Stem Cell Therapies: Reality in the Making

The following two articles outline the current state of stem cell research, address its potential application to several conditions, and pinpoint a need for scientific studies to establish efficacy for this exciting potential avenue of treatment.

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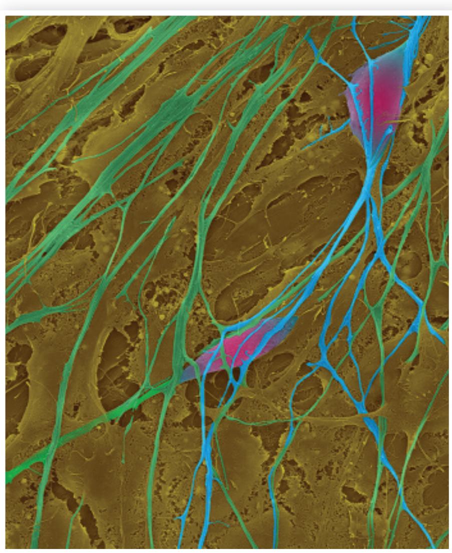

Appreciation for the potential of stem cell therapies should be balanced with healthy doses of optimism and skepticism.

Stem cell therapy has captivated worldwide audiences. As with any new discovery, stem cells may seem foreign, but enduring interest has sustained scientific investigation and clinical use. Promising early results coupled with accessibility to electronic media have helped increase enthusiasm for stem cell therapies. Despite unanswered questions, the understanding of stem cells has grown exponentially, and expectations of novel therapies for seemingly untreatable conditions are high.

The perpetual search for a panacea should be balanced, however, with healthy skepticism and discerning assessments. Compared with other treatment modalities, stem cell therapies are in their infancy; however, stem cell treatments may someday be standard medical care alongside similar "medical miracles" (eg, antibiotic therapies, vaccinations, artificial joint replacement).

What Are Stem Cells?

Stem cell is a relatively nonspecific term, often categorized into two broad sources:

- *Embryonic* stem cells (obtained from embryo)
- *Adult* stem cells (obtained from fully differentiated tissue or organs)

An additional distinction is the capacity of the cell to differentiate into other tissues:

- *Totipotent* cells (differentiate into all tissue types)
- *Pluripotent* cells (differentiate into most tissues from any of the 3 germ layers)

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- *Multipotent* cells (differentiate into tissues from same germ layer)
- *Unipotent* cells (differentiate into 1 tissue type)

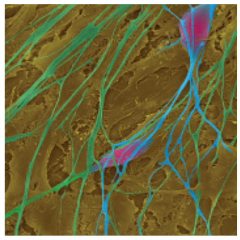
Additional terms that classify the relationship between donor and recipient include:

- *Autologous* cells (obtained from and instilled into same organism)
- *Allogeneic* cells (obtained from different donor of same species as recipient)
- *Heterologous* cells (instilled into recipient from different species than donor)

To categorize a stem cell on a genetic level:

- *Allogeneic* stem cells are obtained from and instilled into organisms of the same species but antigenically distinct.
- *Syngeneic* stem cells are obtained from and instilled into genetically similar organisms.
- *Multipotent* stromal cells are commonly available in the veterinary market.

How Are They Grown?



Another distinction among stem cells is the length of time they are grown in the laboratory. Cells are grown in plastic cultureware at a set number of cells per unit of surface area. As cells divide, they cover the surface. When the process is nearly completed (typically 80% covered), the cells undergo passage (ie, are released from the surface with an enzyme solution and added to new vessels at the same number per surface area). The number of passages is related to how many times the cells divide. Evidence has shown that cultured cells change as the number of passages increases. The cells may have a different appearance, tend to divide more slowly, express different surface proteins, and have a lower capacity to mature into different cell types.[1,2]

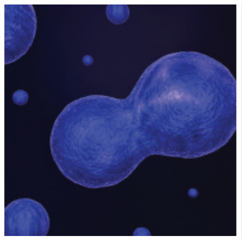
Where Do They Come From?

