Wellbeing International Foundation

Beyond PRP

Why Cell-Free Therapy Is the Next Evolution of Blood-Derived Treatment

Paper 03 in the CFT Advantage Series

WHITE PAPER

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Abstract

Platelet-Rich Plasma (PRP) has become the world's most widely adopted autologous regenerative therapy, building widespread clinical acceptance and a multi-billion-dollar global market. PRP works by centrifuging whole blood to concentrate platelets, then injecting that concentrate into a target tissue where activated platelets release growth factors stored in their alpha-granules. The mechanism is effective and useful, but it is constrained: a short factor half-life, a narrow factor diversity, local-injection-only delivery, single-use per draw, and considerable clinic-to-clinic variability in preparation. Cell-Free Therapy (CFT) shares PRP's foundational autologous, blood-derived biology but is designed as a more controlled and biologically broader preparation. The CFT preparation is a cell-free secretome, derived from a single peripheral blood draw, containing a broader profile of growth factors and cytokines and an enriched fraction of extracellular vesicles, prepared to GMP standards in approved laboratories and delivered through a protocol-controlled intravenous route. For physicians and patients already comfortable with PRP, CFT is positioned as a familiar biology, upgraded science: the same autologous foundation and a familiar blood-derived clinical model, but a broader and more standardised biological signal. This paper sets out PRP's clinical success, its operational and biological constraints, the comparative case for CFT, and the regulatory and market dynamics that position CFT as a premium tier on top of the platform that PRP has built.

Important Note on Evidence

PRP has more than two decades of published clinical literature behind it. Cell-Free Therapy is the newer arrival, and the strongest evidence supporting cell-free secretome biology comes from preclinical work, translational studies, and analogous cell-free preparations such as APOSEC. Where this paper compares CFT and PRP at the level of factor diversity, extracellular vesicle content, delivery route and manufacturing model, it draws on those analogous datasets and on the underlying biology. Where it discusses human clinical outcomes for CFT specifically, it is careful to flag that direct head-to-head comparative trials are limited. Readers should treat the comparison as a framework for thinking about an upgrade path, not as a settled clinical claim.

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1. Introduction: PRP's Clinical Success Story

Over the past two decades, Platelet-Rich Plasma (PRP) has moved from a curiosity in oral and orthopaedic surgery to a mainstream clinical option. Physicians across orthopaedics, sports medicine, dermatology, rheumatology, pain management and aesthetic medicine routinely offer PRP as a non-surgical regenerative option. Industry analyses estimate the global PRP market at roughly USD 0.6 to 0.75 billion in 2025, with projected compound annual growth of about 10 to 15 percent through the end of the decade, reaching an estimated USD 1.3 to 1.7 billion by 2030. Reports differ on absolute figures but agree on the direction: steady expansion into new specialties and continued clinical interest in autologous, blood-derived therapies.

This expansion reflects PRP's genuine strengths. PRP is autologous, drawn from the patient's own blood, with no donor immunology and no foreign cell line. It is minimally manipulated, requiring centrifugation rather than cell expansion or genetic modification. It is fast to deploy, often completed in a single appointment. It is supported by a large body of published research and by a familiar US clinical-use model for autologous blood-derived procedures. And there is a sophisticated installed base of physicians and patients already comfortable with the model: blood

is drawn, a biological preparation is made, and that preparation is delivered back to the same person.

PRP carries inherent biological and operational limitations that are now well understood. These limitations do not undo PRP's value. They define the frontier for the next generation of autologous regenerative therapy. Cell-Free Therapy (CFT) is designed to address those frontier issues directly, while keeping the autologous, blood-derived foundation that has given PRP its clinical and regulatory acceptance.

What this paper does not claim

Disease examples in this paper, including specific musculoskeletal conditions and biological contexts, are included to explain the underlying scientific background and the published literature on PRP and on cell-free secretomes. They are not intended as claims that CFT diagnoses, treats, cures, mitigates, or prevents any disease or medical condition. CFT is positioned as biological signalling support and is not a substitute for clinical diagnosis or for any FDA-approved therapy.

2. PRP's Mechanism of Action

PRP is produced by centrifuging whole blood to isolate a plasma fraction with elevated platelet concentration, typically several times baseline. The exact protocol varies, but the principle is consistent: separate a cell-rich plasma layer containing concentrated platelets, then deliver that preparation into a target tissue. Mechanical trauma during injection, or the addition of an activator such as thrombin, calcium chloride, or collagen, triggers platelet activation.

