Platelet-Rich Plasma and Stem Cells: How Biologics Work Together

Table 1

Mechanism of Action (Characteristic)	PRP	Stem Cell
Responsive cell with nucleus that can replicate		X
Can produce specific cytokines in response to injury type		X
Can deliver cytokines and growth factors	X	X
Can attract mesenchymal stem cells to a site of injury	X	
Modulate the immune system		X
Antibacterial	X	X
Antiviral	X	X
Hemostatic	X	
Stimulate wound healing	X	X
Reduce pain	X	X
Anti-inflammatory	X	X

Comparison of mechanisms of action of PRP and mesenchymal stem cells

Figure 1

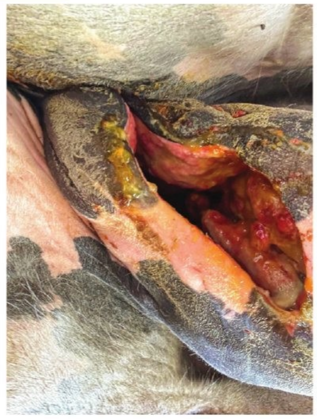
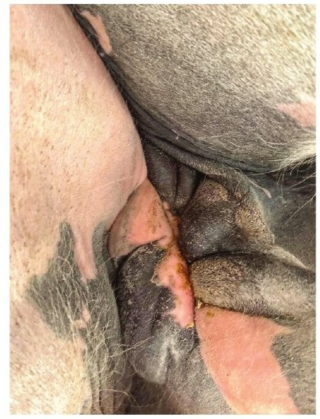


Figure 2



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Introduction

Platelet-rich plasma (PRP) is used commonly in canine and equine practice. A very common question is if there is any advantage of combining PRP with a stem cell product. Recent scientific publications demonstrate that not only is it possible, but the combination has a synergistic effect compared to each product individually. Clearly, they have different mechanisms of action as seen in Table 1, but let's explore how they work in synergy.

Mechanisms of Action

Platelets are provided to supply the growth factors and cytokines predominately located in the alpha granules. After administration, the growth factors and cytokines are released into the area of injection and provide anti-inflammatory cytokines and repair signaling. Platelets also release factors that attract or "home" mesenchymal stem cells, leucocytes, and other mononuclear immune cells to assist in the repair process. It has been reported that PRP injected into the joint or lesion reduces pain signaling.

Mesenchymal stem cells (MSC), on the other hand, are tissue/injury responsive drug stores that manufacture and release injury specific drugs to promote healing, reduce inflammation, modulate the immune system, and reduce pain. Additionally, they are directly antibacterial and antiviral.

PRP and Stem Cells Work Synergistically

PRP is immediately available naturally any time there is an injury, and the stem cell synergy assists the body in providing all the necessary components to treat an injury and promote healing. As you can see from Table 1, these key natural components provide complementary and supportive functions.

In a hallmark study of osteoarthritis in beagle dogs, PRP combined with adipose derived stem cells was superior to either therapy alone and better than placebo controls.[1] These benefits were evident in lameness score, compressive strength of the cartilage, COL and GAG content of cartilage, as well as a reduction in cartilage content of proinflammatory cytokines like TNF-α, IL-1α, and COX2. The author's conclusion was "taken together, this study shows that the combination of MSC and PRP has a beneficial and synergistic effect on OA via the ECM synthesis and chondrocyte proliferation and via the anti-inflammatory reaction."

In a recent review publication, models of periodontal disease, tendon repair strength, osteoarthritis, bone repair, skin and soft tissue repair, and in cardiovascular disease demonstrated that the combination of PRP and MSC was superior to the individual components alone.[2] The same synergy was demonstrated in a rat spinal cord injury model where the authors concluded "this study showed that combination of MSCs and PRP synergistically promotes their therapeutic effects in the SCI (spinal cord injury)."[3]

Case Report

A 15-month-old Clydesdale gelding presented for regenerative care to resolve a large, post-surgical wound. After routine castration, bacterial infection, and surgical debridement, a 9cm x 3cm x 11cm surgical wound extending from the internal inguinal ring to the surface of the prepuce was open and draining serosanguinous discharge (Figure 1). The horse was discharged to home care which included daily cleaning with hypertonic saline and topical application of silver/manuka honey. At recheck after one week at home, the wound was clean but still substantial.

Expected timeline for healing was discussed at 4 months. To speed healing and slow the serosanguinous discharge, cellular biologic therapy was discussed.

The owner had banked stem cells at the time of castration with VetStem, Inc. for later orthobiologic care. This meant that stem cells were immediately available for use. In addition, the allogeneic PRP, PrecisePRP™ Equine, was available for use. PrecisePRP™ Equine is currently under final review with the FDA ACTP program. Based on the availability of these two biologics, a treatment plan was developed.

