AURAGENS

UNDERSTANDING STEM CELL THERAPY

Stem Cell Therapy for Complex Sports Injuries

Cartilage restoration, joint preservation, and the science of human umbilical cord–derived mesenchymal stem cells from Wharton's Jelly.

ACCREDITED

auragens.com · Panama | USA

Advancing Regenerative Medicine — treatments & empathy amplified by science and technology.

A NOTE BEFORE WE BEGIN

Welcome

Thank you for taking the time to explore what regenerative medicine may offer for your musculoskeletal health. At Auragens, we understand that living with joint pain, cartilage damage, a sports injury, or a degenerative condition of the hip, knee, spine, or ankle can fundamentally alter your daily life — your mobility, your independence, your ability to do the things you love.

Whether you are an athlete hoping to return to sport, an active adult striving to preserve joint function, or someone navigating the progressive challenges of osteoarthritis or disc degeneration, we recognize the physical and emotional weight you carry.

This guide explains how human umbilical cord–derived mesenchymal stem cells (hUC-MSCs) from Wharton's Jelly — and the bioactive molecules they secrete, including exosomes — are being investigated as a regenerative approach for a wide range of musculoskeletal disorders. We will explain what these cells are, where they come from, how they may work, what the research shows, and what thoughtful questions to consider.

We want to be transparent from the outset: stem cell therapy for musculoskeletal conditions is an active and growing area of scientific investigation. Early clinical studies have shown meaningful promise in safety and symptomatic improvement. At the same time, most evidence comes from early-phase trials, and outcomes vary between individuals. This guide presents the science honestly — with appropriate optimism where the evidence supports it, and appropriate humility where it does not.

> *"Our goal is not to sell you on a treatment. Our goal is to equip you with the knowledge to have an informed, productive conversation with your physician and the Auragens medical team."*
>
> — THE AURAGENS MEDICAL TEAM

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SECTION 01

Understanding the Conditions — and the Limits of Current Treatment

The musculoskeletal system — the network of bones, cartilage, ligaments, tendons, discs, and joints that gives your body its structure and movement — is remarkably resilient. Yet it is also vulnerable to injury, wear, and degeneration. The conditions in this guide span a broad and interconnected spectrum.

Complex sports injuries

Damage to ligaments (such as the anterior cruciate ligament, or ACL), menisci, tendons, and articular cartilage occurring during athletic activity or trauma. These injuries are often compounded by the limited regenerative capacity of cartilage and other avascular tissues — meaning the body struggles to fully repair itself.

Cartilage disorders & restoration

Focal cartilage defects — localized areas of damage within an otherwise healthy joint — as well as the broader loss of articular cartilage that characterizes osteoarthritis. Articular cartilage has no blood supply and very few resident stem cells, making self-repair extremely limited once damage occurs.

Joint preservation

The clinical goal of maintaining the function and structure of a joint — particularly in younger or more active patients — to delay or avoid joint replacement surgery. It encompasses biological, surgical, and regenerative strategies aimed at restoring tissue integrity and reducing inflammation before irreversible degeneration occurs.

↘ Five regions carry these vulnerabilities — **hip, knee, shoulder, spine & back, and ankle.** The next page looks at each.

WHERE THESE CONDITIONS STRIKE

The major regions, shared biology

Hip

Hip OA, labral tears, impingement, and avascular necrosis — a leading cause of disability worldwide.

Knee

The most common OA globally: cartilage breakdown, synovial inflammation, focal defects, and meniscal injury.

Shoulder

Rotator cuff tears, tendinopathy, and shoulder OA. The tendon-to-bone interface heals poorly, driving high re-tear rates after repair.

Spine & Back

Disc degeneration, facet arthropathy, and chronic discogenic low back pain — the leading cause of disability. The avascular disc resists repair.

Ankle

Osteochondral lesions of the talus, ankle OA, and ligamentous injury. High mechanical load makes cartilage damage hard to treat.

ONE SHARED BIOLOGY

Inflammation, matrix loss, and limited self-repair recur across every one of these tissues — which is why a single regenerative rationale spans them all.

Despite their differences, these conditions share a common biological trajectory. Understanding how they progress reveals why simply managing symptoms is rarely enough — and where regenerative approaches aim to intervene.

HOW THESE CONDITIONS PROGRESS

Five shared biological drivers

Cartilage degradation — breakdown of the extracellular matrix (ECM), cartilage's structural scaffold, driven by enzymes such as MMPs and ADAMTS proteins.

Chronic inflammation — sustained pro-inflammatory cytokines (IL-1β, TNF-α, IL-6) perpetuate damage, inhibit repair, and sensitize pain pathways.

Cellular senescence & loss — chondrocytes, nucleus pulposus cells, and other resident cells undergo stress-induced aging or death, reducing the tissue's ability to maintain itself.

Oxidative stress — accumulation of reactive oxygen species damages cells and ECM components, accelerating degeneration.

Synovial & immune dysregulation — the synovial membrane becomes inflamed, contributing to pain and further cartilage breakdown.

Current treatment options & their limits

TREATMENT	VALUE & LIMITATION
Medications — NSAIDs, analgesics, steroid injections	Symptomatic relief, but do not halt or reverse tissue damage; long-term GI, cardiovascular, and cartilage-related risks.
Physical therapy & rehabilitation	Essential for function and strength, but cannot restore lost cartilage or repair structural damage.
Hyaluronic acid & PRP injections	May provide temporary relief; evidence for structural benefit is limited and inconsistent.
Surgery — microfracture, osteotomy, debridement, reconstruction	Useful in specific scenarios, but often yields fibrocartilage rather than true hyaline cartilage; outcomes can deteriorate over time.
Joint replacement surgery	Highly effective for end-stage disease, but carries surgical risk, has a finite implant lifespan, and may not suit younger patients.

These limitations have motivated regenerative strategies — particularly cell-based therapies — that aim not merely to manage symptoms, but to support the biological environment needed for tissue protection and repair [12].

SECTION 02

What Are hUC-MSCs from Wharton's Jelly?

