Photo courtesy of Dr. Songtao Shi

# Science vs. the Tooth Fairy

## New Promise in Baby Teeth

*By Tina Cauller*

Songtao Shi, DDS, PhD, Associate Professor, Herman Ostrow School of Dentistry of USC (University of Southern California, Los Angeles, CA) in the laboratory.

**How much is a baby tooth worth — fifty cents? A dollar? Ten dollars? Some researchers think a single baby tooth could be priceless, providing you plan ahead instead of giving it away to the tooth fairy.**

When intellect, inspiration and serendipity converge, interesting things can happen. Dr. Songtao Shi certainly has the first element of the equation. He earned a D.D.S. and M.S. degree from Peking University and a Ph.D. from USC. After serving on the faculty at Beijing Medical University, Shi opened a private pediatric dentistry practice in Los Angeles. He was eventually lured to the laboratories of the NIH, where he quickly earned accolades in the scientific world for his brilliant work in the area of stem cells taken from bone marrow. Then in 2003, along came serendipity.

Shi's little girl showed her dentist-scientist daddy a wiggly front tooth and asked him for help. She needed to get it to the tooth fairy. He obliged, and while cleaning the tooth off, he noticed a tiny bit of tissue inside the tooth. That got Shi thinking. In 2000, he and another NIH researcher had found mesenchymal stem cells (MSCs) in the dental pulp of adult teeth. A few days later, when his daughter lost her other front tooth at bedtime, Shi zipped off to his lab. Sure enough, his inspiration had led him to an exciting discovery – there were young stem cells in the tooth pulp left behind in the baby tooth!

### A singularly special cell

Stem cells have a unique job. They are the only cells in our body that can regenerate. A specific type of stem cell can differentiate into a variety of specialized tissue types in order to regenerate organs, tissues, and bones. Because stem cells are the building blocks of organ tissue, the immune system and blood, scientists have pondered their healing potential for decades. Stem cells from bone marrow were first used to save the lives of cancer patients who need help regenerating blood and immune cells after chemotherapy. Then, in the '80s, scientists began looking at stem cells taken from umbilical cord blood, which offer a number of advantages over bone marrow stem cells.

Youth, as it turns out, is particularly significant when it comes to a stem cell. In fact, we age partly because the ravages of time outpace our adult stem cells' weakened ability to regenerate cells. Stem cells taken from cord blood and teeth are vital and powerful, with only minimal degradation from age. Cryopreserving stem cells protects them from damage from aging, environmental factors, and viruses that occurs naturally in our bodies as we grow older.

Cryopreserved stem cells are available right away as opposed to waiting for cells from bone marrow, and collection is safe and painless. They are very young but not taken from embryos, so they are not associated with the same ethical controversy as embryonic stem cells. Because

the cells are autologous – taken from the patient's own body – there is less risk of complication and no need for immunosuppressive medications to prevent rejection.

After the discovery of stem cells in his daughter's tooth, Songtao Shi began collecting newly-lost baby teeth from her friends and any other cooperative 7- and 8-year olds he could enlist. He named the cells SHED (stem cells from human exfoliated deciduous teeth). He found that they proliferated rapidly into clusters, much faster than stem cells isolated from bone marrow or adult teeth.

Shi hypothesized that SHED are responsible for giving the order to make bone around the permanent tooth as it comes in, and with the proper cues, might be able to induce bone formation. He was right. When he implanted SHED under the skin of mice, they triggered the formation of bone. This was exciting – an earlier trial using stem cells from adult wisdom teeth had been unsuccessful. Shi knew that the stem cells in teeth share a common origin with neural tissue. With careful direction, he managed to coax the SHED to form neural cells in the brain and fat cells. Stem cells from adult teeth are much less potent generators of neural cells and incapable of inducing fat cell formation. Researchers believe that SHED may be able to restore cells damaged by diseases like Parkinson's or restore the cells that make dopamine so nerve cells can function properly.

## Tooth or fiction?

When it comes to therapies using stem cells, the future is here. It isn't science fiction and its promise, while still continuing to unfold, has arrived. Whole bladders grown in the laboratory from a patient's own stem cells have been successfully implanted. Doctors have grown patches to cover a hole or weakening in a blood vessel, as well as knee cartilage and tendons. Stem cells are being used to grow cardiac tissue, bone, insulin-producing pancreatic beta cells and other tissues. In some cases, a biological or synthetic scaffold is required to direct the growth of the cells into the desired form. Doctors recently replaced a British teenager's trachea with one grown from her own stem cells over a donor scaffold. Dr. Jeremy Mao of Columbia University Medical Center recently developed a growth factor-infused scaffold with the potential to regenerate an anatomically correct tooth in just nine weeks from implantation. Once the stem cells have colonized the scaffold, a tooth can grow in the socket and then merge with the surrounding tissue.