Stem cells have been isolated from nearly every tissue, with bone marrow and adipose tissue among the most common in veterinary medicine.[3] According to current knowledge, multipotent stromal cells must adhere to plastic, be capable of differentiating into adipocytes, osteoblasts, and chondrocytes, and express specific proteins on their surface without expressing others.[4]

Cells are typically removed from harvested tissue through a series of isolation steps. The original cell population is heterogeneous but becomes more homogeneous with each passage.

Evidence has also suggested that multipotent stromal cells function largely through a paracrine effect—recruiting native cells capable of tissue generation, reducing inflammation, and providing critical stimulation and environmental optimization with a cascade of protein factors.[5] Tissue source, isolation technique, number of passages, and confirmation steps (ie, surface antigens, microscopic appearance, ability to become other tissue) are important to consider when evaluating stem cell products.

What Are the Risks?



Veterinary regenerative products and their commercialization are the jurisdiction of the FDA Center for Veterinary Medicine (CVM). Distinction between a drug and a nondrug is made based on the level of processing required to manufacture a proposed product. Some stem cell therapies may fall under the regulation of veterinary medicine because of their autologous nature, so product approval should not be required.

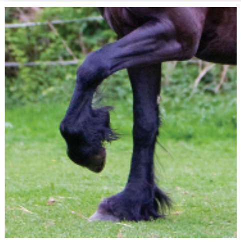
The CVM has not yet published official guidance on its regulatory position for veterinary stem cell products. However, the FDA's position on the use of stem cells in human medicine may serve as the template for future regulation of veterinary stem cell therapy.[6]

Because the stem cell field is relatively new, large, and diverse, few limitations have been identified and contraindications are even less readily available. Major advances in the use of stem cells combined with customized templates to generate tissue (eg, from bladder, bone, brain, cartilage, heart, skin) intended for implantation have the potential to revolutionize many veterinary specialties.

Unlike chemical molecules that have a finite half-life with an established elimination pathway, stem cells appear capable of surviving and migrating in the body. Stem cells reportedly have immunomodulatory properties—the degree of which varies among cells and isolation techniques.[7] Interactions between stem cells or between stem cell–based tissues and normal, injured, or diseased environments are the focus of contemporary research. The ability to predict implanted cell and tissue behavior is critical in designing effective treatment strategies.

Cell preparations can be administered IV, intraarticularly, and locally in diseased or injured tissue. The application site is often different than the harvest site. Based on current knowledge, it appears that the role of stem cells may be to modulate and direct native cells in tissue generation. The local environment may influence how implanted stem cells interact with existing cells. Therefore, normal tissue may respond differently than diseased or injured tissue would to stem cell signals.

Should I Use Them?



Restoration of injured, diseased, or aged tissue through stem cell therapy continues to hold promise. Positive results from laboratory research and studies involving adult stem cells for equine tendon and cartilage lesions and canine bone, intervertebral disk, and spinal cord injuries support the potential role of stem cells in tissue restoration.

However, studies with appropriate controls, adequate populations, validation steps, and repeatability are necessary to establish the safety and efficacy of individual stem cell products for specific clinical applications. Clinical trials are necessary to bring laboratory findings to the general practitioner.

Furthermore, the rapid and dynamic nature of the discovery process in this field has caused regulatory standards to lag behind advances. For the use of stem cell therapy in practice, it is important to carefully research the points described here. In addition, seeking reliable sources for the current status of indications for stem cell therapy, following available recommendations, and striving to objectively evaluate outcomes are also important.

With a healthy balance of optimism and skepticism, stem cell therapies can become reality in the ongoing quest for optimum care. ■ cb

See **Aids & Resources**, back page, for references & suggested reading.

Dr. Lopez is a researcher and has been granted select funding to explore the potential role of equine adult stem cells in bone injury repair.