Understanding mesenchymal stem cells

Mesenchymal stem cells (MSCs) are multipotent stromal cells found in many tissues of the body. They can differentiate into several cell types — including bone cells, cartilage cells (chondrocytes), and fat cells — under appropriate conditions. More importantly for therapy, MSCs are highly active secretory cells: they release a rich array of bioactive molecules, growth factors, cytokines, and extracellular vesicles (including exosomes) that modulate the local cellular environment, regulate immune responses, and support tissue repair.

MSCs can be sourced from bone marrow, adipose (fat) tissue, dental pulp, and the umbilical cord. The source has meaningful implications for the cells' properties, availability, and therapeutic potential.

What is Wharton's Jelly?

Wharton's Jelly is the gelatinous connective tissue that surrounds the blood vessels of the umbilical cord. It is a rich, naturally occurring repository of mesenchymal stem cells, collected from donated umbilical cords following healthy, full-term births — a process that is entirely non-invasive for both mother and newborn, requiring no procedures beyond what would otherwise occur at delivery.

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WHY THIS SOURCE SHOWS PROMISE

Four reasons researchers favor Wharton's Jelly

Youth & potency

Among the most primitive MSCs available, retaining higher proliferative capacity and biological activity than MSCs from adult tissues like bone marrow or fat.

Low immunogenicity

Low expression of markers (e.g. MHC class II) that trigger rejection — candidates for allogeneic, "off-the-shelf" use without immune matching.

Rich secretory profile

Abundant trophic factors, anti-inflammatory cytokines, and exosomes that act through paracrine signaling — influencing neighboring cells without permanent engraftment.

Ethical sourcing

Collected from donated umbilical cords after birth — raising none of the ethical concerns associated with embryonic tissue.

From donation to treatment

Every step from cord donation to patient treatment follows rigorous quality and safety protocols.

1. **Donor screening** — Comprehensive health & infectious-disease testing
2. **Lab processing** — Isolated & expanded under GMP-aligned protocols
3. **Quality control** — Identity, purity, viability & sterility verified
4. **Cryopreservation** — Frozen under controlled conditions to retain potency
5. **Pre-treatment prep** — Thawed & prepared per validated protocols at point of care

> The result is a carefully characterized, quality-controlled cellular product — **not** an unregulated or uncharacterized preparation.

WHY AURAGENS

AABB Accreditation — the gold standard

Auragens Stem Cell Center is proud to be AABB accredited — a distinction that sets us apart from unaccredited clinics. AABB (the Association for the Advancement of Blood & Biotherapies) is the internationally recognized leader in quality and safety standards for cellular therapies. As an FDA deemed-status organization, AABB accreditation represents the most rigorous, comprehensive certification available for facilities that process and administer cellular products.

aabb™ ACCREDITED

ASSOCIATION FOR THE ADVANCEMENT OF BLOOD & BIOTHERAPIES

WHAT ACCREDITATION MEANS FOR YOU

- ✓ **Cell processing excellence** — pharmaceutical-grade quality specifications.
- ✓ **Laboratory practices** — regular inspection for sterility & environmental control.
- ✓ **Staff expertise** — specialized training & competency requirements.
- ✓ **Continuous quality improvement** — audits, proficiency testing & reviews.
- ✓ **Donor screening & safety** — thorough testing against stringent criteria.
- ✓ **Patient safety** — every step monitored, from cell arrival through follow-up.
- ✓ **Traceability & documentation** — complete tracking and accountability.

> *"An external, FDA-recognized expert organization has thoroughly inspected and validated our practices — giving you independent verification, proven quality systems, and genuine peace of mind."*

AABB accreditation is not easy to achieve or maintain — it requires significant investment in infrastructure, training, quality systems, and ongoing compliance. We've made this commitment because you deserve nothing less than the highest standard of care.

SECTION 03

How hUC-MSCs May Help Restore & Preserve Joints

The biology of hUC-MSC therapy is multifaceted. Rather than acting through a single mechanism, these cells and the molecules they secrete appear to work through several complementary pathways particularly relevant to joint and musculoskeletal disease.

3.1 Anti-inflammatory effects

Chronic, low-grade inflammation is a central driver of cartilage degradation, pain sensitization, and disease progression — from knee OA to disc degeneration to post-traumatic joint disease. In preclinical studies, hUC-MSCs and their exosomes suppress key pro-inflammatory mediators including IL-1β, TNF-α, and COX-2 — the same molecular targets addressed by many anti-inflammatory medications, but through biological rather than pharmacological means [4][18][19]. By dampening the inflammatory microenvironment, MSC-derived factors may help interrupt the cycle of inflammation-driven destruction.

3.2 Immunomodulation & macrophage polarization

Joints affected by OA or injury contain elevated pro-inflammatory (M1-type) macrophages that perpetuate synovial inflammation and cartilage damage. One of the better-characterized mechanisms of UC-MSC-derived extracellular vesicles is their ability to shift macrophages from a pro-inflammatory (M1) to an anti-inflammatory (M2-like) phenotype. A 2025 study by Figueroa-Valdés and colleagues showed clinical-grade vesicles polarized macrophages to an M2b-like phenotype via the STAT1 pathway, in vitro and in vivo [10].

12 mo no adverse effects in first-in-human intra-articular EV application [10]

3.3 ECM modulation & chondroprotection

Healthy cartilage depends on a well-maintained extracellular matrix — a scaffold rich in collagen type II and proteoglycans such as aggrecan. In OA and cartilage injury, catabolic enzymes (particularly ADAMTS5 and various MMPs) degrade this matrix faster than it can be rebuilt. MSC-derived exosomes shift the balance toward repair: increasing anabolic markers including Collagen II, SOX9, and aggrecan, while reducing catabolic enzyme activity [4][18]. A key 2017 study by Wang and colleagues showed MSC exosomes can alleviate osteoarthritis by balancing ECM synthesis and degradation — among the most consistently reported mechanisms in the literature [4].

3.4 Paracrine & exosome signaling

Growing evidence suggests the primary therapeutic mechanism of MSCs is not direct engraftment, but the rich array of paracrine signals they release — exosomes, microvesicles, soluble growth factors, and cytokines [14][17]. Exosomes are nanoscale vesicles carrying microRNAs, proteins, and lipids. Once internalized by target cells (chondrocytes, nucleus pulposus cells, synovial cells), their cargo can reprogram gene expression, reduce apoptosis, promote proliferation, and modulate inflammatory signaling [13][14].

