Scarring of the mouth or throat, losing portions of the tongue to cancer, traumatic damage to the facial nerves—even with the latest medical treatment, all of these can dramatically change how a person talks, eats, and looks.

“When patients sustain trauma or injury to one of the oral and maxillofacial structures, reconstruction of the lost tissue is a major challenge,” explains Dr. Anh Le, Chair and Norman Vine Endowed Professor of Oral Rehabilitation at Penn Dental Medicine. She and her team are advancing research that may enhance regeneration of the soft tissues of the face, mouth, and throat, including nerve tissue. Dr. Le’s research focuses on mesenchymal stem cells (MSCs) derived from a uniquely accessible source: human gingival (gum) tissue.

RESPONSIVE REPAIRS COAXED FROM UNLIKELY SOURCES

Dr. Le and her colleagues are among the first to successfully regrow tongue tissue in animals using human gingival stem cells. In their 2017 paper published in the journal Tissue Engineering, they found that a bioengineered tissue “scaffold” combined with these gingival-derived stem cells accelerated wound healing and muscle regeneration. Findings like these can be applied to healing many different tissues. Inserting a stem-cell-laden scaffold in place of an excised throat tumor, for example, can encourage healthy tissue to regenerate around the surgically closed wound and ideally could reduce the formation of scar tissue for improved long-term outcomes.

Obtaining stem cells from bone marrow or fat cells requires invasive procedures, says Dr. Le, “but in our situation, it’s basically discarded tissue.” When you extract teeth, for example, they come out with gingival tissue attached. It’s also easy to take a small sample from the mouth without much collateral damage.

HEALING THE NERVES

Mesenchymal stem cells, found in many adult tissues of humans and other animals, can develop into several different types of tissue depending on their environment and the chemical signals they receive. Dr. Le and her team have explored the use of gingival MSCs to repair bone damage caused by trauma, benign tumors, and cancer treatment, and now they want to do the same for nerve cells.

Efforts to regenerate nerves have mostly relied on neural stem cells, which naturally differentiate into nerve tissue; however, researchers haven’t been able to cultivate them efficiently. Dr. Le
A PRESSING NEED

Precisely controlled organs like the tongue—the most common site for oral cancer among Americans—are especially difficult to reconstruct if large portions are lost. Replacement graft tissue harvested from elsewhere in the body doesn’t have quite the same functionality, and the process creates wounds somewhere else, which is risky for patients with compromised healing or immune function. Scarring and contraction around the injury site further interfere with function. Dr. Le and her surgical colleagues use gold-standard reconstructive techniques, but those techniques can only go so far.

“I had a patient with a cancerous lesion on her tongue,” recalls Rabie Shanti, assistant professor of oral and maxillofacial surgery at Penn Dental Medicine. “Even though it was picked up early, in order to clear her tumor roughly one-third of the patient’s tongue had to be removed and reconstructed with skin and blood vessels from the forearm. With regenerative medicine we aim to use tissue engineering/regenerative technologies instead of borrowing tissue from other body sites. We’re finally starting to push forward new treatment modalities for oral diseases that have been managed the same way for decades.”

COLLABORATION OPENS NEW DOORS

Despite the great need and the promise of gingival stem cell-based research, it’s a long path from studies in animals to cures in humans. In 2015, the National Institute of Dental and Craniofacial Research (NIDCR) funded 10 institutions, including Penn, to develop strategies to translate these earlier-stage studies into tissue-regenerative treatments. Dr. Le leads the Penn Multidisciplinary Consortium on Personalized Dental, Oral, and Craniofacial Tissue Regeneration, a multidisciplinary team of clinicians and scientists from schools across the University. The aim is to enable rapid translation of engineered tissue and regenerative medicine products into preclinical and clinical use.

Among Dr. Le’s many collaborators are Songtao Shi, chair of anatomy and cell biology at Penn Dental Medicine; Bert O’Malley, Jr., chair of otorhinolaryngology/head and neck surgery at Penn Medicine; Phuong Nguyen, a plastic and reconstructive surgeon at the Children’s Hospital of Philadelphia; and colleagues at the VA Hospital. She hopes their collective efforts will eventually lead to FDA-approved clinical treatment for people with oral and maxillofacial damage—whether from cancer, trauma, or a genetic condition.

MORE INFORMATION

For more information on how to support the research of Dr. Le, contact Elizabeth Ketterlinus, Senior Associate Dean for Development & Alumni Relations, ekett@upenn.edu, 215-898-3328.