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Review Article

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Next-Generation Regenerative Therapies in Horses and Camels: Integrating Stem Cells, Mitochondrial Peptides, and Nanomized Peptides for Targeted Tissue Repair

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Abstract

Background: Veterinary regenerative medicine has advanced rapidly in companion animals, yet its application in large species such as horses and camels remains underexplored. Equine medicine, driven by the athletic demands of racehorses and sport horses, focuses heavily on musculoskeletal injuries. Camels, uniquely adapted to desert climates, face challenges in musculoskeletal, metabolic, and infectious disease management. Stem cell xenografts, mitochondrial peptides, and nanomized peptide delivery systems offer new avenues for enhancing tissue regeneration, performance recovery, and systemic resilience in these species.

Objective: To critically evaluate regenerative and peptide-based therapies in horses and camels, and to propose an integrative framework for clinical translation.

Methods: This review synthesizes recent preclinical and clinical evidence for xenografts, neural precursor cells, mitochondrial peptides, and nanomized peptide formulations. Mechanistic insights, therapeutic potential, delivery innovations, safety considerations, and regulatory frameworks are discussed.

Results: Equine studies demonstrate efficacy of regenerative therapy in tendon, ligament, and joint repair, while early work in camels suggests applications in wound healing and metabolic regulation. Mitochondrial peptides improve bioenergetics, reduce oxidative stress, and may enhance athletic recovery in horses or metabolic stability in camels. Nanomized peptides improve stability, targeted delivery, and bioavailability in large animals, supporting applications in arthritis, respiratory disease, and immune modulation.

Conclusions: Integrative regenerative strategies hold significant promise for equine performance medicine and camelid health in arid climates. Advances in stem cell biology, peptide therapeutics, and nanotechnology may transform veterinary care for these species, though rigorous trials and regulatory frameworks remain essential.

Keywords: Stem cells, Mitochondrial Peptides, Nanomized Peptides, Equine Regenerative Medicine, Camelid Regenerative Medicine, Personalized Veterinary Therapy

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Introduction

Regenerative medicine has emerged as a transformative field in veterinary science, leveraging the body's inherent healing capabilities to address conditions resistant to conventional therapies. In equine medicine, regenerative therapies are widely investigated for musculoskeletal injuries, a leading cause of morbidity and loss of athletic function in sport horses [1]. In camels, interest is expanding due to their economic and cultural importance in arid regions, where they are essential for transport, racing, and dairy production [2].

Stem cell therapies, particularly mesenchymal stem cells (MSCs), are at the forefront of equine regenerative medicine due to their ability to differentiate into chondrocytes, osteocytes, and tenocytes while exerting immunomodulatory effects [3]. In camels, MSCs and other precursor cell populations have shown potential for wound healing, reproductive support, and systemic modulation under extreme physiological stress [4]. The therapeutic efficacy of MSC–based interventions is increasingly recognized as being highly contingent on their intrinsic biological characteristics and the specific repertoire of bioactive factors they secrete, often referred to as the MSC secretome. Careful characterization of these properties can provide critical insights into the rational selection of MSC subpopulations most suitable for disease-specific regenerative applications. A key determinant of MSC functionality lies in the tissue of origin and the physiological state of the donor. Stem cells harvested from diseased or aged donors may exhibit diminished proliferative capacity, altered differentiation potential, and impaired paracrine signaling. Indeed, accumulating evidence suggests that endogenous stem cell populations are progressively compromised during chronic or degenerative disorders, and their dysfunction actively contributes to the progression of pathological symptoms. Moreover, the local inflammatory microenvironment exerts a profound influence on stem cell behavior, often exacerbating functional decline by altering survival, engraftment, and paracrine output. Given these constraints, allogeneic MSC therapy offers distinct advantages over autologous approaches, as cells derived from young, healthy donors are more likely to retain robust functional competence. Such "off-the-shelf" allogeneic products not only ensure a more consistent therapeutic effect but also allow for scalable and timely application in clinical settings. This has prompted growing interest in complementary or alternative strategies that act directly at the subcellular level. In particular, mitochondrial organelle peptides (MDPs) and nano-organelle peptide formulations are emerging as powerful candidates for targeted organ repair [5]. These peptides bypass many of the challenges associated with whole-cell therapies by modulating core processes such as oxidative phosphorylation, redox signaling, and stress adaptation. When engineered within nanocarrier systems, they can be delivered with high precision to diseased tissues, thereby restoring cellular bioenergetics, attenuating inflammation, and supporting regenerative pathways. Together, these advances position organelle-targeted peptides as a next-generation approach that complements and, in some cases, may surpass the therapeutic potential of MSC-based interventions. This review examines the integration of stem cell transplantation with peptide therapeutics in horses and camels, emphasizing translational potential, species-specific applications, and regulatory challenges.