30–150 nm the size range of MSC-derived exosomes

3.5 Trophic factor support

MSCs secrete tissue-supporting factors including vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), transforming growth factor-beta (TGF-β), and insulin-like growth factor-1 (IGF-1), which support cell survival, tissue maintenance, and repair signaling. In avascular tissues such as articular cartilage and intervertebral discs — where nutrient supply is already limited — this trophic support may help sustain the viability and function of resident cells under stress [13][17].

3.6 Oxidative stress reduction

Reactive oxygen species (ROS) — generated by mechanical stress, inflammation, and cellular aging — accumulate in degenerating joints and discs, accelerating senescence and ECM breakdown. In a 2026 study by Zhang and colleagues, hypoxic MSC-derived exosomes delivered via PLGA microspheres activated the PPAR-γ pathway in nucleus pulposus cells, reducing oxidative-stress senescence markers and increasing key ECM components (Collagen II, aggrecan) in disc-degeneration models [15].

59.8%

approximate reduction in oxidative-stress-induced **cellular senescence markers** in nucleus pulposus cells (preclinical disc model) [15]

3.7 Antifibrotic & tissue-supportive signaling

In chronic joint and disc disease, fibrotic remodeling — the replacement of healthy tissue with scar-like fibrous tissue — can further compromise function. MSC-derived factors have demonstrated antifibrotic properties across multiple tissue contexts, potentially helping to preserve the structural integrity of joints and discs by modulating the signaling pathways that drive fibrotic change [13][14].

ⓘ Several of these mechanisms are most consistently reported in **preclinical** models. They illustrate the biological depth of MSC and exosome signaling — while human confirmation continues across the studies summarized in the next section.

SECTION 04

Clinical Evidence & Research Findings

A NOTE ON THE EVIDENCE LANDSCAPE

The evidence is genuinely promising, but early-stage. Most published human studies are early-phase (I or I/II), with small numbers of patients and short follow-up. Larger randomized controlled trials with long-term follow-up are needed before definitive conclusions. What follows reflects the current science honestly — strengths and limitations alike.

Sports injuries & cartilage repair

[2] 2016
RCT · 2-yr

Koh et al. — Arthroscopy

Adipose-derived MSCs + microfracture vs microfracture alone. The MSC-augmented group showed improved clinical and structural outcomes, suggesting cell-based augmentation may enhance standard cartilage repair.

[1] 2020
Phase IIa

Qiao et al. — Regenerative Medicine

Human adipose-derived progenitor cells + microfracture + hyaluronic acid for cartilage repair, with clinical and structural outcomes consistent with a benefit from cellular augmentation.

[3] 2017
RCT · 24-mo

Wang et al. — Arthritis Research & Therapy

A single intra-articular injection of allogeneic mesenchymal precursor cells following ACL reconstruction. Favorable safety and tolerability with structural and clinical signals supporting further study.

[5] 2023
Phase I

Huang et al. — Signal Transduction & Targeted Therapy

Immunity-and-matrix-regulatory cells (IMRCs) for meniscal injury — safety, MRI-documented improvements, and functional gains, with strong immunomodulatory potential in preclinical assays.

Taken together, these results suggest MSC-based augmentation of cartilage repair may improve outcomes versus standard surgery alone — though larger, more definitive trials are needed.

THE MOST-STUDIED JOINT

Knee Osteoarthritis

Phase I, single-arm study — **Ao et al., 2023 (BMC Musculoskeletal Disorders)**. Repeated intra-articular UC-MSC injections in 14 patients with knee OA, over three months of follow-up:

PAIN · VAS	FUNCTION · WOMAC	CARTILAGE · MOCART	QUALITY OF LIFE
6.0 → 3.5	26 → 8.5	42 → 58	SF-12 ↑

Transient adverse reactions in 5 of 14 patients; no serious adverse events reported [6]. Lower VAS/WOMAC = better; higher MOCART = better cartilage.

Further knee OA studies

[7] 2023 **Yusoff et al.** — Chondrogen™ (Wharton's Jelly MSCs): significant reductions in analgesic use, improved IKDC and KOOS scores, no significant adverse events over 6 months.

[8] 2019 **Khalifeh Soltani et al.** — allogenic placental MSCs in a pilot study: safety and early efficacy signals in a small cohort.

[9] 2025 **Wang et al.** — hUC-MSC-derived exosomes: preclinical → randomized, double-blind, dose-escalation first-in-human study with safety and early clinical/MRI signals.

[10] 2025 **Figueroa-Valdés et al.** — clinical-grade small EVs: M2b macrophage polarization via STAT1, cartilage regeneration in animals, safe retention with no adverse effects at 12 months.

[11] 2024 **Lohrasbi et al.** — systematic appraisal: UC-MSC therapy appears effective and safe across available trials, noting heterogeneity and the early-phase nature of evidence.

IN-HOUSE CASE SERIES · N = 7 PATIENTS · 10 KNEE OBSERVATIONS · M1–M12

Allogeneic Umbilical-Cord MSC Therapy for Knee Osteoarthritis in Professional Athletes

Patient-reported KOOS outcomes from a single-center case series. Knee-level changes from baseline benchmarked against the published MCID of 0.08 on the $KOOS_5$ Total composite (0–1 scale).

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01 Cohort overview

Enrollment · retention · demographics

ENROLLED
19
Total treated patients

FOLLOW-UP
7
36.8% follow-up rate

KNEE OBS.
10
6 L · 4 R · 3 bilateral

MEAN AGE
28.6y
Range 23–32 · pro athletes

RESPONDER RATE
7/10
70% met MCID (Δ ≥ 0.08)

02 Per-knee KOOS outcomes

Anonymized · $KOOS_5$ Total (0–1)

