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INTRODUCTION

The Second International Symposium on Regenerative Medicine is an academic and scientific forum designed to promote the exchange of knowledge on cellular therapies, regenerative medicine, and advanced biotechnology. It brings together national and international experts with the aim of strengthening translational research, driving clinical innovation, and fostering collaboration among academia, industry, and the healthcare sector. This event contributes to the development of safe and ethical practices, aligned with international standards, to improve patients' quality of life.

CONTENTS

Current status of Regenerative Medicine

Wendy V. Jaraba-Álvarez[1]

Abstract

Introduction: Regenerative medicine is consolidating as one of the most dynamic areas of contemporary biomedicine, focused on restoring the structure and function of tissues or organs by stimulating or replacing natural repair processes. This field integrates advances in cell biology, tissue engineering, biomaterials, biotechnology, and gene therapies, with the aim of developing effective treatments for chronic, degenerative diseases and injuries with limited recovery capacity. **Objective:** To describe the principles, current therapeutic strategies, and clinical applications of regenerative medicine, as well as the main challenges associated with its implementation. **Methods:** A narrative review of recent scientific literature was conducted, integrating preclinical and clinical evidence related to cell-based therapies, stem cell–derived products, tissue engineering, and emerging technologies applied to regenerative medicine. **Results:** Current therapeutic strategies include the use of induced pluripotent stem cells (iPSCs), mesenchymal stem cells (MSCs) derived from different sources, cell-derived products such as exosomes and growth factors, as well as 3D bioprinting techniques and biomimetic scaffolds. These approaches aim to promote tissue regeneration and modulate inflammatory responses, thereby supporting functional recovery at both cellular and systemic levels. In the clinical setting, regenerative medicine has shown promising results in orthopedics, cardiology, neurology, dermatology, and aesthetic medicine. However, its implementation faces significant challenges related to protocol standardization, preclinical and clinical validation, regulation of biological products, and ethical considerations. **Conclusion:** The sustained advancement of scientific evidence, together with technological innovation and interdisciplinary collaboration, suggests a transition toward personalized regenerative therapies that redefine the paradigms of modern medicine, guiding clinical practice toward comprehensive restoration of biological function and improved quality of life.

Keywords

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Regenerative medicine, mesenchymal stem cells, advanced therapies.

ThermoStem®: Brown Adipose Tissue–Derived Stem Cell Platform for Advanced Metabolic Therapies

Francisco Silva[2]

Abstract

Introduction: Obesity and metabolic disorders represent a global challenge. Brown adipose tissue (BAT) regulates metabolism through thermogenesis; however, its direct clinical use is not feasible. ThermoStem® proposes a solution based on BAT-derived stem cells to generate bioengineered constructs that increase functional brown fat mass in humans. **Objective:** To develop and validate a cellular platform capable of modulating metabolism through transplantation of artificial brown adipose tissue, evaluating safety and efficacy in preclinical models. **Methods:** Human brown adipose–derived stem cells (BADSCs) were isolated, and differentiation protocols toward functional brown adipocytes were established (UCP1, FNDC5 expression). Successive generations were designed incorporating scaffolds, encapsulation strategies, and xeno-free media. Studies were conducted in obese animal models (SCID) to assess effects on body weight and glucose metabolism. **Results:** Differentiated BADSCs exhibited a brown adipocyte phenotype with high mitochondrial activity. Transplantation reduced weight gain (~5% over 5 weeks) and improved glucose tolerance ($p < 0.05$). Increased mitochondrial respiration and fatty acid uptake were also observed. **Conclusion:** ThermoStem® demonstrates potential as a cell-based therapy for obesity and metabolic diseases. Further development is projected toward biodistribution, toxicology studies, and clinical trials in humans.

Keywords

Obesity, brown adipose tissue, stem cells, ThermoStem®, metabolism, cell therapy.

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From Cell to Patient: Quality as a Fundamental Principle in Cell Therapy.

Laura Duque Medina[3]

