Breath of Fresh Air: Regenerative Medicine Bringing Hope to Patients Needing New Airways
By Josh Martinez

For the many thousands of patients suffering from diseases of the airway, life can be a constant struggle to get enough air. Injury, disease, tumors and developmental abnormalities of the windpipe leave many patients persistently suffocating.

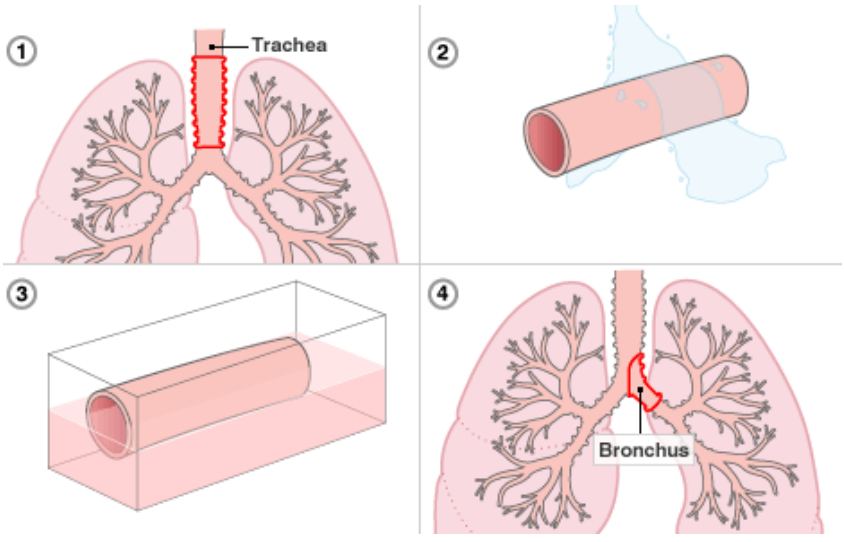
One such person, Claudia Castillo, was suffering from a collapsed airway damaged by a severe case of tuberculosis (shown in the CT image on the right).

The 30-year-old mother of two children was living in a state of constant suffocation. Her shortness of breath was so severe that she could barely get enough air in her body to keep up with her two children or climb a flight of stairs. Claudia desired nothing more than to return to her normal life. The problem was that the only medical procedures available were very risky and would've likely left Claudia with a poor quality of life.

Just when it seemed Claudia was out of options, a team of surgeons and biomedical researchers offered her a revolutionary alternative: an experimental transplant with a trachea that would be made using her own stem cells. Scientists had used this procedure successfully with rats and pigs, but it had never been attempted in a human.

Claudia took a risk and agreed to make medical history by becoming the first human patient to receive this this new transplant technology.

Figure 1 shows the steps that Dr. Martin Birchall and a team of pioneering throat surgeons took to construct Claudia's airway replacement.



1. A donor's trachea was removed.

2. The donor trachea was treated with chemicals to strip away all of the cells leaving behind only a protein scaffold.

3. This scaffold was seeded with adult stem cells from Claudia's bone marrow to replace the tracheal cartilage. The inside of the scaffold was seeded with airway cells scraped from Claudia's healthy bronchus. Claudia's cells repopulated the scaffold to form her airway replacement.

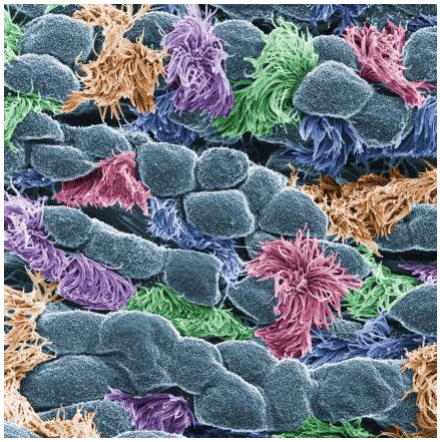
4. The new airway construct was then transplanted into Claudia to replace the damaged portion of her airway. As a bonus, Claudia did not require the use of harsh immunosuppressive drugs because the immune system does not reject cells or tissues it recognizes as "self."

Years later, Claudia has had no post-surgical complications and gives credit to this procedure for giving her back a normal life. In his recent STEM lecture at Sac State, Dr. Birchall (shown in figure 1) described Claudia's miraculous procedure, as well as his work replacing a child's trachea using a similar procedure. These medical breakthroughs have established the feasibility of fabricating tissues and organs using patients' own cells, and have revolutionized transplantation using tissue engineering.

There is an ever-increasing population of patients in need of transplants and an extremely short supply of donor organs, demonstrating the clinical need for an innovative new solution. Tissue engineering and regenerative medicine is a breath of fresh air for biomedical research, and is poised to revolutionize the way we look at medicine. Tissue engineering involves growing 3D tissues and organs in a lab and then using them to replace, repair or reconstruct body parts. This technology can overcome two major limitations with transplantation: the shortage of donor tissue available to patients in need and the complications associated with the use of harsh drugs required to prevent rejection of transplanted tissue.

To bioengineer an airway replacement, scientists must regenerate a layer of cells called "airway epithelium" that will line the inside of the windpipe. Unfortunately, there is little known about how to effectively regenerate the airway epithelium, so this has been a great challenge. One part of the challenge is figuring out the best source of cells (that would be taken from the patient) to use to make the new airway epithelium.

The airway epithelium (figure 2) is a specialized protective barrier that uses mucous to trap germs, particles, and cells with finger-like structures called cilia, which escalate the mucous away from the lungs. Making sure the new airway epithelium provides this protective is key to the survival of the bioengineered trachea. Without knowing how to effectively regenerate airway epithelium, we cannot utilize tissue engineering on a large scale for replacing large segments of airways.



Obtaining epithelial cells from the airway requires a biopsy, which can be dangerous for a patient population that already has airway complications. Damaged airways also means patients will have limited healthy airway tissue available to biopsy. Furthermore, when scientists try to grow cells in a petri dish from airway biopsies they have found the biopsied cells do not create enough epithelial cells to completely regenerate a trachea. It is therefore critical for other sources of epithelium to be investigated for their potential to regenerate airway epithelium.

In the laboratory of Dr. Alice Tarantal at the University of California, Davis we are focused on finding a feasible cell source to regenerate the airway lining. One possibility are cells obtained from the inside of the cheeks, referred to as the buccal mucosa. The buccal mucosa epithelium has many unique properties that make it an attractive candidate for airway tissue engineering. In fact, the buccal mucosa has already been used in this capacity; small biopsies taken from the inside of the cheek have been used to replace and rebuild damaged or lost epithelium of the eye, esophagus, and urethra,. Thus, we are hopeful that issue engineered buccal mucosa may also efficiently regenerate the inner lining of the trachea.

Tissue engineering can improve and even save lives of many, like Claudia, in need of a new organ. Surgeons and scientists at UC Davis are currently working to establish safe and effective methods for constructing and implanting airway replacements using animal models to enable movement of this technology to human clinical trials. While we have already demonstrated the possibility of utilizing this technology, preclinical studies like those being done at UC Davis are moving us closer to making stem cell cures a reality for all patients.