiation treatment for head and neck cancers.

PITTSBURGH, PA (PRWEB) October 20, 2015 -- A promising gene therapy technique developed by physicians and researchers at Allegheny Health Network (AHN) may one day offer new hope for cancer patients who suffer from xerostomia, a common and debilitating side effect of radiation therapy, according to a pre-clinical study presented today at the American Society for Radiation Oncology (ASTRO) annual conference in San Antonio, TX.

Led by Michael J. Passineau, PhD, Director of the Network’s Gene Therapy Program, and Mark Trombetta, MD, FACS, Director of Clinical Programs for the AHN Radiation Oncology Network, AHN’s groundbreaking research involved the use of an innovative ultrasound procedure, instead of a virus, to facilitate the transfer of therapeutic DNA into cells.

The project was supported by a $1.7 million National Institutes of Health (NIH) grant and is among just 360 studies selected for oral presentation at the ASTRO conference from more than 3,000 submissions.

“About two-thirds of people treated for cancer of the head and neck region will receive radiation therapy, and many of them will suffer from xerostomia, severe dry mouth, that dramatically decreases their quality of life and impacts their overall health,” Dr. Passineau said. “Our research holds great promise for helping patients who struggle with this difficult complication of treatment.”

Xerostomia is a life-altering side effect of radiation therapy that makes it very difficult for cancer patients to eat properly, subsequently affecting their oral health, mental health and physical well-being. For some patients, dry mouth can linger even after radiation treatment is complete. Medications offer little relief, and researchers have turned to gene therapy in search of a cure.

“While newer techniques have tempered radiation’s impact on patients, treating or preventing xerostomia has proved to be an elusive goal,” Dr. Trombetta said. “We are excited to lead the development of this potential breakthrough in gene therapy that may finally help patients with chronic dry mouth.”

Gene therapy uses DNA as a pharmaceutical agent to treat disease, introducing new cells to a patient’s genes to replace missing or malfunctioning genes. The biggest challenges with the treatment are the process of directing DNA into the cells and sustaining the benefit.

Therapeutic DNA must be packaged in a vector, usually a virus, which can penetrate cells within the body. Viral gene transfer has been used successfully in the past; however it induces a strong immune response and is most often only temporally effective.

Ultrasound-assisted gene transfer is based on a process called sonoporation – or the use of sound (typically ultrasonic frequencies) to modify the permeability of cell membranes and allow DNA to pass through. After mixing a gene drug with a solution of microbubbles and infusing it into the treatment site, a very powerful, low
frequency ultrasound beam is directed into the area. Like an opera singer shattering a crystal glass, the ultrasonic beam causes the bubbles to vibrate in the acoustic field and eventually implode. The implosion creates a shock wave that briefly opens the cell membrane and allows the gene drug to enter.

Dr. Passineau and his team used the ultrasound technique to transfer Aquaporin-1, a protein encoded in the AQP1 gene that functions as a molecular water channel, into the genes of mini-pigs which had experienced profound loss of saliva by four weeks following radiation therapy.

Gene therapy was administered 12 or 14 weeks post-radiation therapy, with transfer accomplished via a catheter inserted into a duct inside the mouth. An ultrasound field was then applied to the parotid (salivary) glands in four 30-second treatments.

The technique restored salivary flow to pre-treatment levels for all of the test subjects.

“These results demonstrate, for the first time, the efficacy of ultrasound-assisted, non-viral gene transfer to the parotid glands of swine. Using ultrasound rather than a virus to facilitate transfer increases safety and decreases the possibility that the therapy will lose effectiveness,” Dr. Passineau said. “We look forward to advancing our work to a Phase I human clinical trial."

“Drs. Passineau and Dr. Trombetta and their colleagues are on the forefront of a new direction in gene therapy that holds great promise for treating chronic diseases like xerostomia,” said David Parda, MD, Chair, Allegheny Health Network Cancer Institute. “This impressive work exemplifies the exceptional quality and scope of medical research being conducted at AHN and our commitment to advancing innovations that elevate standards of care.”

Others involved in the AHN study include cardiologist Robert Biederman, MD; Zhimin Wang, PhD, Changgong Wu, PhD, Lee Zourelias, PhD, and Olivier Gayou, PhD of the AHN Gene Therapy Program; Day Werts, PhD, AHN Radiation Oncology, and Paul Edwards, DDS, Indiana University School of Dentistry.

About Allegheny Health Network
Allegheny Health Network is a western Pennsylvania-based integrated healthcare system that serves patients from across a five state region that includes Pennsylvania, Ohio, West Virginia, Maryland and New York. The Network’s Cancer Institute offers a complete spectrum of oncology care, including access to state-of-the-art technologies and new therapies being explored in clinical cancer trials. The Network’s radiation oncology program is the largest in the country and the only one in Pittsburgh dually accredited by both the American Society for Radiation Oncology and the American College of Radiology and the first. Allegheny Health Network’s Cancer Institute provides the complete spectrum of advanced oncology care and is a leading center for cancer research and new treatments being explored in clinical trials. AHN also has a formal affiliation with the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, one of the nation’s 41 comprehensive cancer centers designated by the National Cancer Institute, for research, medical education and clinical services.

To schedule an appointment with an AHN oncologist, please call 412.DOCTORS or visit www.ahn.org/find-a-doctor.
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