Abstract

Introduction: Cell therapy products represent one of the most promising advances in modern regenerative medicine due to their ability to repair, replace, or regenerate damaged tissues. Unlike conventional drugs, they are living, complex biological systems whose quality, safety, and efficacy depend on multiple intrinsic and extrinsic factors. Because they cannot be sterilized or corrected once manufactured, ensuring quality from the earliest stages of production, rather than at the end, is essential. **Objective:** To emphasize the importance of conceiving quality as a transversal principle throughout the entire life cycle of cell therapy products from donor selection to patient administration, in accordance with international standards governing advanced therapy medicinal products (ATMPs). **Methods:** This work is based on professional experience and technical expertise in the implementation of quality management systems for advanced therapy products. It provides a descriptive and integrative overview of the critical quality aspects that must be ensured at each stage of the cell product life cycle, incorporating regulatory frameworks and best practices established under national and international guidelines. **Results:** The structured implementation of these principles at every stage of the process ensures the production of fully traceable, viable, safe, and effective cell therapy products. This integrated approach reinforces the quality, integrity, and consistency of the biological material while strengthening control over critical processes and the reliability of outcomes. Expected achievements include the preservation of product identity, purity, potency, and stability, as well as a reduction in the risks of contamination, handling errors, or loss of cell viability. **Conclusion:** Quality in cell therapy is not achieved at a single stage but is continuously built throughout the product's life cycle. The adoption of robust quality systems, environmental control, validated procedures, and competent personnel are fundamental to ensuring safe, effective, and reproducible therapies that strengthen the field of regenerative medicine and improve patient outcomes.

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Keywords

Cell therapy, stem cells, quality, safety, efficacy.

Quality, Potency, and Functionality Outcomes: Validating the Impact of WJ-MSCs and Their Derivatives.

Hector Ortega-Arellano[4]

Abstract

Introduction: Mesenchymal stem cells (MSCs) derived from Wharton's jelly have proven to be a highly promising cellular source for regenerative medicine applications due to their differentiation capacity, immunomodulatory properties, and secretion of bioactive molecules. Acellular products derived from MSCs, such as secretome and exosomes, offer significant advantages over conventional cell-based therapies, including greater stability, lower immunogenicity, and ease of storage and transportation. **Objective:** This study aimed to characterize the quality, potency, and functional attributes of Wharton's jelly–derived MSCs, as well as their exosomes and secretome, with a view toward their application in regenerative therapies. **Methods:** MSCs were cultured under controlled conditions and characterized morphologically and by flow cytometry, confirming positive expression of CD73, CD90, and CD105, and absence of CD45, CD34, and HLA-DR. Their differentiation capacity toward mesodermal lineages was evaluated. Exosomes were isolated, characterized by size and surface markers, and analyzed proteomically. Functional assays were performed in human fibroblasts to assess cell proliferation, COL1A2 expression, and senescence. **Results:** MSCs met international quality criteria and demonstrated trilineage differentiation capacity. Exosomes exhibited proteomic profiles enriched in biological pathways associated with extracellular matrix organization, immune regulation, and vesicular trafficking. In treated fibroblasts, increased cell proliferation, upregulation of COL1A2, and a reduction in senescence markers were observed. **Conclusion:** The results confirm the high therapeutic potential of Wharton's jelly–derived MSCs and their acellular derivatives. Their functional profile and stability position them as robust candidates for the development of advanced therapies in regenerative medicine.

Keywords

Mesenchymal stem cells (MSCs), wharton's jelly, exosomes, secretome, regenerative medicine.

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Safety of Intravenous Mesenchymal Stem Cell Therapy: Integration of Evidence from Randomized Trials and Real-World Clinical Data.

Jhyld Carolaind Camacho Barbosa[5], Luz Adriana Palacio[6]

Abstract

Introduction: Mesenchymal stem cell (MSC) therapy, administered intravenously (IV), has gained widespread use in regenerative medicine due to its systemic immunomodulatory potential. While numerous clinical trials support its safety, continued pharmacovigilance in real-world settings remains essential to detect rare or delayed adverse events (AEs). **Objective:** To comprehensively evaluate the safety profile of IV MSC therapy by integrating findings from evidence from randomized clinical trials (RCTs) meta-analyzed in a recent systematic literature review (SLR), with longitudinal safety data from patients treated under the BioXcellerator Clinical Care Program (CCP) through structured follow-up assessments. **Methods:** Safety data from 36 RCTs were analyzed in the SLR by Habiba et al. (2025), encompassing diverse pathologies and cell sources. Meta-analytic estimates of AEs frequency were compared with prospective surveillance outcomes collected at BioXcellerator, where patients receiving IV MSCs are followed at three time points: 24–72 h, 15 days, and 3, 6, 12 months post-infusion. AEs are recorded through standardized follow-up by CCP. **Results:** Across trials, IV MSC infusion did not significantly increase the risk of general, musculoskeletal, gastrointestinal, respiratory, renal, or immune AEs compared with controls. A small, non-significant trend toward nervous system events and a modest increase in infection-related events were noted, but without severe consequences. Real-world data at BioXcellerator corroborated these findings: the most frequent events were transient fever, mild fatigue, and local discomfort, which resolved within 72 hours. No serious infusion-related complications or delayed AEs were identified during one-year follow-up. **Conclusion:** Combined evidence from clinical trials and structured real-world data confirms that IV administration of MSCs has a favorable safety profile when performed under standardized conditions. The integration of post-treatment surveillance into clinical practice

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enhances early detection and continuous evaluation of safety signals, reinforcing confidence in the clinical use of MSC therapies.