Further research has proven that the tooth bud of the mandibular third molar is an especially rich source of multipotent stem cells, which can form enamel, dentin, blood vessels, dental pulp, neural tissues, muscle, bone, organs, insulin-producing pancreatic cells, skin, cartilage, and hepatocytes. Researchers are currently developing stem cell therapies to treat a host of ailments including Type I diabetes, Parkinson's, Alzheimer's, arthritis, cardiac disease, multiple sclerosis, spinal cord injury and numerous others. Even some genetic conditions may be treated using stem cells from a healthy sibling.

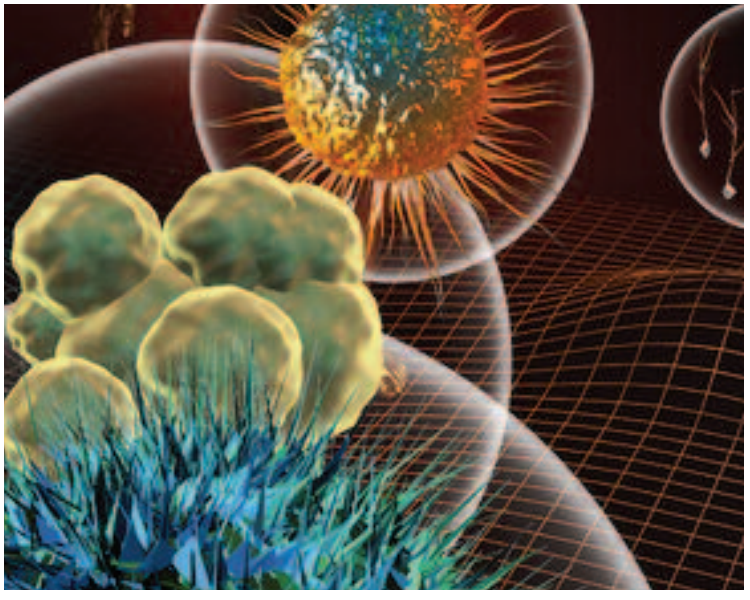
For dentistry, stem cell therapy could mean the ability to regrow natural teeth. How far off is this? A whole tooth is complicated structure. Most experts think that growing a whole tooth in a human mouth is a decade or more in the offing. "We have a long way to go," says Dr. Songtao Shi. "A whole human tooth is no less complex an organ than a human heart." For now, Shi and his team at USC are working on growing a "bio root" – a living tooth root – and he predicts that this milestone could be just a year or two away. They have already grown a living root and supporting periodontal ligaments in a pig sufficient to support a crown restoration and hope to go to clinical trials in the near future.

"We are using the background information and experience from dental implants and looking for ways to replace the artificial root substitute with a functional bioimplant," Shi notes. When asked about research goals that are closer to realization, Shi shares his excitement about the team's proximity to success in treating periodontal disease. "At present, we can treat periodontitis, but we lack an effective method to reverse the damage done by disease. We are very close to being able to use cell regeneration to grow new tissue to firmly support a tooth affected by disease. This is a very promising development."

## Saving for the future

While NIH is prohibited by conflict of interest considerations from operating a stem cell bank, private companies are springing up to meet the demand for this promising new area of medical technology. One company at the forefront of this new technology is StemSave, an FDA-registered company based In New York.

StemSave works with dentists to recover teeth at the optimal time, before they become very loose, to assure the highest probability of stem cell viability. (The pulp chamber of the deciduous tooth may be obliterated by the erupting tooth by the time the tooth actually becomes loose.) To participate, patients enroll at www.StemSave.com or by calling 877-STEMSAVE. Prior to the planned procedure, the patient's dentist receives a patented kit that contains a vial with a special solution to nourish and protect the cells during transport. When the tooth is extracted, the dentist simply places the extracted tooth into the kit. The kit is then sealed and sent to StemSave laboratories where the specimen is processed. Once the presence and viability of the cells is confirmed, the cells are cryopreserved. If the patient has a need for their stem cells in the future, they contact StemSave directly to arrange



transport from storage. The StemSave process was carefully designed to take less than a minute of a dentist's time. The company maintains the contractual relationship with the patient for cryopreservation so there is no paperwork or payments for the dentist's office to manage.