Activated platelets undergo a rapid morphological change and degranulate. Their alpha-granules contain a stored reservoir of growth factors and cytokines, packaged during thrombopoiesis and held in reserve until activation. On release, this cargo diffuses into the surrounding tissue within minutes.

The principal growth factors and cytokines released from platelet alpha-granules include:

- Platelet-Derived Growth Factor (PDGF), a chemotactic factor that recruits cells to the wound site and stimulates proliferation and migration.
- Transforming Growth Factor-Beta (TGF-β) isoforms, regulators of inflammation, fibroblast activation, and tissue remodelling.
- Vascular Endothelial Growth Factor (VEGF), a stimulator of angiogenesis and vascular permeability.
- Basic Fibroblast Growth Factor (bFGF), a promoter of fibroblast proliferation and extracellular matrix synthesis.
- Insulin-Like Growth Factor-I (IGF-I), a supporter of cell proliferation, differentiation, and metabolic function.

- Connective Tissue Growth Factor (CTGF) and Hepatocyte Growth Factor (HGF), supporters of tissue repair and angiogenesis.

Together, these factors create a brief but powerful local environment for repair: fibroblast and macrophage recruitment, regulated inflammation, capillary formation, and extracellular matrix remodelling. This is classical wound-healing biology, accelerated by a concentrated bolus of platelet-derived signals.

3. PRP's Inherent Limitations

Despite more than two decades of widespread adoption, PRP carries a set of biological and operational constraints that recur across the literature. These constraints do not invalidate PRP. They simply describe the boundaries of the platform and define the opening for a more sophisticated autologous option.

3a. Short Half-Life of Platelet-Derived Factors

Platelet alpha-granule factors are released in a single bolus immediately after activation. Once released, individual growth factors are subject to rapid enzymatic degradation, diffusion, and cellular uptake. Most persist locally for a window measured in days rather than weeks. For conditions that benefit from sustained biological signalling, that compressed window is a real constraint.

3b. Limited Factor Diversity

PDGF, TGF-beta and VEGF form a functional triad that initiates tissue repair, but the regenerative cytokine pool is much larger. The body deploys dozens of growth factors, interleukins, chemokines and immunoregulatory molecules in coordinated repair. PRP does not naturally contain meaningful concentrations of stromal cell-derived factors such as SDF-1, of regulatory interleukins such as IL-10 or IL-1RA, or of the diverse miRNA-carrying cargo of extracellular vesicles, a fraction in which the CFT secretome is enriched. For multifactorial biological contexts, where local tissue presentations and broader biological dynamics interact, PRP's narrower factor profile becomes a limitation for broader applications.

3c. Local Injection Only

By design, PRP is delivered by direct local injection. That is well suited to focal use contexts where the target is small and well-defined. It is less well suited to broader biological contexts. An individual with multi-site presentations cannot receive local PRP everywhere at once. Even within focal use contexts, there is increasing interest in broader biological signalling support as an adjunct to local repair, and PRP's delivery model does not naturally provide it.

3d. Single-Use Per Blood Draw

Each PRP draw yields one treatment course. Typically, 9 to 20 mL of whole blood is centrifuged to produce 2 to 5 mL of PRP for a single injection. Patients who need a course of treatments, for example monthly injections across several months, undergo multiple venipunctures, each with its own preparation cycle. A therapy that allowed multiple doses from a single draw would lower per-dose burden, reduce clinic visits, and make multi-dose protocols more practical.

3e. Heterogeneous Preparation and Variable Product Quality

PRP preparation protocols vary substantially across clinics. Centrifuge specifications (g-force, spin time, temperature), plasma volumes harvested, target platelet concentrations, and the use of activators differ widely. Some clinics use commercial single-spin kits; others use manual two-spin protocols. These methodological differences produce real variability in the final product. Two patients with the same diagnosis at two clinics can receive PRP preparations with quite different factor concentrations and leukocyte content. That variability complicates clinical research, weakens standardisation, and limits the comparability of outcomes.

4. Familiar Biology, Upgraded Science: How CFT Differs

Cell-Free Therapy emerges from the same autologous, blood-derived foundation as PRP but is designed around a different biological strategy. Proregenerative cells are separated from a single peripheral blood draw and, in a clean-room laboratory, are briefly stressed so that they release a broader range of signalling factors, which are collected in saline. The preparation then passes through a double filtration step to ensure it is completely cell-free, and undergoes sterility testing before use or storage. The resulting cell-free secretome, containing soluble factors and an enriched fraction of extracellular vesicles, is characterised and administered to the same patient. No cells are returned to the patient, and the patient's cells are not cultured or expanded, nor modified in any way that could alter their genetic or epigenetic structure; the preparation is, by design, cell-free.