Keywords:

Mesenchymal stem cells, intravenous infusions, safety.

From the Exposome to the Clinical Reparome: Stem Cells, Exosomes, and Precision Medicine for the Treatment of Multisystem Environmental Toxicity

Marie Claire Berrouet Mejía[7]

Abstract

Introduction: Cumulative exposure to environmental contaminants—metals, endocrine-disrupting compounds, particulate matter, and microcontaminants—triggers chronic inflammation, immune–endocrine disruption, and multisystem damage (lungs, liver, nervous system, skin, and cardiovascular system). The exposome framework connects these environmental burdens with clinical phenotypes. In parallel, exosomes and other extracellular vesicles capture biological signatures of injury and repair; and mesenchymal stem cells and their vesicles have shown immunomodulatory and pro-regenerative potential. **Objective:** To present a clinical-technology framework, "Exposome → Reparome," that combines: (1) risk stratification using exosome-derived biomarkers and omics profiles; (2) personalized intervention with mesenchymal stem cells and extracellular vesicles aimed at tissue repair and inflammation modulation; and (3) bioregulatory medicine to restore physiological networks altered by environmental toxicity. **Methods:** Critical review (2015–2025) of methodological guidelines for extracellular vesicles, preclinical and clinical studies on the safety and effectiveness of mesenchymal stem cells and vesicles; and translational synthesis of mechanisms (inflammation resolution, antifibrosis, pro-angiogenesis, neuroprotection), biomarkers (circulating exosomes), and regulatory and quality criteria. **Results:** Extracellular vesicles derived from mesenchymal stem cells attenuate pro-inflammatory pathways, reprogram immune profiles toward repair, and promote regeneration in pulmonary, hepatic, neurological, muscular, and cutaneous tissues. Circulating exosomes enable non-invasive monitoring of exposure and progression of organ damage, supporting precision medicine. Clinical evidence reports a favorable safety profile for intravenous administration of mesenchymal stem cells across multiple indications. **Conclusion:** Integrating exosomal biomarkers, exposome profiles, and therapies with mesenchymal stem cells and vesicles within a precision-medicine and

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bioregulatory framework allows personalization and acceleration of tissue recovery in environmental toxicity. Priorities include robust standardization of vesicle characterization, long-term safety surveillance, and multicenter clinical trials with clinically meaningful endpoints.

Keywords

Exposome, exosomes, mesenchymal stem cells, environmental toxicology, precision medicine.

Mesenchymal Stem Cell Therapy in Multiple Sclerosis: Current Evidence and Clinical Perspectives

Jorge Andrés Jiménez[8]

Abstract

Introduction: Multiple sclerosis (MS) affects approximately 2.8 million people worldwide and remains a disease with a high burden of disability. Although disease-modifying therapies can reduce relapse rates by up to 68%, their impact is limited in progressive forms of MS, and a significant proportion of patients experience serious adverse events. This has driven growing interest in regenerative strategies such as mesenchymal stem cells (MSCs), whose immunomodulatory and neuroprotective potential may address pathological mechanisms not covered by current treatments. **Objective:** To review the preclinical and clinical evidence supporting the use of MSCs in MS, describe their mechanisms of action, and analyze the results of phase I and II clinical trials, as well as future perspectives in advanced therapies. **Methods:** This presentation analyzes data from preclinical studies in experimental autoimmune encephalomyelitis (EAE) models, phase I/II clinical trials (including MESCAMS, ACTiMUS, and others), immunological and neurotrophic biomarkers, and neuroimaging assessments. Routes of administration (intravenous and intrathecal) and their pharmacokinetic profiles are also reviewed. **Results:** Preclinical studies demonstrate a 71% reduction in inflammatory infiltrates and 89% preservation of axons. In remyelination models, MSCs increase repair by 2.3-fold. Phase I trials show an excellent safety profile with no serious adverse events. Phase II trials report improvements in EDSS scores, reduction in T2 lesion volume, and decreased T1 gadolinium-enhancing lesions. Biomarker analyses support dual mechanisms of action, including a significant increase in regulatory T cells (Tregs), reduction of Th17 cells, and increased BDNF levels correlated with clinical improvement. **Conclusion:** MSC therapy demonstrates a strong safety profile and consistent signals of efficacy in MS, particularly in progressive forms of the disease. Its immunomodulatory and neuroprotective mechanisms represent a complementary therapeutic approach to current pharmacological treatments, with multiple trials advancing

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toward phase III. Future progress will depend on optimizing dosing, routes of administration, and integration of biomarkers to enable personalized therapy.

Keywords

Multiple sclerosis, MSCs, immunomodulation, neuroprotection, MESCAMS, cell therapy.