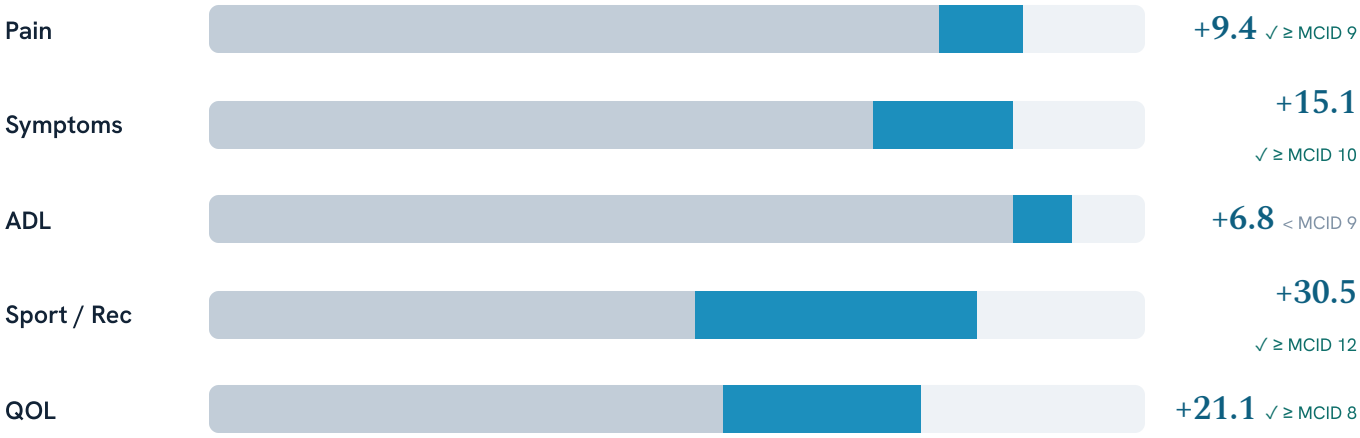
KNEE	SIDE	BASELINE	TIME	FOLLOW-UP	Δ	MCID
Knee 1	L	0.92	M3	0.98	+0.06	—
Knee 2	R	0.80	M3	0.94	+0.14	✓
Knee 3	L	0.76	M12	0.78	+0.02	—
Knee 4	R	0.46	M12	0.78	+0.32	✓
Knee 5	L	0.61	M1	0.80	+0.19	✓
Knee 6	R	0.69	M3	0.84	+0.15	✓
Knee 7	L	0.66	M9	0.90	+0.24	✓
Knee 8	L	0.60	M12	0.99	+0.38	✓
Knee 9	L	0.69	M12	0.73	+0.04	—
Knee 10	R	0.62	M12	0.73	+0.11	✓

L, left; R, right; M, months post-treatment; Δ, change from baseline on $KOOS_5$ Total. **7/10 (70%) met MCID**; **10/10 (100%) improved** on the composite score.

03 KOOS subscale outcomes

Mean change · 0–100 scale

Bar extends from baseline (gray) to follow-up mean (blue). All five subscales exceeded their respective MCIDs at the cohort level.



Largest gains: **Sport / Recreation +30.5** and **Quality of Life +21.1** — the domains most relevant to return-to-play in professional athletes.

04 Aggregate statistics

Stratified by side · KOOS$_5$ Total (0–1)

SUBGROUP	N	MEAN Δ	MEDIAN	SD	RANGE	MCID MET
Left knee	6	+0.155	+0.125	0.141	+0.02 to +0.38	3/6 (50%)
Right knee	4	+0.180	+0.145	0.095	+0.11 to +0.32	4/4 (100%)
Combined	**10**	**+0.165**	**+0.145**	**0.119**	**+0.02 to +0.38**	7/10 (70%)

05 Adverse events

No serious adverse events (SAEs)

PATIENT A	PATIENT B	PATIENT C	PATIENT D
Knees 1,2	Knees 3,4	Knee 5	Knee 6
Chills · transient	None reported	Chills · transient	None reported

PATIENT E	PATIENT F	PATIENT G
Knee 7	Knee 8	Knees 9,10
None reported	None reported	Chills · transient

Transient chills resolved within 30 min without intervention.

A single intra-articular injection of allogeneic hUC-MSCs was associated with clinically meaningful improvement in **7 of 10 knees (70%)**, with **all 10 knees improving** over baseline and a favorable short-term safety profile.

+0.165	10/10	0
2.06× MCID	IMPROVED	SERIOUS AEs

Single-center case series (n=7, 10 knees), mixed M1–M12 follow-up, no control arm and 63.2% loss to follow-up — hypothesis-generating, not a controlled efficacy claim. MCID 0.08 per Collins et al., *OAC* 2016 [30].

TENDON-TO-BONE HEALING

Shoulder & Rotator Cuff

Rotator cuff tears are a leading cause of shoulder pain and disability. Even after arthroscopic repair, re-tear rates remain high because the tendon-to-bone interface tends to heal as mechanically weaker scar tissue rather than its original structure. MSCs are being investigated both as a **surgical augment** and as a **non-operative injection** to improve that biology.

Representative outcome signals from controlled and first-in-human studies:

RE-TEAR RATE	PAIN / DISABILITY	TENDON DEFECT · MRI
28.5% → 14.3%	SPADI ↓ ~80%	↓ ~90%
control vs MSC [22]	high-dose group [23]	bursal-side volume [23]

[21] 2014
Case-control · 10-yr

Hernigou et al. — International Orthopaedics

Bone-marrow MSC augmentation during arthroscopic repair improved the healing rate and reduced further tears versus matched controls — with a dose-response in which higher cell counts at the tendon–bone interface tracked with markedly lower re-tear rates out to 10 years.

[22] 2017
Comparative · MRI

Kim et al. — American Journal of Sports Medicine

Adipose-derived MSCs in fibrin glue applied at the repair site. Re-tear fell to 14.3% versus 28.5% in controls, with a higher MRI-confirmed tendon-healing rate (84.7% vs 70.4%).

[23] 2018
Phase I · First-in-human

Jo et al. — Stem Cells

Intratendinous injection of autologous adipose MSCs (dose-escalation) for partial-thickness tears. No adverse events; SPADI improved ~77–80% and bursal-side defect volume fell ~90% on MRI, with benefits sustained at two years.

Functional scores have not always separated from controls, but a consistent **protective effect against re-tear** and improved structural healing has emerged. These trials used adipose- and bone-marrow-derived MSCs; Wharton's Jelly hUC-MSC-specific shoulder data remain limited, though the same tendon-to-bone rationale applies. Larger randomized trials are underway.