For parents who missed out on the chance to bank cord blood, harvesting and preserving a child's stem cells from baby teeth could be a golden opportunity. Parents of older children may be relieved to know that the opportunity to bank immature tooth-derived stem cells does not end at the kindergarten door. Adolescents can bank dental stem cells when bicuspid teeth are extracted in preparation for orthodontic treatment, when a tooth is fractured, or after the extraction of wisdom teeth. It is best to recover these teeth during the developmental stage, between age 16 and 20, since this is when the stem cells are most active in formation of the root. However, even third molars or permanent teeth with healthy pulp that are extracted later in life can be a source of viable stem cells.

## Tooth wisdom

The value of tooth-derived stem cell banking is questioned by some who argue that the future potential of the cells to provide useful therapy is uncertain and speculative. Others argue that the companies are preying on parents' natural concerns for their child's health, nudging them toward excessive anxiety. There are concerns about what will happen to the saved cells if the company goes under. Skeptics are critical of the initial and annual costs of cryopreservation. Banking companies have responded with assurances that their fees are fair and worthwhile and that they have a plan in place for the continuity of their services should the company fail.

Still, the NIH and HHS (Department of Health and Human Services) are waving off these reservations. Both are putting a lot of eggs into the basket of regenerative medicine, and these organizations are not known to commit funds without good reason. Experts at both agencies are banking on regenerative medicine to improve our quality of life and reduce health care costs and have committed significant resources to the field. The U.S. military's Armed Forces Institute of Regenerative Medicine is channeling hundreds of millions of dollars into efforts to develop stem cell therapies to treat wounded soldiers.

While the practical payoff may be years away, research is advancing our knowledge by leaps and bounds every day. Many informed and thoughtful people who can afford to pay the fees for cryopreserving cells from teeth are deciding that the potential benefit far outweighs the cost. After all, how do you put a price on even the slightest possibility that your child might someday be helped by investing in a simple, painless procedure? Dentists are finding that the service is simple and convenient. More important, they are finding that it is being enthusiastically received by patients who appreciate that their dentist is looking out for them by offering an option that might someday save the life of their child.

Of course, no one is looking to send the tooth fairy into quaint obsolescence. Just hoping that she might become a lifesaving fairy godmother for someone should the need arise. ■

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textbook perfect with slight inflammation and bleeding only to have the patient return in six months with bleeding and probe depths that were progressing and a noticeable odor in the mouth.

Dentistry is revolutionized when biofilm pathogens are known and quantified. Judicious care can be prescribed in treating and eradicating the pathogens doing the damage when we use this powerful tool in every day practice. A patient's genetic risk assessment and biofilm test all become part of the diagnostics equation along with x-rays and clinical examination. Enabling practitioners to assess and know what a patient's inflammatory response and bacterial infection is as an adjunct to prescribed therapy. By embracing the knowledge that saliva's DNA provides, dentists can prevent the oral cavity from being of any negative consequence on the overall health of the body.

Today, patients are better educated in the care of their teeth and gums, and have a better understanding of how this relates to their body's overall health. Patients are more ready than ever to embrace and accept partnering with their doctors in their overall care, and fully expect to keep their teeth for their lifetime. The integration of salivary diagnostics into dentistry today will fuel the growth of the next century of dentistry.

Creating a shift in the nature of today's dental practice requires an approach from many different angles. Currently, dentists are afforded the opportunity to be at the forefront of integrating salivary diagnostics into their practices and learn how this will grow and change the way dentistry is practiced. Clinical research continues to give us the empirical data needed as evidence grows on the oral-systemic links. Indicators show there is a visionary shift in dentistry moving dental practices toward evidence-based dentistry utilizing salivary diagnostics. Salivary diagnostics presents an adjunct for educating, motivating and changing the way dentistry is practiced both today and in the future. Salivary diagnostics, as with any new technique, product or service, demands due diligence and proper training to employ the new tool and interpret the results in order to utilize the product to its full potential and benefit the patient and practices of today. Financially, this creates a revenue stream much like the boost dental practices received from intraoral cameras. "A picture is worth a thousand words." In the case of salivary diagnostics, the picture is the lab report.

Go to **www.mydentalgenetics.com** for more information on salivary diagnostics. ■