Regenerative Medicine in Otolaryngology: The Role of Stem Cells

Verónica Rodríguez Rivera[9]

Abstract

Introduction: Stem cells promise to be an innovative therapeutic alternative in otorhinolaryngology, given their capacity for self-renewal and differentiation. **Objective:** To review the current and potential applications of stem cells in otorhinolaryngology. **Methods:** A systematic review of scientific literature in biomedical databases was conducted to evaluate the application of stem cells in different areas of our specialty. **Results:** Preclinical studies and clinical trials have shown benefits in sensorineural hearing loss, tympanic perforation, vertigo, vocal cord disorders, impaired saliva production, neuropathic pain management, and mucosal regeneration, among others. **Conclusion:** Stem cells represent a promising option; however, standardized protocols and safety studies are required for their clinical implementation.

Keywords

Otolaryngology, stem cells, hearing loss, vertigo.

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Regenerative Therapies and the Musculoskeletal System: Evidence and Clinical Experience

Mario Mercado[10]

Abstract

Introduction: Degenerative disorders of the musculoskeletal system, such as tendinopathies, osteoarthritis, and ligament injuries, are highly prevalent and significantly impair quality of life. These tissues are characterized by low vascularization and cellularity, which hinders repair processes and drug delivery. Regenerative therapies have emerged as an alternative to improve function and reduce pain. **Objective:** To evaluate the evidence and clinical experience regarding the use of regenerative therapies for musculoskeletal conditions, including osteoarthritis and tendon injuries. **Methods:** A literature review and analysis of observational data from BioXcellerator were conducted on patients treated with Wharton's jelly–derived mesenchymal stem cells (WJ-MSCs), platelet-rich plasma (PRP), and other orthobiologics. Standardized protocols and follow-up assessments using WOMAC and DASH scales were included. **Results:** In knee osteoarthritis, 51% of treated knees receiving WJ-MSCs showed clinical improvement at 12 months, as assessed by WOMAC. In shoulder and elbow injuries, 58% of patients demonstrated functional improvement according to DASH scores. Therapies such as PRP and viscosupplementation also showed benefits in pain reduction and improved mobility. **Conclusion:** Regenerative therapies are promising for the management of musculoskeletal conditions; however, controlled studies and protocol standardization are required to ensure safety and efficacy.

Keywords

Regenerative therapies, osteoarthritis, tendinopathies, mesenchymal stem cells, exosomes.

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Imaging Changes Following Cell Therapy Applications: Focus on MRI

Miguel Vega Arango[11], Freddy Barrios Arroyave[12]

Abstract

Introduction: Imaging plays a central role in regenerative disc therapy—not only for post-treatment evaluation but also for pre-treatment assessment. Identifying target levels, characterizing endplate and marrow integrity, and excluding confounding pathology all depend on reproducible imaging. However, protocol heterogeneity across scanners and institutions complicates interpretation and limits comparability. **Objective:** To explore the value of structured MRI analysis in regenerative medicine imaging, focusing on the spine. Rather than relying on broad grading systems, which often obscure subtle interval changes, we center on reproducible metrics such as bone marrow edema (BME) signal and protrusion dimensions—two of the most responsive biomarkers observed in our cohort. These changes were evident even in the presence of variable acquisition protocols, underscoring the need for standardization. **Methods:** A conceptual framework was developed based on retrospective review of a multi-level MRI dataset of pre- and post-treatment imaging using standardized metrics. Variability due to scanner type and acquisition settings was acknowledged and factored into the interpretation. **Results:** Post-treatment data revealed measurable increases in disc height and signal at multiple levels. Interval changes in BME signal and protrusion morphology offer greater diagnostic value but protocol heterogeneity significantly affects image interpretation and reproducibility. Broad grading systems obscure clinically relevant subtleties, limiting their utility in longitudinal assessment. **Conclusion:** Structured MRI analysis provides a reproducible framework for quantifying regenerative outcomes. Dedicated pretreatment imaging protocols are required for better patient selection and adequate interval change monitoring. This approach enhances clinical decision-making and may set basis for future protocol standardization for regenerative medicine imaging.

Keywords

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Regenerative disc therapy, MRI, bone marrow edema (BME), imaging protocol.