Regenerative Therapies in Equine and Camel Medicine

Traditional MSCs have been extensively investigated in horses, most derived from bone marrow, adipose tissue, or umbilical cord. These cells exhibit robust self-renewal and multilineage differentiation capacity, and their paracrine secretion of trophic factors contributes to angiogenesis, immunomodulation, and extracellular matrix remodeling [6]. In camels, MSCs have been successfully isolated from adipose tissue and peripheral blood [7], demonstrating notable resilience under oxidative stress conditions, an adaptation that likely reflects their evolutionary adjustment to arid and metabolically challenging environments. This intrinsic resistance highlights their translational potential in managing systemic and stress-related disorders.

Beyond cell-based therapies, peptide-based therapeutics such as MDPs and antimicrobial peptides (AMPs) have emerged as promising adjuncts due to their capacity to enhance cellular resilience, mitigate oxidative damage, and promote tissue regeneration [8]. Recent advances in nanotechnology have further optimized their clinical applicability by enabling stable, targeted delivery and controlled release, thereby extending their utility to chronic musculoskeletal, respiratory, and metabolic diseases in large animals [9].

More recently, regenerative strategies have expanded to include xenografting of mitochondrial organelles and the engineering of nano-encapsulated pluripotent stem cells (nPSCs) for organ-specific repair. Transplantation of functional mitochondria into ischemic or degenerative tissues has been shown to restore oxidative phosphorylation, improve ATP generation, and reduce reactive oxygen species, offering a mechanistically rational approach for tissues subject to repetitive strain in equine athletes or metabolic stress in camelids. In parallel, nPSCs delivered via nanocarrier platforms provide enhanced survival, precise homing, and lineage-specific differentiation into chondrocytes, tenocytes, or neuroglia, depending on the target tissue. Taken together, these advances point toward a future in which mitochondrial organelle peptides and nano-organelle peptide systems serve as highly targeted tools for organ repair. By directly addressing the subcellular deficits underlying tissue degeneration, these therapeutics hold the potential to complement, and in some contexts, surpass the regenerative benefits of MSC-based interventions.

Clinical Applications

In horses with tendon and ligament injuries, the combined delivery of nano-engineered pluripotent stem cells (nPSCs) and mitochondrial xenografts has been reported to accelerate collagen fiber alignment, enhance biomechanical strength, and prolong repair capacity [9]. Beyond musculoskeletal applications, alternative stem cell pools are under investigation. For example, hoof progenitor cells (HPCs) have been evaluated as a potential therapeutic option for equine laminitis. Studies demonstrate that while HPCs exhibit local reparative capacity, they appear to have a reduced ability to migrate across injured tissues, suggesting their effects are predominantly localized rather than systemic [10-12]. Emerging work has also explored direct mitochondrial transplantation (mitotherapy) as a novel strategy for equine joint disease. In a pilot study, autologous blood-derived mitochondria were isolated using a commercially available kit and injected intra-articularly into the left carpal joint of three horses. Over a 28-day observation period, the procedure was well tolerated, with no clinical or ultrasonographic evidence of inflammation, supporting the feasibility and safety of intra-articular mitochondrial delivery and providing a foundation for future efficacy studies. In parallel, preclinical studies indicate that nano-engineered neural precursor cells (NPCs) derived from induced pluripotent stem cells (iPSCs) can integrate into host neural networks, offering promise for treating equine spinal cord injuries. Notably, when NPC transplantation is combined with xenografted mitochondria, the supplemented organelles support axonal energy metabolism, enhance neuronal survival, and improve the likelihood of functional recovery [13].

In camels with musculoskeletal disorders, the integration of mitochondrial xenografts with nano-engineered pluripotent stem cells (nPSCs) holds significant promise for enhancing both structural repair and metabolic resilience. By restoring oxidative phosphorylation and reducing reactive oxygen species, xenografted mitochondria may stabilize the energy balance of stressed chondrocytes and synoviocytes, while nPSCs contribute lineage-specific differentiation to support cartilage and tendon regeneration [13]. Similar strategies in equine models have demonstrated improved collagen alignment and functional recovery following tendon injury, providing a translational rationale for applying this approach to working camels [14].

In wound healing applications, nano-delivered stem cells encapsulated in protective carriers have been shown to improve survival and homing, while their paracrine factors stimulate fibroblast proliferation and angiogenesis. When combined with mitochondrial supplementation, this dual therapy enhances energy availability in regenerating tissues, thereby accelerating closure of traumatic soft-tissue injuries [15]. Reports in large-animal models support the feasibility of mitochondrial transfer for tissue repair, suggesting that camelid applications could build on this foundation [16].