Hip disorders

Published literature on hUC-MSC therapy specifically for hip OA and hip preservation is limited, and the current evidence does not yet include robust clinical trials. Broader cartilage-restoration reviews include the hip within joint-preserving biological approaches [12], and the mechanistic rationale is sound (shared pathobiology with knee OA). Still, hip-specific clinical evidence remains early and exploratory.

Spine disorders & intervertebral disc degeneration

For spinal conditions, the evidence base is primarily preclinical — robust mechanistic data from animal and in-vitro systems, with limited human trial data so far.

[13] 2022 **Bhujel et al.** — review of how MSC exosomes may support disc regeneration: NP cell proliferation, reduced apoptosis/senescence, ECM modulation, less inflammation.

[14] 2022 **Liang et al.** — paracrine and exosome-mediated pathways for disc repair and bone regeneration, emphasizing the pleiotropic nature of MSC exosome biology.

[15] 2026 **Zhang et al.** — controlled release of hypoxic exosomes via PLGA microspheres activated PPAR-γ, suppressed NP senescence, and attenuated disc degeneration in animal models.

[16] 2026 **Wei et al.** — systematic review & meta-analysis: consistent histological and functional benefits across animal IVDD models, with noted heterogeneity.

The translational gap is narrowing: beyond the mechanistic work above, early human clinical trials for back & spine are now emerging — summarized on the next page.

Ankle disorders

Literature specific to ankle OA, osteochondral lesions of the talus, and ankle preservation with hUC-MSCs or Wharton's Jelly MSCs is currently limited. Ankle cartilage shares the same vulnerabilities as other joints, so the mechanistic rationale applies — but ankle-specific evidence is at an early stage, and consultation with an orthopedic specialist is particularly important here.

FROM MECHANISM TO PATIENTS

Back & Spine — Human Clinical Evidence

Beyond the preclinical disc-regeneration data, a growing set of human studies has tested MSCs for degenerative disc disease and chronic low back pain — the world's leading cause of disability. Most deliver cells by **intradiscal injection**, avoiding open surgery.

Directional signals across pilot studies, cohorts, and randomized trials (2011–2021):

LOW BACK PAIN	DISABILITY	DISC QUALITY · MRI
VAS ↓	ODI ↓	Hydration ↑
sustained relief [24-26]	improved function [26][28]	structural signal [24]

[24] 2011
Pilot

Orozco et al. — Transplantation
Autologous bone-marrow MSCs injected into degenerated lumbar discs produced rapid, sustained improvement in pain and disability, with improved disc water content on MRI — among the first human evidence for intradiscal MSC therapy.

[25] 2017
RCT

Noriega et al. — Transplantation
A randomized controlled trial of allogeneic bone-marrow MSCs for degenerative disc disease: significant pain relief and improved disc quality versus control, delivered by a simple injection without surgery.

[26] 2017
Cohort · 3-yr

Pettine et al. — International Orthopaedics
Intradiscal autologous bone-marrow concentrate produced reductions in pain (VAS) and disability (ODI) that were sustained through three-year follow-up.

[27] 2017
Pilot

Centeno et al. — Journal of Translational Medicine
Culture-expanded autologous MSCs for disc-degeneration-associated radicular (nerve-related) pain reported safety and encouraging early efficacy signals.

[28] 2021
RCT · 36-mo

Amirdelfan et al. — The Spine Journal
A prospective, randomized, placebo-controlled 36-month study of allogeneic mesenchymal precursor cells for chronic low back pain from disc degeneration, supporting durable safety and efficacy signals.

Most human spine data come from autologous or allogeneic bone-marrow and precursor cells; Wharton's Jelly hUC-MSC-specific trials remain limited. The preclinical exosome work in Section 3 points in the same direction, and larger trials are ongoing.

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Erector Spinae Infiltration with MSCs in Chronic Lumbar Pain

Díaz C, Padrón M, Benedito V, Regis M, Gormaz C, et al. — *Journal of Stem Cell Research* (2024) 5(2):1-16. Published July 10, 2024 · A case-report series authored by the Auragens Clinic & Laboratory team.

Four men (ages 51–56) with chronic lumbar pain from disc disease, protrusions, stenosis, and facet pathology were treated with **intravenous hUC-MSCs** plus **MSC-derived exosomes delivered locally via ultrasound-guided erector spinae plane (ESP) infiltration** — a regional-anesthesia route repurposed to place biologics precisely at the spine. Pain was tracked by Visual Analogue Scale (VAS).

Systemic
IV hUC-MSC 1-2 M/kg — 50 M/day over 3-4 days (150-200 M total)

Local · ESP block
10×10⁹ MSC-derived exosomes per side; one patient also facet-joint hUC-MSC

PT	AGE/SEX	DIAGNOSIS & OUTCOME	VAS	RELIEF
A	51 · M	L3–L4 degenerative disc disease Off gabapentin & meloxicam; pain-free through 9 mo	8 → 0	100%
B	56 · M	Chronic lumbar pain No new medications; pain-free at 10 mo	7 → 2	71.4%
C	53 · M	T12/L1 protrusion, canal stenosis, L4/L5 retrolisthesis Off opioids; resumed MMA & weightlifting at 12 mo	10 → 1	90%
D	52 · M	L2–L3 DDD + L5/S1 disc protrusion Off celecoxib; improved mobility at 6 mo	7 → 3	57.1%

80.7%
MEDIAN VAS RELIEF

Zero adverse events
No short- or long-term complications from systemic or localized therapy in any patient. Most discontinued analgesics and resumed daily activities within days, with relief sustained 6–12 months.

A small, uncontrolled case series intended to describe safety and signal efficacy — not a controlled trial. Cells were manufactured at the Auragens Laboratory in a GMP-grade ISO-7 cleanroom under ISCT guidelines; exosomes purified to an 80–130 nm size range. Larger controlled studies are needed to confirm these findings [29].

IN-HOUSE RESULTS · TREATED & DOCUMENTED AT AURAGENS

Game-Changing Regeneration

Orthobiologic therapy in a professional athlete

29-year-old | Elite cricket player | Left knee | Injured Dec 2023 | Treated Jan 2024

A 29-year-old elite athlete with a history of repetitive knee trauma sustained an acute injury during a match in December 2023 — a snapping sensation in the left knee, followed by joint effusion, limited range of motion, and mechanical instability. Despite prior conservative interventions, symptoms persisted and significantly affected performance and quality of life.

