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Vet-Stem
Regenerative Veterinary Medicine

# Regenerative Stem Cell Therapy

*Stem cells are being used to help facilitate tendon and ligament injury healing in horses*

Athletic horses are prone to musculoskeletal injury of tendons or ligaments, any of which can be performance-limiting or career-ending. These tissues tend to have a relatively poor blood supply and limited cell populations, making it difficult for them to heal with other than scar tissue. Fibrous scar tissue at the "healed" site has less elasticity and function than normal surrounding tendon or ligament. Thus, the risk of reinjury increases, particularly in adult equine athletes, with recurrence of tendonitis (inflammation of a tendon or tendon muscle attachment) as high as 43% of horses returning to competition.[1]

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Recent medical advances are relying on the use of regenerative therapy to stimulate healing for many orthopedic injuries as well as for treating bone and joint injuries and laminitis. Using the body's original cell line—stem cells—is one form of regenerative medicine. Stem cells are unique in their capability to develop into different cell lines to facilitate tissue repair.

## Regenerative Medicine

The objective in using regenerative medicine with stem cell therapy is to restore injured tendon or ligament tissue to a more normal architecture. Several types of stem cells could be potentially useful for regenerative medicine: embryonic, fetal, placental, umbilical, and adult. The most practical and effective stem cell sources for equine tendon and ligament repair are adult stem cells, also known as mesenchymal stem cells (MSCs).

When stem cells are transplanted into a tendon or ligament injury, tissue regeneration occurs via two possible mechanisms: 1) directly, by differentiation into various tissue-specific cell types; and/or 2) indirectly, by contributing to the production of proteins that reduce inflammation, stop cell death, and assist tissue growth and healing.

Researchers believe anti-inflammatory effects along with increased cell types from stem cell differentiation help slow the disruption and degeneration of tendon fibers in an injury.[1] Additionally, growth factors provided by stem cell transplantation improve the blood supply within an injured tendon or ligament. Research suggests "the effect is more in maintaining or inducing organized tendon architecture, rather than in provision of an increased pool of cells to participate in the healing response."[1]

## Adipose Versus Bone Marrow Stem Cells

Both adipose- and bone marrow-derived stem cells contain a varied population of nucleated cells that can differentiate into the target tissue for repair. Nucleated stem cells include endothelial cells (that line blood vessel), fibroblastic cells (found in connective tissue), pericytes (multipotent cells found in small blood vessels), smooth muscles cells, macrophages (specialized white blood cells), and blood cells, although it is as yet unknown which cell type best facilitates tendon healing.[1]

Bone marrow-derived stem cells have been the initial source used for injecting into a tendon or ligament lesion. Bone marrow aspirates are typically collected from the horse's sternum or ileum (hip bone). However, dilution of the stem cells by rich bone marrow blood makes it necessary to rely on culture expansion of stem cells in a laboratory. This additional procedure delays stem cell use for several weeks.[1]

Adipose-derived stem cells come from fatty tissue harvested from the base of the tail, which is easily accessible in a standing horse. This site provides a concentrated population of adipose-derived stem cells that can be injected into an injury site within 48 hours of harvest. The collection sample can also be processed in a commercial lab for increased tissue propagation for future injection.[1,4]

The simplified procedure for obtaining adipose-derived stem cells as compared to the more labor-intensive bone marrow aspirate cultures has several advantages: Not only is there a considerably reduced cost in obtaining adipose stem cell material, but a tendon or ligament injury can be treated within 48 hours following stem cell harvest. This speed of treatment has merit since granulation tissue that builds scar tissue appears in injured tendon or ligament within two weeks. Bone marrow

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cultures require time to develop adequate cell concentrations, necessitating a treatment delay of three to six weeks, which potentially misses a window of opportunity for healing.

Stem cell injection is usually performed with the help of ultrasound to guide the cells directly and accurately into the tendon or ligament lesion.

## Research Results

Studies of tendon repair using stem cells have shown promising results. Not only are anti-inflammatory effects achieved through the immune modulating tendencies of stem cells, but tendon lesions also are healed with improved structural organization.[1]

A retrospective study of 66 horses evaluated their return to athletic function following treatment with adipose-derived stem cell therapy. For horses with chronic tendon injuries lasting longer than three months, 84% returned to full work at their previous level of performance. Of horses with acute injuries, 73% were able to return to their previous athletic performance.[5] In comparison, only 40-60% of horses with tendonitis lesions treated by conventional therapies returned to soundness after one year.

Suspensory ligament (SL) injury has proven to be considerably difficult to resolve with conventional therapies such as time and rest. Injecting adipose-derived stem cell into the injured ligament site, 71% of 62 treated horses with chronic SL injury were able to return to their previous performance level while 16% returned to work, but at a lesser level. Of horses treated with adipose-derived stem cells for acute SL injuries, 92% returned to their previous performance level.[5]

## Take-Home Message

It might take six to 12 months of rest and rehabilitation to achieve the best resolution of a soft tissue injury, and stem cell treatment does not necessarily speed this healing process. The intent of using regenerative medicine with stem cells is to improve the strength and function of the tendon or ligament architecture for a successful healing outcome. Gradual increases in controlled exercise should be monitored via ultrasound exam of the injury following the initial treatment and rest period. This should help a horse return to his previous performance level with less chance of injury recurrence.[4]

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