Regenerative Medicine in Modern Dermatology: Clinical Applications of MSCs, Exosomes, and Secretome

Leidy Gallego Vidales[13]

Abstract

Introduction: Skin aging is a multifactorial biological process influenced by genetic, environmental, and lifestyle factors. Dysfunction of keratinocytes, fibroblasts, and the extracellular matrix, together with increased reactive oxygen species and metalloproteinases, contributes to the loss of skin elasticity, hydration, and barrier function. Regenerative medicine offers innovative alternatives through therapies based on mesenchymal stem cells (MSCs), exosomes, and secretome, aimed at restoring cellular homeostasis and delaying cutaneous senescence. **Objective:** To describe the biological foundations and clinical evidence supporting the use of MSCs, exosomes, and secretome in dermatology, highlighting their role in skin rejuvenation, tissue repair, and the treatment of complex mucocutaneous diseases. **Methods:** A review of preclinical and clinical evidence on MSCs derived from bone marrow, adipose tissue, and umbilical cord was conducted, along with studies on exosomes and secretome. Data from phase I/II clinical trials and studies on alopecia, diabetic foot ulcers, psoriasis, pemphigus foliaceus, and epidermolysis bullosa were included, evaluating safety, efficacy, and underlying mechanisms. **Results:** MSCs demonstrated immunomodulatory, antifibrotic, and antioxidant effects, with improvements in skin elasticity (+27%), wrinkle reduction (>10%), and increased hydration (>20%). Exosomes showed benefits in keratinocyte and fibroblast proliferation, reduction of reactive oxygen species, and regulation of inflammatory cytokines. In complex diseases, umbilical cord–derived MSCs (UC-MSCs) showed safety and partial efficacy in psoriasis, accelerated wound healing in diabetic foot ulcers, and significant reduction of pain and pruritus in epidermolysis bullosa. Clinical trials reported low immunogenicity and absence of serious adverse events. **Conclusion:** Regenerative medicine represents a safe and promising therapeutic alternative in dermatology. MSCs, exosomes, and secretome provide targeted cellular mechanisms that enable skin rejuvenation, immune modulation, and deep tissue repair. Their

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clinical potential continues to expand, supported by growing evidence and applications in conditions with limited treatment options.

Keywords

Regenerative dermatology, mesenchymal stem cells, exosomes, secretome, skin rejuvenation.

Regenerative Medicine and Fertility: Emerging Applications in the Ovary and Endometrium

Mariana Velásquez Corrales[14]

Abstract

Introduction: Infertility affects more than 186 million people worldwide, and its prevalence increases with advancing reproductive age. Decline in ovarian reserve, oocyte quality, and alterations in endometrial receptivity represent central factors contributing to reduced fertility. Regenerative medicine has emerged as a promising field aimed at modulating ovarian and endometrial function through interventions based on platelet-rich plasma (PRP), mesenchymal stem cells (MSCs), and advanced biological therapies. **Objective:** To review the available scientific evidence on the potential of regenerative medicine to improve ovarian reserve, oocyte quality, and endometrial receptivity, and to evaluate its clinical impact in patients with infertility. **Methods:** Evidence was integrated from preclinical animal studies, case reports, cohort studies, phase I/II clinical trials, and systematic reviews published between 2015 and 2025. Interventions evaluated included intraovarian PRP, umbilical cord–derived MSCs, cell transplantation approaches, and regenerative therapies for thin endometrium, as well as their effects on markers such as AMH, FSH, AFC, ovarian volume, and endometrial thickness. **Results:** PRP has shown increases in antral follicle count and potential follicular activation, although outcomes are strongly dependent on maternal age. Ovarian MSCs demonstrated partial restoration of reproductive function in animal models, and human studies suggest increases in AMH, reductions in FSH, and improved follicular recovery. In thin endometrium, umbilical cord–derived MSCs resulted in significant increases in endometrial thickness (from 4.08 ± 0.26 mm to 5.87 ± 0.77 mm) and successful pregnancies following frozen embryo transfer (FET). Recent studies using UC-MSCs in premature ovarian insufficiency report increases in AFC and a higher number of retrieved oocytes. **Conclusion:** Regenerative medicine applied to fertility represents an experimental strategy with promising results in ovarian reserve enhancement and endometrial receptivity. Current evidence suggests potential benefits for patients with poor ovarian response

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or refractory endometrium; however, high-quality randomized controlled trials are required to establish standardized protocols and determine true clinical efficacy.

Keywords

Infertility, regenerative medicine, mesenchymal stem cells, PRP, ovarian reserve, endometrium.