KOOS · BASELINE → 18 MO	REPORTED IMPROVEMENT	9-MONTH MRI
65 → 90	+71.4%	Effusion resolved

Diagnosis · Jan 2024

- Large suprapatellar effusion
- Wrisberg rip, Class 1-B of the lateral meniscocapsular structures
- Grade III distension & fraying of the ACL — chronic mechanical stress
- Exam: Anterior Drawer positive; paradoxical maneuvers positive, lateral aspect

Treatment protocol · Jan 2024

Intravenous
1.5 million hUC-MSC / kg body weight

USG-guided intra-articular (L knee)
5 million hUC-MSC

CELL IDENTITY & PURITY · FLOW CYTOMETRY

CD90+ 99.74% **CD73+** 100.0% **CD105+** 94.87% **CD44+** 99.98%

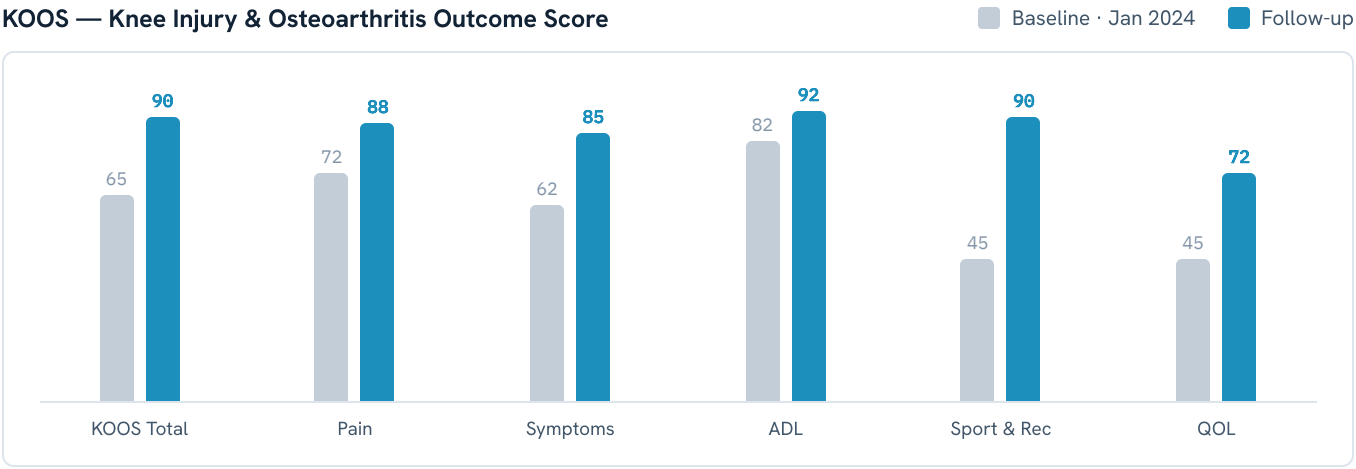
Negative for CD34, CD11b, CD45, CD19, HLA-DR · non-MSC phenotype 0.31% · processed at Auragens Laboratory under GMP & ISCT guidelines in an ISO-7 cleanroom.

Auragens clinical team: C. Díaz, A. Ortíz, V. Benedito, M. Regis, G. Nachio, C. Díaz-Urriola (MD); D. Briggs (PhD).

OUTCOMES AT 18 MONTHS

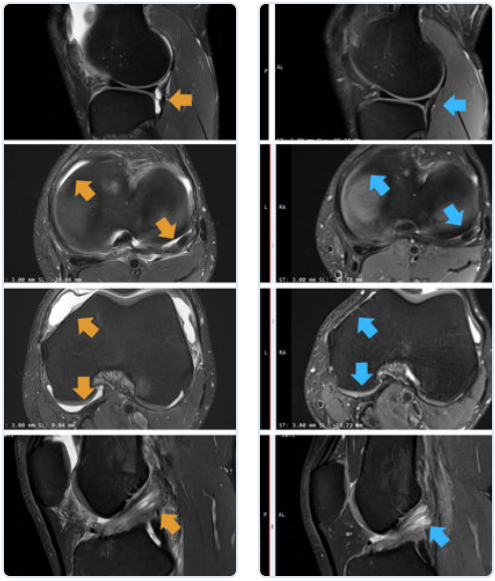
Measured recovery

KOOS — Knee Injury & Osteoarthritis Outcome Score



BASELINE · JAN

FOLLOW-UP · SEP



Radiologic resolution

Follow-up MRI at 9 months evidenced **complete resolution of the intra-articular effusion**, signs of healing of the meniscocapsular junction in the postero-lateral aspect, and **organized ACL morphology** compared with the initial lesion.

- Baseline lesion / effusion
- Same site at 9-month follow-up

KOOS rose from **65%** at baseline to **90%** on the self-administered 18-month assessment.

An intra-articular injection of allogeneic hUC-MSCs produced clinically significant improvement in this professional athlete with chronic knee pain — KOOS +71.4% at 18 months alongside radiologic resolution of joint effusion and healing of the meniscocapsular injury. The case reinforces the anti-inflammatory and regenerative potential of hUC-MSCs in musculoskeletal injuries of active, high-performance athletes.

SECTION 05

Safety Profile — What the Research Shows

Across early-phase human studies, the safety picture has been generally favorable — though limited by small samples and short follow-up. The most common adverse events were transient, localized injection-site reactions (temporary pain, swelling, or stiffness) that resolved without intervention [6][7][10]. No consistent serious adverse events — tumor formation, systemic immune reactions, or infection — were reported in the early-phase trials reviewed.

STUDY	SAFETY FINDING
Ao et al., 2023	14 patients, repeated UC-MSC injections; transient reactions in 5; no serious AEs over 3 months [6]
Yusoff et al., 2023	No significant adverse events over 6 months (Chondrogen™) [7]
Wang et al., 2017	Favorable safety & tolerability over 24 months (post-ACL) [3]
Figueroa-Valdés et al., 2025	No adverse effects at 12 months (first-in-human EVs) [10]
Wang et al., 2025	Safety across dose levels (exosomes, dose-escalation) [9]

The low-immunogenicity advantage

Low HLA class II expression and active immunosuppressive signaling may allow allogeneic administration without immune matching in many cases [10][11]. This immune privilege isn't absolute and continues to be studied.

