Regenerative Medicine Zoetis

Point-of-Care Regenerative Medicine
Prepared Under 30 Minutes
Natural - Drug-Free

What is Regenerative Medicine?

Regenerative medicine is the process of healing and restoring the normal function of damaged tissues or joints through the use of biological materials such as cells, platelets and plasma. Regenerative medicine boosts the natural healing processes by stimulating the body's own repair mechanisms.

Regenerative medicine therapies may take many forms including, stem cells, platelets, and natural cell signals (e.g. growth factors). The goal is to change the course of acute and chronic disease/injury and improve outcomes by restoring normal issue or joint function and speeding recovery.

Zoetis' portfolio of regenerative medicine devices spans nearly 20 years of development and commercialization. Focusing on the outputs of signaling proteins, matrix proteins and cells, our regenerative medicine devices, blood or bone marrow aspirate are harvested from the animal and prepared on-site in less than 30 minutes. This offers convenience, peace-of-mind, and cost savings to the caregiver and owner.

Signals

Pro-Stride APS
(Autologous Protein Solution w/ IL-1ra) w/IRAP)

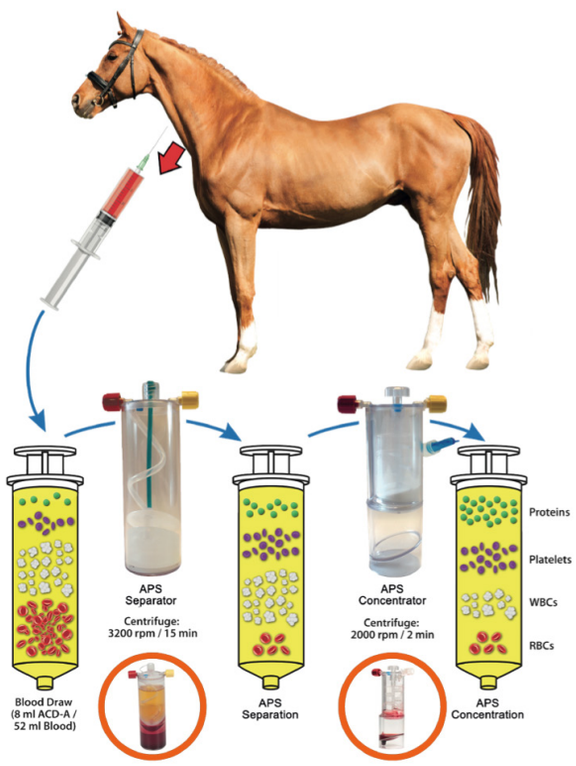
Stem cells are the building blocks of tissue regeneration, but they need a plan. That plan comes from soluble signals such as growth factors which orchestrate tissue regeneration. Platelets guide the initial steps, and use of PRP can "jump-start" healing in acute injuries. However, in chronic injury such as osteoarthritis (OA), healing is stuck in the initial inflammatory phase. Before healing can begin in earnest, the inflammatory signals must be silenced and replaced with signals which promote tissue regeneration.

Interleukin-1-receptor antagonist

(IL-1ra or otherwise known as "IRAP") is an important mediator of this redirection. IL-1ra produced primarily by WBCs orchestrates the inflammatory response. WBCs are the traffic cops of inflammation and can incite or stanch it, depending on environmental cues. **Not all "IRAP" containing products are the same.** Zoetis' Pro-Stride begins with a high platelet recovery/high concentration PRP fraction, rich with WBCs, and further stimulates to release IL-1ra and other anti-inflammatory factors (ex. sIL1R, sTNF-R). **There is no incubation period, rather the output is ready for immediate use following a short centrifugation time.**

Pro-Stride is an autologous platelet concentration, different from an autologous conditioned serum (ASC). With an autologous platelet concentration, cells are less disrupted and left more intact at time of treatment. This supports the idea of more natural degranulation into the soft tissue while live monocytes continue to promote the cascading effect of cells and produce additional IL-1ra within the patient. The Pro-Stride system produces a concentrated mix or "supercharged soup" of cells, platelets, growth factors and anti-inflammatory proteins, all within a concentrated plasma. Use of the Pro-Stride system has been clinically demonstrated to provide pain relief up to one year from a single treatment, with the potential for disease-modifying effects.*

*A. Bertone, Am J Vet Res 2014;75:141–151



Matrix

Restigen PRP
Platelet Buffy Coat Concentrate

Regenerative cells need a roadway before they begin their work of regeneration. Matrix proteins form these roadways and include collagen and fibrin. These large proteins form continuous porous networks along which the cells grab hold and pull themselves along. Fibrin comes from the plasma, the liquid part of blood, when activated by the platelets. **Platelet Rich Plasma (PRP)** contains the matrix proteins and all the signals to form super-highways for the cells.

PRP contains both the signals and the matrix proteins to jump-start the regeneration process. **Not all PRP systems or capture methods are the same.** Platelets can vary between reparation in recovery percentage, concentration factor, and activation state. Zoetis Veterinary's **Restigen PRP** consistently yields 90% or more of platelets at a 9-fold concentration. In healing, platelets in an intact, resting state supports the idea of preserving the potency of signals until application to the site of injury. This also serves to facilitate matrix adhesion.

The Restigen Device is designed to utilize white blood cells (WBC) as part of its buffy coat output solution. WBCs are the mediators of the immune system. Some believe that WBCs are inflammatory or harmful to regeneration, but they are also responsible for restricting inflammation. The action of WBCs in inflammation is a direct result of the signals that they receive. Restigen works through a rapid yet gentle isolation process. Minimizing the risk of cell aggravation and inflammation will support an environment where WBCs can act as cytokine factories and promote tissue regeneration beyond the standard action of PRP alone.

Cells

Centrate BMA
Bone Marrow Aspirate Concentrate

Most adult tissues contain cells that can regenerate a variety of tissue structures. These cells are sometimes called "adult stem cells". Immediately after collection of the patient's bone marrow aspirate, Zoetis Veterinary's CenTrate Device isolates and concentrates cells from bone marrow at the point of care, rapidly producing an enriched concentrate of mesenchymal cells (MSCs) for immediate application.

The CenTrate Device features a dual buoy design that produces an output of natural fibrin matrix with 5-19x increase in MSCs compared to original bone marrow in a convenient 15-minute processing time. There is no required shipping or laboratory culture, allowing for immediate processing.

Treatments

CenTrate® BMA

- Tendon Injuries
- Ligament Injuries
- Lesions
- Wounds (acute and chronic)
- Tissue Repair

Restigen® PRP

- Tendon Injuries
- Ligament Injuries
- Lesions
- Wounds (acute and chronic)
- Tissue Repair

Pro-Stride® APS

- Joint Inflammation
- Joint Disease / Osteoarthritis