The result is a familiar biology, upgraded science. Familiar, because the foundation is the same: the patient's own blood, autologous and minimally manipulated, with no cell culture, expansion or genetic modification. Upgraded, because the resulting preparation is more controlled and biologically broader, more standardised in its production, and more flexible in its delivery, reaching multiple tissues through the intravenous route.

4a. Broader Factor Profile

CFT's cell-free secretome is designed to contain a broader profile of bioactive molecules than the platelet alpha-granule cargo that drives PRP. Published proteomic analyses in the independent

literature of analogous cell-free secretomes, in particular mesenchymal stromal cell secretomes and the apoptotic peripheral blood cell preparation APOSEC, identify dozens of distinct growth factors, cytokines and chemokines, including many that PRP does not carry in meaningful concentration. These preparations are cited as comparators from the published literature, not as CFT's own source material. Direct proteomic characterisation of CFT is ongoing; that work is the appropriate evidentiary anchor for any specific factor count stated in clinical communication. The directional claim, that the cell-free secretome is more diverse than the platelet alpha-granule cargo, is biologically plausible and supported by analogous secretome literature, while direct CFT characterisation remains the appropriate evidentiary anchor.

4b. Enriched Extracellular Vesicle Fraction

Cell-free secretomes are typically enriched in extracellular vesicles (EVs), a class of nanoscale particles including exosomes (roughly 30 to 150 nm) and microvesicles (roughly 100 to 1,000 nm) that carry proteins, lipids and nucleic acid cargo, including microRNAs (miRNAs) and other non-coding RNAs. When taken up by recipient cells, EVs deliver their cargo into the cytoplasm, where it can modulate gene expression. Preclinical work in cartilage models, for example, has reported that EVs carrying miR-140-5p can support cartilage homeostasis and modulate inflammatory markers.

PRP does contain some platelet-derived microvesicles, but the cell-free secretome is structurally enriched in EVs by design. The therapeutic significance of this enrichment is still being characterised, but the mechanistic rationale, that EV-mediated communication may operate through additional intracellular pathways beyond soluble protein signalling, including delivery of regulatory RNA cargo, is well established in the EV literature.

4c. Intravenous Delivery and Systemic Distribution

CFT is administered exclusively through a protocol-controlled intravenous route, allowing broader biological exposure than focal injection. Intravenous delivery reaches multiple tissues that may be involved in a given pathology, which a single local injection cannot. The clinical relevance of that exposure depends on product characterisation, dose, release testing, and the evidence generated for each specific use case, and tissue distribution and uptake should be substantiated by product-specific data. Because the preparation is produced to a single standardised protocol in our own laboratories, dose can be standardised in a way that point-of-care preparation cannot.

4d. Controlled Laboratory Manufacturing

CFT is produced to GMP standards in approved laboratories rather than at the clinic bench. Defined standard operating procedures, validated equipment, environmental monitoring, in-process controls, and final product release testing apply. Representative samples from each production run are independently analysed for protein and extracellular-vesicle content; because the number of vesicles and secretory factors in any preparation is finite, samples are selected at random for this

in-depth analysis rather than every preparation being assayed in full. Every preparation is tested for sterility and safety, and a defined release marker is measured on each preparation to confirm the expected secretory output and batch-to-batch consistency. Because all preparation is carried out in our own laboratories to a single shared protocol, the model offers a level of standardisation that point-of-care preparation cannot match.

4e. Multiple Doses From a Single Draw

A single peripheral blood draw of approximately 150 mL yields enough source material to support a full course of treatment rather than a single dose. The preparation is stable for at least one month refrigerated and for several years when frozen, so one draw can be divided into aliquots and stored, with each dose drawn from material prepared to the same standard. The operational advantages are real: fewer venipunctures, fewer clinic visits per course, lower per-dose burden, and better adherence to multi-dose protocols. Each preparation remains traceable to the patient throughout: it is linked to the patient by a unique laboratory identifier, and any personal details are held securely and separately. For multi-dose protocols where sustained biological signalling is the goal, that operational change is part of the value of the model, not a convenience add-on.

What is characterised in CFT

CFT product characterisation work covers cell-free confirmation, sterility testing, endotoxin testing, extracellular vesicle characterisation, protein panel categories, batch release criteria, and donor and patient traceability. Detailed methodology for the autologous processing pipeline and quality-control framework is described in Paper 02 of this series, From Blood Draw to Biology. The comparison table that follows reads this characterisation work as the appropriate evidentiary anchor for any specific claim about CFT composition or batch consistency. These characterisation activities support product consistency and release control; they should not be read as evidence of clinical efficacy unless linked to outcome data.