Cell-free approaches & safety

Exosome and small-EV therapies may carry lower risks of immune reaction, pulmonary embolism, and other cell-related events, while preserving many paracrine benefits [9][10][14].

⚠ IMPORTANT CAVEATS

Safety evidence comes from small, early-phase studies with 3–24 month follow-up. Long-term data — surveillance for tumor formation, immune sensitization, and other delayed effects — are not yet available from large, controlled trials. Discuss the current evidence and its limits with the Auragens medical team and your physician.

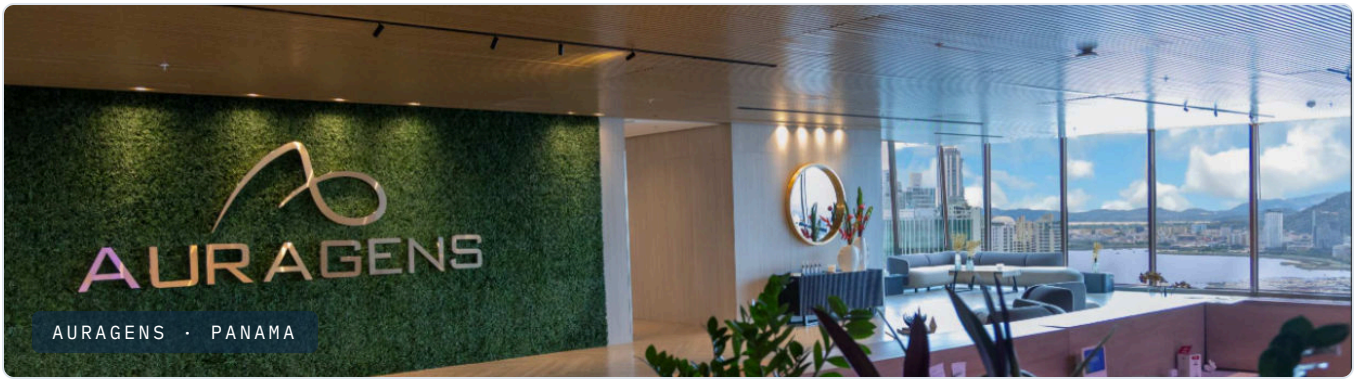
SECTION 06

What to Expect Next at Auragens

Your consultation

If you're considering hUC-MSC therapy, your journey begins with a comprehensive medical consultation — a clinical conversation, not a sales appointment — designed to understand your situation in full and discuss, transparently, whether this investigational therapy may be appropriate for you. During your consultation, the Auragens medical team will:

- ✓ Review your medical history — condition, duration, prior treatments, imaging, current function.
- ✓ Explain the proposed approach — cell source & preparation, route of administration, sessions, rationale.
- ✓ Discuss risks and benefits in the context of your specific situation and history.
- ✓ Discuss your goals and realistic expectations based on current evidence.
- ✓ Present the evidence honestly — what's supported, what's limited, what's investigational.
- ✓ Answer all your questions — without pressure or rush.



Personalized treatment planning

No single protocol fits every condition or person. We develop a plan reflecting your diagnosis, the tissues involved, your overall health, and your goals — often coordinating with your existing orthopedic, sports-medicine, or spine specialist.

Transparency about investigational treatment

We will never represent MSC therapy as a guaranteed cure or a replacement for standard care. We always present the current evidence, including its limitations, and support you in making a truly informed decision with your full healthcare team.

References

[1] Qiao Z, Tang J, Yue B, et al. (2020). Human adipose-derived mesenchymal progenitor cells plus microfracture and hyaluronic acid for cartilage repair: a Phase IIa trial. *Regenerative Medicine*, 15(1), 1193–1214.

[2] Koh YG, Kwon OR, Kim YS, Choi YJ, Tak DH. (2016). Adipose-derived MSCs with microfracture versus microfracture alone: 2-year follow-up of a prospective randomized trial. *Arthroscopy*, 32(1), 97–109.

[3] Wang Y, Shimmin A, Ghosh P, et al. (2017). Safety, tolerability, clinical, and joint structural outcomes of a single intra-articular injection of allogeneic mesenchymal precursor cells after ACL reconstruction. *Arthritis Research & Therapy*, 19(1), 180.

[4] Wang Y, Yu D, Liu Z, et al. (2017). Exosomes from embryonic mesenchymal stem cells alleviate osteoarthritis through balancing synthesis and degradation of cartilage ECM. *Stem Cell Research & Therapy*, 8(1), 189.

[5] Huang J, Ye Z, Hu X, et al. (2023). Immunity-and-matrix-regulatory cells enhance cartilage regeneration for meniscus injuries: a Phase I dose-escalation trial. *Signal Transduction and Targeted Therapy*, 8(1), 431.

[6] Ao Y, Qian N, Zhang R, et al. (2023). Repeated intra-articular injections of umbilical cord-derived MSCs for knee osteoarthritis: a Phase I, single-arm study. *BMC Musculoskeletal Disorders*, 24(1), 481.

[7] Yusoff BAHM, Don AFBM, Mohamad NB, et al. (2023). Chondrogen™ injection for knee osteoarthritis using stem cells from Wharton's Jelly. *Sains Malaysiana*, 52(10).

[8] Khalifeh Soltani S, Forogh B, Ahmadbeigi N, et al. (2019). Safety and efficacy of allogenic placental MSCs for treating knee osteoarthritis: a pilot study. *Cytotherapy*, 21(1), 54–63.

[9] Wang Y, Du J, Liu A. (2025). Injection of hUC-MSC exosomes for the treatment of knee osteoarthritis: from preclinical to clinical research. *Journal of Translational Medicine*, 23(1), 642.

[10] Figueroa-Valdés AI, de la Fuente C, Matas J, et al. (2025). Clinical-grade extracellular vesicles from umbilical cord MSCs: preclinical development and first-in-human intra-articular validation for knee osteoarthritis. *Journal of Nanobiotechnology*, 23(1), 22.