Mesenchymal Stem Cell Therapy in Spinal Cord Injury: Current Clinical Evidence

Julián Andrés España Peña[15]

Abstract

Introduction: Spinal cord injury (SCI) affects more than 20 million people worldwide and results in severe disability with significant functional, social, and economic impact. Despite advances in acute management and rehabilitation, the regenerative capacity of nervous tissue remains limited. Mesenchymal stem cells (MSCs) have emerged as a promising therapeutic alternative due to their immunomodulatory, anti-inflammatory, and neuroregenerative properties. **Objective:** To describe the available clinical evidence on the use of MSCs in patients with spinal cord injury, highlighting their main mechanisms of action, functional benefits, and safety in real-world clinical settings. **Methods:** A review of phase I/II clinical studies, recent meta-analyses, and institutional experiences using MSCs derived from bone marrow and Wharton's jelly was conducted. Outcomes related to the ASIA scale, motor function, sensory recovery, activities of daily living (ADL), and quality of life were considered, as well as reported safety profiles. **Results:** Clinical data demonstrate significant improvements in motor and sensory function in patients with SCI, particularly in ASIA grades B–D. A meta-analysis of 18 studies reported sustained benefits in ASIA motor scores, ASIA sensory scores, and ADL between 3 and 18 months post-treatment. Umbilical cord–derived MSCs (UC-MSCs) showed greater efficacy compared with bone marrow–derived MSCs. Institutional evidence from cohorts treated with Wharton's jelly–derived MSCs (WJ-MSCs) demonstrated functional improvement, pain reduction, and favorable imaging progression without serious adverse events. **Conclusion:** MSC therapy represents a promising strategy for patients with spinal cord injury, with accumulating evidence of functional improvement and a favorable safety profile. Although the results are encouraging, larger controlled trials are required to optimize treatment protocols, determine the ideal route of administration, and standardize patient selection criteria.

Keywords

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Spinal cord injury, MSCs, neuro-regeneration, ASIA, cell therapy.

Advanced Cell Therapy in Rheumatoid Arthritis: Clinical Experience at BioXcellerator

Leonardo Ramírez[16]

Abstract

Introduction: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease characterized by persistent synovitis, progressive joint destruction, and functional impairment. Many patients are refractory to conventional and biologic DMARDs, continuing to experience pain, stiffness, and high inflammatory activity. Wharton's jelly–derived mesenchymal stem cells (WJ-MSCs) have emerged as an immunomodulatory alternative with clinical potential. **Objective:** To describe BioXcellerator's clinical experience in the management of patients with refractory RA treated with WJ-MSCs and exosomes, assessing their impact on pain, function, quality of life, and inflammatory markers. **Methods:** An observational cohort review of 20 patients with refractory RA treated with a combined intravenous and intra-articular strategy using WJ-MSCs and exosomes was conducted. Clinical and laboratory assessments were performed at 3, 6, and 12 months using VAS, HAQ-DI, SF-12, CRP, and ESR. Data correspond to a case series approved by the ethics committee (CEI-0048042025) with informed consent obtained from all participants. **Results:** Patients showed a reduction in pain scores from approximately 5 to 3 points at 3 months, which was maintained through 12 months. HAQ-DI decreased from 0.77 to 0.40 at 3 months and reached values close to 0.15 at 12 months, reflecting marked functional improvement. The physical component of the SF-12 increased from 50.6 to 92.9 at 3 months. Reductions in CRP and ESR were observed, along with radiological improvement in affected joints. No serious adverse events were reported, with a safety profile consistent with international literature. **Conclusion:** Cell therapy with WJ-MSCs and exosomes represents a safe and promising alternative for patients with refractory RA. The combined IV and intra-articular strategy reduced pain, improved physical function, and enhanced quality of life. These results support the potential of this therapy as a complement to DMARDs and biologic agents, highlighting the need for phase III-controlled studies.

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Keywords

Rheumatoid arthritis, MSCs, exosomes, advanced cell therapy, immunomodulation.

From the Laboratory to the Patient: Ensuring Quality in Regenerative Medicine.

Claudia Valeria Cruz Saucedo[17]

Abstract

Introduction: Regenerative medicine represents a transformative frontier in healthcare, posing complex challenges in quality management, traceability, and regulatory compliance. When dealing with living, personalized, and highly sensitive products, comprehensive quality systems are required to support every stage of development, from basic research to clinical application. **Objective:** To provide a comprehensive perspective that bridges scientific innovation with clinical responsibility, promoting regenerative therapies that transform lives. **Method:** A comprehensive approach is proposed to ensure quality across all phases of the ATMP lifecycle: from basic research, through manufacturing in GMP environments, storage and transportation, to clinical application and post-treatment monitoring, integrating international regulatory frameworks. **Results:** This approach aims not only to meet regulatory standards but also to strengthen infrastructural resilience, operational excellence, and ethical commitment in contemporary regenerative medicine. **Conclusion:** Regenerative medicine represents not only a scientific promise but also a clinical responsibility. Every cultured cell, every biomaterial design, and every applied protocol must adhere to one fundamental principle: quality.

Keywords

Quality, GMP, stem cells, bioethics, regulation.

