lead story

Dental Stem Cells in Research and Practice

By ***Jean Majeski***

Introduction

Stem cells are cells that meet the two conditions of self-replication and the ability to differentiate into at least two different types of cell.[1] Types of stem cells are determined based on their source and differ in regard to the types of cells into which they differentiate (see Table I).

Embryonic stem cells, the use of which is controversial due to the need to destroy an embryo to harvest them, are the most versatile stem cells in that they are pluripotent; that is, they can differentiate into any other type of cell. However, their capacity for differentiation, coupled with their ability to self-replicate for many generations, presents a potential disadvantage to anyone who wants to guide and control their development for therapeutic use in the creation of new tissue.[1]

Adult stem cells, also called somatic stem cells, lack the potency of their embryonic counterparts, but have been used successfully to treat disease and do not require destruction of an embryo.[2] Adult stem cells can be harvested from an individual and, should the need occur, be used later to regenerate tissue by transplantation into the same (autologous transplant) or another individual (allogeneic transplant).[2]

Induced pluripotent stem cells—adult stem cells treated so that they behave like embryonic stem cells—have the potential to serve as the source of a large number of autologous stem cells, but more research is indicated prior to their therapeutic application due to their capacity for proliferation and concomitant potential for carcinogenicity.[1]

Among the types of adult stem cells, those derived from tooth structures have been receiving the attention of researchers over the past decade and inspiring hope for practical applications in the future. This article considers their status in research, their potential in practice, and the role of the dental hygienist in educating patients to make decisions about collecting and storing them.

Dental Stem Cells in Current Practice and Research

Dental stem cells, along with other stem cells from the craniofacial region, develop from material that is created during the development of the nervous system and have the potential to differentiate into neural cell lines. Researchers are examining what role they might play in the regeneration of tissue both in the orofacial region and in other areas of the body (see sidebar opposite).[1]

"Mesenchymal stem cells—the type found in dental pulp, among other tissues—were only discovered in 2003, and are being used in research for a number of diseases including Parkinson's, heart disease, diabetes, spinal cord and brain injuries, cranial bone repair and root formation," said David Matzilevich, MD, PhD, chief scientific officer of the National Dental Pulp Laboratory (NDPL), a division of the New England Cryogenics Center that specializes in the collection and storage of stem cells found in dental pulp.

Greg Chotkowski, DMD, president of StemSave™, a leading company in the field of stem cell recovery and cryo-preservation, said, "Dental stem cells have been transdifferentiated in the laboratory to form bone, nervous tissue and beta islet cells that produce insulin. These stem cells could prove to be a valuable source in the treatment of a number of degenerative diseases in addition to those that directly affect the oral cavity."

"Currently, there are no medically approved regenerative treatments using dental stem cells," said Ann Eshenaur Spolarich, RDH, PhD, associate director of the National Center for Dental Hygiene Research. "However, research has shown that dental stem cells can be used to regenerate a variety of tissue types in the body."

According to Matzilevich, a number of animal studies are currently under way to explore such regenerative applications. "The hope is that these cells will be used to regenerate bone, cartilage, skin, nerve and brain tissue, fat tissue, heart and muscle tissue," he said.

"We feel the first applications for dental pulp stem cells will be in the oral cavity," added Jeanne Coupe, RDH, NDPL clinical relations specialist, "which would include root regeneration, cranial bone repair and jaw regeneration."

According to Chotkowski, most of the current regenerative therapies in dentistry do not utilize stem cells directly. "The current approach is to enhance and mobilize a host's own stem cells through the introduction of commercially derived extrinsic growth factors," he said. "These factors, such as bone morphogenetic proteins, will induce the formation of bone by attracting stem cells and turning them into osteogenic cells.

"Presently, there is a commercial company that is supplying allogenic stem cells (from cadavers and processed to reduce their immunogenicity) for use in orthopedic applications. When used in sinus lifts [surgeries performed when there is insufficient bone in the maxilla or when the sinuses are too close to the jaw for implants to be placed] and periodontal defects, they shortened the time to bone formation and will prove to be a viable substitute to autologous bone grafting."

For now, autologous bone grafting, or the moving of a host's stem cells from one area or donor site to another area of the body, is the gold standard in regenerative bone therapy, Chotkowski explained. "This approach requires a donor site; most often it is a separate procedure and carries all the associated risks and complications. A proposed major advancement in regenerative therapies is to utilize an individual's own cells, which would be processed and expanded outside of the body and then reintroduced.

"The source of these stem cells could be previously recovered and cryopreserved dental stem cells found in baby teeth, wisdom teeth or other extracted healthy permanent teeth."