[11] Lohrasbi P, Ghasemi-Dehkordi P, et al. (2024). Regenerative therapy in osteoarthritis using umbilical cord-origin MSCs: a critical appraisal of clinical safety and efficacy. *Stem Cells International*, 2024, 4261166.

[12] Lee DH, Kim SJ, Kim SA, et al. (2022). Past, present, and future of cartilage restoration: from localized defect to arthritis. *Knee Surgery and Related Research*, 34(1), 9.

[13] Bhujel B, Shin HE, Choi DJ, Han I. (2022). MSC-derived exosomes and intervertebral disc regeneration: review. *International Journal of Molecular Sciences*, 23(13), 7306.

[14] Liang WG, Han B, Hai Y. (2022). Mechanism of action of MSC-derived exosomes in intervertebral disc degeneration treatment and bone repair. *Frontiers in Cell and Developmental Biology*, 9, 833840.

[15] Zhang W, Yin H, Wang C, et al. (2026). Controlled release of hypoxic exosomes from PLGA microspheres attenuates IVDD via PPAR-γ activation and oxidative-stress suppression. *Biomedicine & Pharmacotherapy*, 174, 118940.

[16] Wei H, et al. (2026). Therapeutic effects of stem cell-derived extracellular vesicles in animal models of IVDD: a systematic review and meta-analysis. *Frontiers in Bioengineering and Biotechnology*, 14, 1749916.

[17] Vizoso FJ, Eiro N, Cid S, Schneider J, Perez-Fernandez R. (2017). Mechanisms and therapeutic potential of stem cell-derived extracellular vesicles in musculoskeletal disorders. *Biotechnology Journal*, 12(12).

[18] Fazaeli H, Kalhor N, Naserpour L, et al. (2021). A comparative study of exosomes from adipose- and bone marrow-derived MSCs in an osteoarthritis mouse model. *BioMed Research International*, 2021, 9688138.

[19] Lou A, Gao J, Li S, et al. (2025). Quercetin-primed MSC exosomes synergistically attenuate osteoarthritis progression. *Journal of Orthopaedic Surgery and Research*, 20(1), 45.

[20] AABB. (2026). Association for the Advancement of Blood & Biotherapies. aabb.org

[21] Hernigou P, Flouzat Lachaniette CH, Delambre J, et al. (2014). Biologic augmentation of rotator cuff repair with mesenchymal stem cells during arthroscopy improves healing and prevents further tears: a case-controlled study. *International Orthopaedics*, 38(9), 1811–1818.

[22] Kim YS, Sung CH, Chung SH, Kwak SJ, Koh YG. (2017). Does an injection of adipose-derived mesenchymal stem cells loaded in fibrin glue influence rotator cuff repair outcomes? A clinical and magnetic resonance imaging study. *American Journal of Sports Medicine*, 45(9), 2010–2018.

[23] Jo CH, Chai JW, Jeong EC, et al. (2018). Intratendinous injection of autologous adipose tissue-derived mesenchymal stem cells for the treatment of rotator cuff disease: a first-in-human trial. *Stem Cells*, 36(9), 1441–1450.

[24] Orozco L, Soler R, Morera C, Alberca M, Sánchez A, García-Sancho J. (2011). Intervertebral disc repair by autologous mesenchymal bone marrow cells: a pilot study. *Transplantation*, 92(7), 822–828.

[25] Noriega DC, Ardura F, Hernández-Ramajo R, et al. (2017). Intervertebral disc repair by allogeneic mesenchymal bone marrow cells: a randomized controlled trial. *Transplantation*, 101(8), 1945–1951.

[26] Pettine KA, Suzuki RK, Sand TT, Murphy MB. (2017). Autologous bone marrow concentrate intradiscal injection for the treatment of degenerative disc disease with three-year follow-up. *International Orthopaedics*, 41(10), 2097–2103.

[27] Centeno C, Markle J, Dodson E, et al. (2017). Treatment of lumbar degenerative disc disease-associated radicular pain with culture-expanded autologous mesenchymal stem cells: a pilot study on safety and efficacy. *Journal of Translational Medicine*, 15(1), 197.

[28] Amirdelfan K, Bae H, McJunkin T, DePalma M, et al. (2021). Allogeneic mesenchymal precursor cells for chronic low back pain associated with degenerative disc disease: a prospective, randomized, placebo-controlled 36-month study of safety and efficacy. *The Spine Journal*, 21(2), 212–230.

[29] Díaz C, Padrón M, Benedito V, Regis M, Gormaz C, et al. (2024). Erector spinae infiltration with mesenchymal stromal cells in chronic lumbar pain: a case report series. *Journal of Stem Cell Research*, 5(2):1–16. Published by the Auragens Clinic & Laboratory Program.

[30] Díaz C, Ortíz A. (2026). Allogeneic umbilical-cord MSC therapy for knee osteoarthritis in professional athletes: patient-reported KOOS outcomes (May 2025–May 2026). Auragens internal clinical-outcomes report. MCID per Collins NJ, et al., *Osteoarthritis Cartilage* (2016) 24(8):1317–29.

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INFORMATIONAL DISCLAIMER

Please read this carefully

This educational document is provided for informational purposes only and does not constitute medical advice, diagnosis, or treatment recommendations. The information is based on a review of peer-reviewed scientific literature current as of 2026 and is intended to support informed patient-physician dialogue, not to replace it.

Mesenchymal stem cell therapy using human umbilical cord-derived cells from Wharton's Jelly is investigational for most musculoskeletal indications addressed in this guide. It is not approved by the U.S. Food and Drug Administration (FDA) as a standard treatment for sports injuries, cartilage disorders, or osteoarthritis of the hip, knee, spine, or ankle. The evidence base, while promising, is primarily derived from small, early-phase clinical studies with limited follow-up. Outcomes vary between individuals and cannot be predicted or guaranteed.

Individual results may vary. Some patients may experience meaningful improvement in pain, function, or quality of life; others may experience minimal or no benefit. The absence of serious adverse events in early-phase studies does not guarantee long-term safety, and continued monitoring and research are essential.

Please consult with your physician and the Auragens medical team to determine whether UC-MSC therapy is appropriate for your specific situation, medical history, and treatment goals. All treatment decisions should be made collaboratively with your qualified healthcare providers.

ACCREDITED

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