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Mesenchymal Exosomes: The Functional Science Behind Regenerative Medicine

Dianny Elizabeth Jiménez Jojoa[18]

Abstract

Introduction: Mesenchymal stem cell–derived exosomes represent an emerging frontier in regenerative medicine, acting as bioactive carriers capable of modulating complex cellular microenvironments. Their composition, enriched with regulatory proteins, lipids, and microRNAs, positions them as mediators of key processes such as immunomodulation, angiogenesis, and tissue repair, thereby overcoming several limitations of conventional cell-based therapies. **Objective:** To describe the molecular mechanisms and translational evidence supporting the therapeutic potential of mesenchymal exosomes, and to highlight their clinical applications and critical quality considerations for responsible implementation in regenerative medicine. **Methods:** A scientific overview was conducted integrating molecular insights, translational findings, and clinical experiences. Particular attention was given to signaling pathways sustaining exosome bioactivity, including PI3K/Akt, Wnt/β-catenin, and TGF-β/SMAD, as well as to quality criteria such as origin, purification, and characterization that define efficacy and reproducibility. **Results:** Evidence from preclinical and early clinical studies demonstrates advances in joint function restoration in degenerative diseases, acceleration of skin regeneration and wound healing, neuroprotective effects and enhanced plasticity in neurological conditions, and myocardial repair in cardiovascular damage. These outcomes illustrate the progressive transition of mesenchymal exosomes from basic research into translational protocols with direct medical relevance. **Conclusion:** Mesenchymal stem cell–derived exosomes are consolidating as an independent bioactive platform with the potential to transform regenerative medicine. Their molecular mechanisms, therapeutic applications, and evolving regulatory frameworks indicate a future in which exosomes will not only complement but also redefine evidence-based strategies for the prevention, treatment, and functional restoration of multiple pathologies.

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Keywords

Mesenchymal exosomes, Regenerative medicine, Immunomodulation, Tissue repair, Clinical translation.

Tympanic membrane regeneration by MSC-secretomes application.

Gabriel Román López Vázquez[19], Julio César Tobón Velasco[20], Ma. Gema Ruiz García[21], Joel De La Cruz Enríquez[22], José Carlos Jiménez Ortega[23]

Abstract

Introduction: Eardrum perforations can cause pain, hearing loss, tinnitus, dizziness, and balance problems. The size and location of the perforation can influence the severity of symptoms, and surgical repair can be risky, expensive, and potentially unsuccessful. MSC-derived secretome has regenerative and anti-inflammatory properties, and its use induces tissue regeneration, improves healing, and reduces the risk of infection. **Objective:** To evaluate the effect of MSC-secretome application on the regeneration of perforated tympanic membranes. **Methods:** A descriptive-explanatory, semi-quantitative, experimental and longitudinal study, where secretome was applied in 7 patients with acute perforations and 3 with chronic perforations, observed by endoscopic microscopy and evaluated by impedance and audiometry, with an applicative approach, which aims to make known the procedure and its use as a safe and viable therapy in this pathological condition. **Results:** Ten patients with tympanic perforations were studied (7 acute, 70%; and 3 chronic, 30%), with a perforation area less than 25% (70%) and greater than 25% (30%). All patients underwent audiometry and impedance testing, indicating hearing defects such as conductive superficial hearing loss. The origin of tympanic perforation was mainly otomycosis (60%), followed by traumatic event (20%), and finally COM and AOM (10% each). Besides, the application of MSC-derived secretomes in acute perforations induced closure in an average time of 14±2 days and in chronic perforations in 85±3 days, and are functional with normal audiometry and logoaudiometry, and with type A curve in tympanometry. **Conclusion:** The application of the MSC-secretome induced eardrum regeneration without generating adverse effects, making it safe, effective, and very promising as an innovative therapy

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Keywords

Tympanic membrane perforation, Regeneration, Wound Healing, MSC-secretome.

Advanced autologous and allogenic therapies in orthobiology: Innovations for osteoarthritis and chondral lesions.

Rodrigo Arancibia[24], Solange Rivas[25]