Spolarich said, "The advantage of banking your own stem cells from your dental pulp is that they are unique to you. Should they be needed in the future for a medical treatment, you will use your own cells, eliminating risk

Table I. Types of Stem Cells	
Type of stem cell	**May differentiate to...**
Embryonic	Any type of cell
Amniotic fluid-derived	Cartilage cells Fat cells Bone cells Muscle cells Endothelial cells Neuron-like cells Liver cells
Umbilical cord	Liver cells Skeletal muscle cells Neural tissue Immune cells
Bone-marrow-derived mesenchymal	Bone cells Cartilage cells Muscle cells Fat cells Neuron-like cells Pancreatic islet beta cells
Tooth-derived	Neural cell lineages Bone cells Cartilage cells Muscle cells Fat cells Pancreatic islet beta cells
Adipose-derived	Fat cells Cartilage cells Muscle cells Neuronal cells Bone cells
Induced pluripotent stem cells	Any type of cell, potentially

Source: Mao JJ. Stem cells and the future of dental care. NY State Dent J 2008; 74(2): 20-24.

Nondental Stem Cells for Dental Applications

Just as dental stem cells have the potential for therapeutic use throughout the body, stem cells from outside the oral cavity may be used for regenerating tissue in the mouth. Ivan Ho, DDS, is the founder of Platinum Dental in Rancho Santa Margarita, Calif. In March 2009, he performed an outpatient procedure called Bone Marrow Aspirate Concentration (BMAC) to strengthen the insufficiently dense mandible of a patient in preparation for a permanent dental implant.

BMAC has been used for many years by neurosurgeons and orthopedic surgeons to generate bone for procedures such as spinal and tibia fusions. It is a minimally invasive, relatively painless outpatient procedure that takes between one and three hours to perform, providing faster healing, less pain and better results than other implant procedures.

"This minimally invasive procedure is an innovative, advanced long-term alternative to existing tooth replacement options such as dentures, bridges and even traditional bone-grafting procedures," Ho explained. "In addition to providing better and faster healing, the transplantation of the patient's own stem cells enables the body to increase bone growth in the jaw through angiogenesis to permanently support the dental implant. Because the use of dentures and bridges carries a high risk of problems—in many cases resulting in gum disease, tooth decay and the loss of viable teeth—additional costly surgical procedures are necessary. Dental implants are the most natural solution and provide the best long-term results."

Ho harvested his patient's own bone marrow mesenchymal stem cells through a small incision in the hip bone the morning of the procedure. Using a centrifuge, he isolated and concentrated the stem cells from the plasma, transplanted them into the patient's jaw and added an allograft. The stem cells then began to work with the surrounding tissue to eventually generate healthy, dense bone tissue in preparation for the implant.

for infection, the need for anti-rejection drugs and the risk for contracting an infection from another donor."

"Because the research is still relatively new, it has not been proven that the stem cells can be used for other people," Matzilevich added. "So at this time, clients are being told that the only person the stem cells can be used for is the one who had the extractions done. There is great hope, however, that in the future, these cells could be matched with others without risk of rejection."

"There is a tremendous amount of research being conducted to characterize these cells," Chotkowski continued. "The stem cells recovered from baby teeth and developing wisdom teeth are immature and have pluripotential and embryonic-like characteristics. In some published research, they have been shown to be low in immunogenicity.

"However, we recommend saving your own stem cells to be used on yourself, because when you reintroduce your own tissue, there is virtually no chance of rejecting the tissue, and it decreases the need for powerful drugs that weaken the immune system. It is also less taxing. Donor cells require the patient to take powerful anti-rejection drugs that suppress the body's immune system."

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The Future of Dental Stem Cell Research

Chotkowski said that this is an exciting time for the dental professional. "We will continue to see the advancement of dental stem cell research and dental stem cells applied to clinical therapies," he explained, noting that several clinical trials utilizing dental stem cells have been proposed outside the United States. "In Japan, they have been able to form a whole tooth from stem cells in mice. Stem cells are being applied to dental implants and they have been shown to form a ligamentous attachment between the implant and bone.

"Regeneration or regrowing the pulp of a tooth is right around the corner, and it will change the specialty of endodontics within the next five years. On a global scale, there is a tremendous investment from both the public and private sectors in stem cell research. The Obama administration has made stem cell research one of the pillars of his health program. The U.S. Army is investing over $250 million in stem cell research to treat injured

How Stem Cells Are Extracted from Banked Tissue

Greg Chotkowski, DMD, president of StemSave™, explained what happens to the stem cells harvested from dental pulp.

"Dental stem cells are preserved within the native tissue that was recovered at the time of the planned dental procedure," he said. "StemSave allows an individual to recover up to four healthy recently extracted teeth per kit. The StemSave recovery and transport kit is rushed, via UPS, from the dental office to our processing and cryopreservation facility.