Reproductive medicine may represent another frontier for these integrative therapies. Application of targeted nPSCs to the ovarian or uterine microenvironment, in conjunction with mitochondrial xenografts, could restore fertility in breeding camels by improving oocyte quality, stabilizing endometrial function, and enhancing the resilience of reproductive tissues under metabolic stress [17]. Evidence from bovine and murine studies indicates that mitochondrial replacement and stem cell–derived trophic support can rescue ovarian insufficiency and improve pregnancy outcomes, underscoring the potential for adaptation to camelid reproductive health [18,19].

Mitochondrial Peptides

Mitochondrial dysfunction is increasingly recognized as a driver of both equine performance decline and camelid metabolic instability, manifesting through impaired oxidative phosphorylation (OXPHOS), excessive reactive oxygen species (ROS) generation, and reduced mitochondrial biogenesis. These alterations compromise energy availability, muscle endurance, and systemic resilience in large animals subjected to environmental or athletic stress. Targeting these deficits with MDPs represents a promising therapeutic avenue in veterinary medicine.

SS-31 (Elamipretide) is an aromatic–cationic tetrapeptide that selectively binds to cardiolipin in the inner mitochondrial membrane. By stabilizing cristae architecture and preserving electron transport chain function, SS-31 enhances ATP synthesis and reduces ROS accumulation [20]. In equine athletes, where high-intensity exercise is associated with mitochondrial disruption, oxidative damage, and muscle fatigue, SS-31 may improve post-exercise recovery, protect against exercise-induced oxidative injury, and enhance cardiac resilience under workload. Supporting this rationale, studies in Thoroughbred horses demonstrate that exercise induces significant alterations in mitochondrial dynamics and ROS handling in skeletal muscle, linking mitochondrial stability to athletic performance [21]. MOTS-c, a mitochondria-encoded peptide, functions as a mitokine with systemic metabolic effects. By activating the AMP-activated protein kinase (AMPK) pathway, MOTS-c stimulates mitochondrial biogenesis, improves insulin sensitivity, and enhances substrate utilization [22]. These effects are particularly relevant for camels, whose survival under heat stress, dehydration, and nutritional scarcity depends on extraordinary metabolic plasticity. Camel studies highlight unique mitochondrial adaptations, including efficient ROS buffering and flexible fuel switching during fasting, underscoring the translational potential of MOTS-c to reinforce metabolic resilience in these conditions [23]. Together, SS-31 and MOTS-c illustrate the translational shift toward organelle-targeted molecules that directly address subcellular dysfunction. By restoring mitochondrial bioenergetics and modulating systemic adaptation, these peptides represent a species-relevant therapeutic strategy to support both equine performance and camelid survival in extreme environments.

Nanomized Peptides

Conventional peptide therapeutics face well-documented challenges, including rapid enzymatic degradation, short plasma half-life, and limited penetration into target tissues. Nanotechnology-enabled peptide formulations, such as liposomes, polymeric nanoparticles, and nanogels, address these barriers by improving pharmacokinetics, protecting peptides from proteolysis, enabling controlled release, and facilitating targeted delivery to specific organs and tissues [24].

In horses, the application of nanomized peptide systems has shown promise in osteoarthritis (OA) and respiratory disease, primarily. Intra-articular delivery of nanocarrier-encapsulated peptides has been demonstrated to reduce synovial inflammation and preserve cartilage matrix integrity in experimental equine OA models, thereby supporting joint health and prolonging athletic function [25]. This is particularly relevant in performance horses, where joint degeneration is a major cause of morbidity and early retirement. Inhalable nanocarrier-based peptides are under investigation for conditions such as equine asthma and recurrent airway obstruction (RAO). Nanoparticle formulations improve pulmonary deposition, prolong residence time in the airways, and provide sustained anti-inflammatory activity, offering an alternative to corticosteroid-based management [26].

In camels, nanotechnology-enabled peptide delivery including encapsulation of AMPs in nanoparticles has been shown to improve stability and enhance efficacy against gastrointestinal and respiratory pathogens, both of which are major contributors to morbidity and economic loss in camel herds [27]. Oral nanocarriers represent a particularly valuable strategy for camels, as they improve gastrointestinal absorption and systemic bioavailability, helping to overcome the logistical challenges of repeated parenteral dosing in large, free-ranging animals [28].

Taken together, these advances demonstrate that nanotechnology not only enhances the biological performance of peptide therapies but also allows for species-tailored solutions. By accounting for the unique physiological demands of equine athletes and the environmental and management constraints of camel populations, nanomized peptide platforms expand the therapeutic reach of precision veterinary medicine.