Stem cells were administered intravenously for the anti-inflammatory effect and potentiation of healing. PRP was administered topically by rehydration of the allogeneic PrecisePRP™ Equine and syringe flushing of 8mls PRP (4 billion platelets) into the deep aspects of the wound. The wound was packed with sterile gauze for 4 hours to allow the PRP to absorb into the wound tissue and release growth factors like PDGF-BB and VEGF to promote angiogenesis. In addition, the PRP releases high mobility group box 1 (HMGB1) which works to mobilize MSC as a chemoattractant.[4]

Daily care was continued with the inclusion of repeat PRP administration, as described above, two weeks after the initial use and MSC administration. Wound size and health were evaluated weekly. On week 5, the wound was assessed as 7cm x 1/2cm x 3cm with healthy granulation tissue present without serosanguinous discharge. By week 6, the wound was completely closed (Figure 2) and the gelding returned to normal turnout during week 6. He was placed back in training on week 8 with no further complications noted. Although this use of PrecisePRP™ Equine is off-label, wound healing is a very commonly reported application.

Conclusions

Based upon the literature, PRP and stem cells are strongly synergistic. There are complementary mechanisms of action that work together to improve healing and tissue repair in many different organs/tissues across multiple species. ●

References

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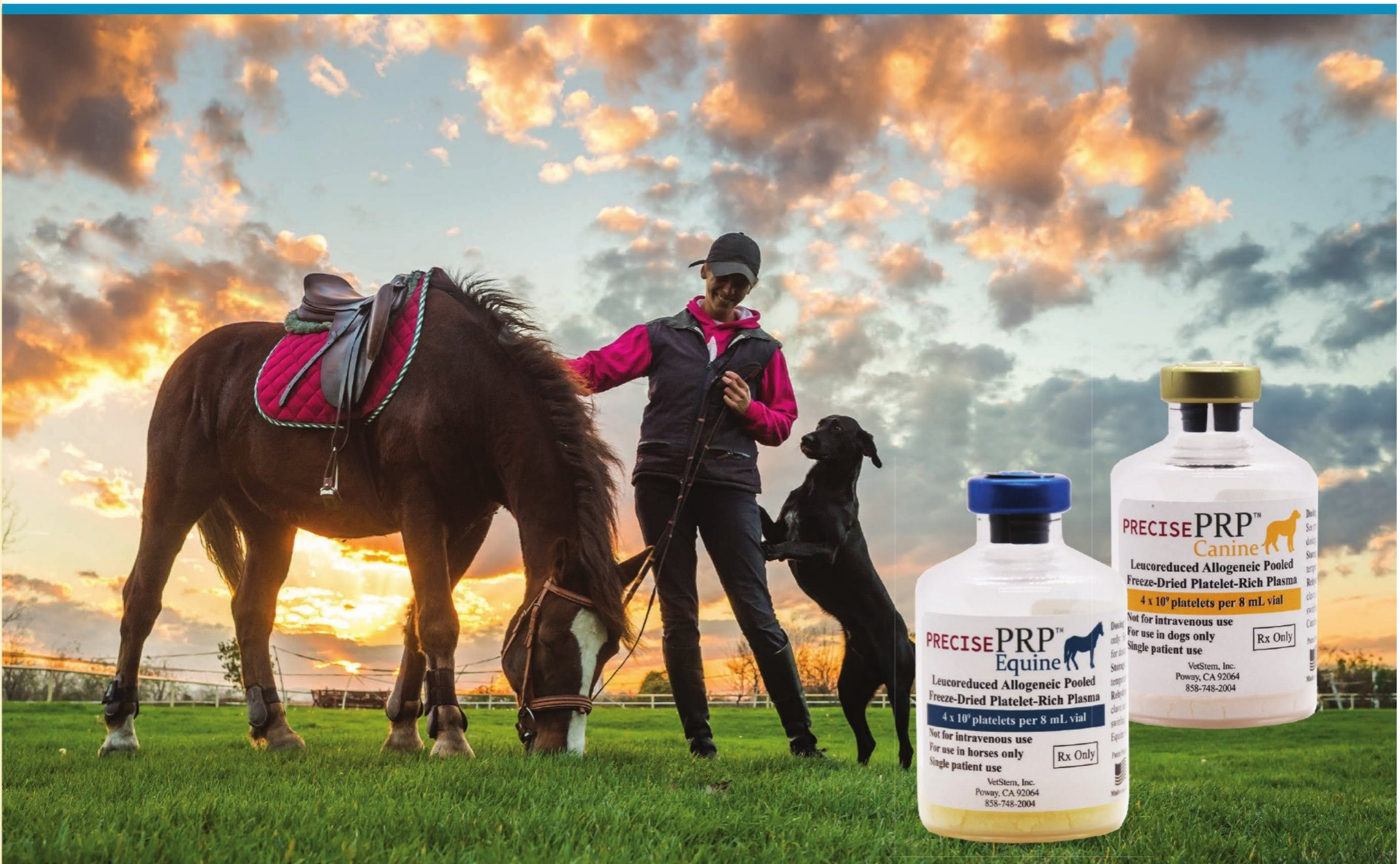

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