"At the processing facility, the teeth are cracked open and the pulpal tissue containing the dental stem cells is collected, washed, processed, tested for cell viability and then cryopreserved. There is a separate process involved for the isolation and expansion of the stem cells.

"When needed, the cryopreserved sample will be removed from the liquid nitrogen and the tissue will go through a thawing process. This tissue can either be digested enzymatically and placed into a cell sorter or, depending on the size and quantity of tissue, placed into a growth medium where the stem cells are allowed to grow into colonies. These colonies are characterized, and specific colonies are separated and allowed to continue to expand to the required number of cells indicated by the planned regenerative therapy protocol."

soldiers in a project called AFIRM (Armed Forces Institute for Regenerative Medicine)."

"Dental stem cells may be able to repair cardiac muscle that becomes damaged during a heart attack or from ischemic heart disease," Spolarich said. "Also, laboratory research has shown that roots of teeth can be regrown in animal models, suggesting that in the future, people may be able to regrow their own tooth roots, replacing the use of traditional metal implants."

Stem Cell Banks

"Dental stem cells are a valuable source of stem cells and are found in teeth with healthy pulp," StemSave's Chotkowski explained. "These teeth could be deciduous teeth, wisdom teeth and other permanent teeth. Presently, these teeth are being discarded as medical waste. A stem cell bank allows an individual the opportunity to preserve their biomaterial for future regenerative therapies."

Chotkowski cited the banking of umbilical cord blood as a source of stem cells, which has been advocated for the past 15 years to parents of newborns. "To date, there have been many lives saved through the transplantation of these stem cells," he said. "Cryopreservation or banking of stem cells maintains the viability of these cells indefinitely.

"During cryopreservation, the cells are put to sleep through a process called vitrification, in which the tissue is placed in liquid nitrogen at a temperature of –196 degrees Celsius. The cryopreservation process stops all cellular metabolism involving both cell growth and cell death. The cells preserved today can be applied to future regenerative therapies. There are many parents who did not have the opportunity to bank their children's cord blood. StemSave allows these parents another chance to bank their children's accessible and valuable stem cells when they are undergoing a routine dental procedure."

"Patients may oftentimes approach the hygienists first with questions and will often ask them for advice on the newest procedures."

The Dental Hygienist's Role

NDPL's Coupe said that as a hygienist, it will be important to inform patients of the future value in preserving teeth that will be exfoliated or extracted. "The mesenchymal stem cells in teeth are the easiest to retrieve and preserve and are typically removed and thrown out as medical waste," she explained. "If they are saved, they could be used in the future to save many lives and remove the problem of waiting for transplants, which so many people face today."

"Dental hygienists play an important role in raising patient awareness of regenerative medicine, stem cells, stem cell research and the benefits of stem cell banking for use in future regenerative therapies," Chotkowski added. "Hygienists are on the front lines of cutting-edge medicine because they spend considerable time with patients during scheduled routine visits and are familiar with the patients' dental history. Patients may oftentimes approach the hygienists first with questions and will often ask them for advice on the newest procedures. This presents an excellent opportunity to educate and inform patients about the ability to save their stem cells from teeth that are scheduled to be extracted and would otherwise get discarded."

Chotkowski also believes that dental hygiene schools should add stem cells and regenerative therapies to the curriculum. "There has been a lot of media attention recently geared toward the general public about stem cells, and patients will be asking the dental hygienist their views on the benefits of banking stem cells from teeth. I think it is our responsibility to educate the dental community on the basics of stem cells and their benefits in future regenerative therapies. We do not expect dental hygienists to become stem cell experts, but we need to make them aware that they will play an important part in the future of medicine and dentistry."

Spolarich agreed. "Dental hygienists can play an important role in educating their patients about the opportunity to bank their own dental stem cells. The best source of these cells is the pulp of deciduous teeth and permanent teeth, which become available naturally on multiple occasions during the course of a child's life: when deciduous teeth become loose, during extraction of premolar teeth for orthodontics and from removal of third molars."

Spolarich explained that during a regularly scheduled dental procedure, the mobile baby tooth or permanent tooth is extracted, stored in a special nutrient solution and shipped for cryopreservation.

"While dental stem cell therapies are not currently FDA approved, certainly, in the course of our children's lifetime, they will have the ability to benefit from life-saving regenerative medical therapies," she said. "So banking dental stem cells is like a form of bioinsurance—saving them now is an easy, affordable and noninvasive strategy to ensure their availability in the future when they will be needed the most."

References

1. Mao JJ. Stem cells and the future of dental care. NY State Dent J 2008; 74(2): 20-24.
2. Schneegans S. teeth will help to shape the future of stem cell research. A World of Science 2008; 6(3): 16-17.

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