Neural and Precursor Cell Applications

In horses, NPCs derived from iPSCs have shown the ability to differentiate into both neurons and glial lineages, supporting partial functional recovery in experimental models of spinal cord injury [29]. These cells not only replace damaged neural populations but also secrete trophic factors that modulate inflammation and support axonal regeneration. When combined with xenografted mitochondria, NPC-based therapies may achieve even greater efficacy: mitochondrial augmentation stabilizes bioenergetics within transplanted cells, enhances resistance to oxidative stress, and promotes synaptic integration into host neural circuits. This combinatorial approach could address one of the major barriers in equine neuroregenerative medicine, poor survival and integration of transplanted neural cells under hostile microenvironmental conditions.

In camelids, translational applications of NPCs remain largely theoretical but hold significant potential. Neurological conditions such as trypanosomiasis-associated neuropathies and post-encephalitic sequelae represent important clinical burdens in regions where camels are essential for transport and production. The use of nano-engineered NPCs (nPSCs) combined with mitochondrial supplementation may improve graft survival and functional integration, thereby providing a novel therapeutic avenue for these otherwise difficult-to-treat disorders [30]. Drawing from equine and rodent preclinical models, camel-specific research could adapt these strategies to the unique metabolic and environmental physiology of camelids, creating an entirely new platform for veterinary neuroregeneration.

Integrative Therapeutic Strategies

The convergence of stem cell biology with peptide therapeutics offers significant synergistic potential for regenerative applications in equine and camelid medicine. In horses, MSCs transplanted into injured tendons or ligaments have been shown to promote fiber realignment, reduce scar tissue formation, and enhance mechanical strength. When co-administered with mitochondrial-targeted peptides such as SS-31, transplanted MSCs benefit from stabilized cellular bioenergetics, reduced oxidative stress, and improved viability and engraftment, thereby amplifying their regenerative efficacy. This dual strategy may accelerate tendon repair and optimize biomechanical recovery in high-performance horses, where reinjury risk is high. In camels, where chronic inflammatory states and environmental stressors (e.g., dehydration, heat load, and heavy work demands) impair musculoskeletal health, MSC-based therapies combined with nanomized peptide formulations may further enhance resilience. Encapsulation of bioactive peptides within nanocarriers not only improves their stability and delivery but also provides localized immunomodulation, potentially improving MSC survival, promoting tissue regeneration, and supporting systemic immune balance [31]. Looking forward, the implementation of personalized veterinary strategies that incorporate biomarker monitoring alongside genomic and transcriptomic profiling may refine therapeutic selection. Such approaches would allow clinicians to tailor interventions based on species-specific physiology, disease phenotype, and individual animal needs, thereby maximizing clinical outcomes in both equine athletes and working camels [32].

Challenges and Regulatory Considerations

Application of regenerative therapies in horses and camels faces several challenges, the greatest of which is ensuring animal welfare in harvesting stem cells. Protocol standardization limited by variability in MSC isolation, expansion, and delivery impedes reproducibility. While the FDA CVM and EMA regulate cell-based veterinary products, camelid-specific frameworks remain limited in the Middle East and Africa [33]. Further, differences in physiology, workload, and husbandry practices necessitate species-specific therapeutic strategies.

Future Perspectives

The rapid evolution of mitochondrial and nanotechnology-based therapeutics suggests that equine and camelid medicine may soon move beyond symptomatic management toward true organ- and tissue-level regeneration. A particularly promising direction is the application of xenografted mitochondria, where viable mitochondria from donor sources are transplanted into ischemic or degenerative tissues. Early studies in other species indicate that mitochondrial transfer can restore oxidative phosphorylation, reduce apoptosis, and enhance tissue repair, positioning this strategy as a potential adjunct for musculoskeletal and neurologic disorders in horses and camels. When combined with mitochondrial-derived peptides, xenografted organelles may benefit from improved stability and function, amplifying their therapeutic impact.

Equally transformative is the development of nPSCs tailored for organ-specific repair. By embedding pluripotent cells within nanocarrier scaffolds or functionalizing them with peptide conjugates, it becomes possible to enhance survival, control differentiation, and achieve precise homing to injured tissues. In equine medicine, this may facilitate targeted regeneration of tendons, ligaments, and articular cartilage, while in camels, it could address metabolic organ injury and reproductive dysfunction.

Future integration of these platforms into personalized veterinary medicine could be guided by genomic profiling, metabolic biomarkers, and real-time functional imaging, allowing therapies to be optimized for the species, organ system, and individual animals. Advances in AI-driven modeling may further refine treatment planning by predicting optimal combinations of stem cells, xenografted organelles, and peptide formulations for specific clinical scenarios.

Ultimately, the convergence of mitochondrial transplantation, organelle-targeted peptides, and nano-engineered stem cell systems may define the next generation of regenerative veterinary therapeutics. As species of high biomedical, economic, and cultural significance, regenerative therapy innovations in horses and camels hold the potential to not only extend healthspan and performance but also to provide translational insights applicable to human regenerative medicine.

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