Abstract

Introduction: Orthobiologic therapies are redefining musculoskeletal medicine by activating endogenous repair mechanisms in degenerative and inflammatory disorders. Osteoarthritis and focal chondral lesions represent major unmet medical needs, affecting more than 600 million people worldwide. In this context, the development of translational platforms that integrate advanced biomanufacturing with clinical practice is essential to ensure the safety, reproducibility, and efficacy of biological therapies. **Objective:** To describe and evaluate a translational orthobiologic therapy platform developed by Cellus, as well as its main clinical and preclinical applications in the treatment of osteoarthritis and articular cartilage repair. **Methods:** Cellus developed a platform that integrates clean rooms certified under ISO 9001:2015 standards within clinical environments, ensuring continuous traceability, manufacturing, and administration of biological products. Several therapeutic strategies were evaluated, including autologous serum rich in growth factors combined with hyaluronic acid (SRF+™); intraoperative autologous cartilage micrografts (CondroMatrix™); adipose tissue–derived stromal vascular fraction (SVF+™); and 3D mesenchymal stem cell spheroids (Cellusphères®), manufactured under xeno-free, hypoxic GMP conditions. Clinical efficacy was assessed using pain (VAS) and functional (WOMAC) scales, imaging studies, and preclinical evidence from osteoarthritis models. **Results:** In a cohort of 102 patients with Kellgren–Lawrence grade II–III knee osteoarthritis, SRF+™ treatment achieved a 68% reduction in pain (VAS) and a 62% improvement in function (WOMAC) at six months, outperforming corticosteroids, hyaluronic acid, and PRP-based therapies. CondroMatrix™ enabled single-stage chondral repair (1–4 cm^2), with appropriate tissue integration quantified by 3D magnetic resonance imaging. SVF+™ expanded same-day procedures by combining autologous cellular concentrates with growth factors and ultrasound-guided intra-articular injection. Meanwhile, Cellusphères® demonstrated

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potent anti-inflammatory, immunomodulatory, and trophic activity, with superior preclinical safety and efficacy compared with traditional 2D cultures. **Conclusion:** The described orthobiologic therapies promote tissue repair, reduce the need for invasive procedures, and significantly improve patients' quality of life. This unified translational approach bridges clinical orthobiology and advanced biomanufacturing, positioning Latin America as an emerging hub for safe, effective, and scalable regenerative medicine. Nevertheless, further research, interdisciplinary collaboration, clear regulatory frameworks, and enhanced clinician education are required to safely and effectively integrate these therapies into standard orthopedic practice.

Keywords

Osteoarthritis, chondral lesion, autologous serum, fibrin matrix, 3D allogeneic spheroids.

Intradiscal Injection of Hypoxic MSCs (BRTX-100) in Lumbar Disc Disease: Phase 2 Safety and Efficacy

Francisco Silva[26]

Abstract

Introduction: Chronic low back pain associated with degenerative disc disease (DDD) is characterized by high recurrence rates and therapeutic options ranging from conservative management to invasive surgeries, with reoperation rates exceeding 30%. The intervertebral disc microenvironment is defined by hypoxia, loss of extracellular matrix, reduced cellularity, and increased inflammatory mediators (IL-1, IL-6, TNF-α), leading to impaired biomechanical function. The use of hypoxia-preconditioned bone marrow–derived mesenchymal stem cells (MSCs) (BRTX-100) is proposed to modulate inflammation and stimulate tissue regeneration in the avascular regions of the nucleus pulposus. **Objective:** To evaluate the safety and preliminary efficacy of a single intradiscal injection of BRTX-100 (40×10^6 cells/1.5 mL) in patients with DDD and chronic low back pain, and to explore imaging signals of disc microenvironment remodeling. **Methods:** Phase 2 randomized, double-blind, sham-controlled clinical trial with blinded assessments. Ninety-nine subjects were randomized (2:1) across 16 U.S. centers. Adverse events (AEs/SAEs), vital signs, physical examinations, and laboratory tests were recorded. Patient-reported outcomes included VAS (pain), ODI, RMDQ, FRI, and SF-12v2 at baseline and weeks 2, 12, 26, 52, and 104. T2-weighted MRI was performed at baseline and at weeks 52 and 104. Key inclusion criteria included low back pain ≥6 months, failure of ≥6 months of conservative management, Pfirrmann grades 2–7, Modic I/II or no Modic changes, disc height ≥50%, and a single disc identified as the pain generator. **Results:** In the initial safety cohort (n=15), no serious adverse events or dose-limiting toxicities were observed; treatment-related AEs included transient post-procedural low back pain and MRI changes in one subject. In preliminary blinded analyses, at week 26, 46% of patients reported >50% improvement in VAS (n=15); at week 52, 90% (n=10); and at week 104, 75% (n=4). For ODI, >50% improvement was observed in 40% at week 26 (n=15), 80% at week 52 (n=10), and 50% at week 104 (n=4). Overall response trends ranged from 60–70%, with MRI signals suggestive of disc

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microenvironment remodeling, including increased T2 signal intensity, reduced protrusion size, and decreased annular tear signal in treated segments. **Conclusion:** Intradiscal injection of hypoxic MSCs (BRTX-100) demonstrates a favorable safety profile and clinically meaningful signals of efficacy, including pain reduction and functional improvement, sustained up to 104 weeks in DDD patients. MRI findings suggest potential extracellular matrix remodeling within the disc. These results support continuation of the clinical development program (FDA Fast Track designation and planning of a Type B meeting to initiate phase 3) and evaluation in cervical indications.

Keywords

Low back pain, Degenerative disc disease, Hypoxic MSCs, BRTX-100, Intradiscal injection, Phase 2 trial.