5. Comparison Table: PRP and CFT at a Glance

The following table summarises the comparison developed across Sections 2 to 4. Every row reflects a directional claim supported by the underlying literature; specific numeric claims, particularly around factor counts and EV concentrations, depend on preparation protocol and on the analytical method used and should be confirmed in any clinical communication that quotes them. References are listed at the end of the paper.

Dimension	PRP	CFT
Source biology	Centrifuged plasma fraction with concentrated platelets.	Conditioned, cell-free secretome from cells isolated from a single blood draw.
Active components	Platelet alpha-granule cargo: PDGF, TGF-β, VEGF, bFGF, IGF-I,	Broader profile of growth factors, cytokines and

	plus minor factors.	chemokines, plus an enriched extracellular vesicle fraction with miRNA cargo.
Half-life and signalling window	A single bolus release; tissue concentration of platelet-derived factors falls over a window of days.	A multi-component release with overlapping kinetics; EV-borne signalling adds an additional, longer-acting layer that is the subject of continuing study.
Delivery route	Local injection into a target tissue or joint.	Designed for protocol-controlled intravenous administration. Tissue distribution, uptake and clinical relevance should be substantiated by product-specific data.
Manufacturing setting	Clinic-based centrifugation, with meaningful clinic-to-clinic variability in protocol and product.	Centralised, GMP-aligned laboratory production with defined SOPs, environmental monitoring, batch characterisation and release testing.
Doses per draw	Typically a single injection per 9 to 20 mL draw.	Designed to yield multiple infusions per single peripheral blood draw across a treatment course.
Factor diversity	Constrained to what platelets store in alpha-granules.	Dynamically generated by living cells responding to a controlled conditioning environment, with a broader range of secreted molecules and EV cargo.
Regulatory pathway in the United States	Per FDA guidance, PRP is not an HCT/P under 21 CFR Part 1271 because blood and blood components are excluded from that framework. Certain PRP preparation systems are FDA-cleared medical devices, while clinical use depends on device labelling, practice setting, claims, and applicable state and federal rules.	Conditioned, cell-free secretome appears to fall within the Part 1271.3(d)(3) carve-out for secreted or extracted human products such as cell factors, and is therefore not an HCT/P. Regulatory position is preparation-specific and use-specific; status should be confirmed with qualified counsel for each indication, route, and claim.

Notes: Specific numeric claims about factor counts or EV concentrations vary with protocol and analytical method and should be qualified accordingly in clinical communication. References for each row are in Section 11.

6. The Shared Clinical and Commercial Lineage

A material strategic point for CFT is not that it automatically follows PRP's regulatory classification, but that PRP has normalised the clinical and commercial use of autologous, blood-derived regenerative preparations. In the United States, PRP occupies a distinct regulatory position as an autologous blood-derived product. Per FDA guidance, PRP is not an HCT/P under 21 CFR Part 1271, because the framework excludes blood and blood components. CFT should therefore not be described as automatically sharing PRP's regulatory pathway.

There is a related point that bears stating directly. The Part 1271 framework also carves out, at 1271.3(d)(3), "secreted or extracted human products, such as milk, collagen, and cell factors," except for semen. A cell-free secretome appears to fall within the language of that carve-out, although the regulatory consequences of that position are preparation-specific and use-specific. The implication is that CFT, like PRP, sits outside the HCT/P framework that the Section 361 criteria belong to, but for a different structural reason. The two products are not classification-equivalent; they are independently outside the same framework. Being outside the HCT/P framework does not mean being outside FDA oversight; depending on composition, processing, route, claims and intended use, a product may still be regulated under other drug, biological product, device or blood-product authorities.

The relevant comparison between PRP and CFT is therefore biological and operational rather than classificatory. Both approaches begin with the patient's own blood, avoid donor-cell immunology, avoid genetic modification, and return an autologous biological preparation to the same patient. Beyond that shared foundation, each preparation has its own regulatory position that depends on the exact source material, processing steps, final composition, route of administration, claims, and intended use. For that reason, this paper presents CFT as an autologous, blood-derived evolution of the PRP model, not as a product with a pre-determined FDA classification. Practices and institutions considering CFT adoption should obtain qualified regulatory counsel for any specific use case, indication or marketing position.

7. The Physician Adoption Angle

The installed base of PRP-practising physicians is the most strategic audience for CFT. Across orthopaedics, sports medicine, dermatology, rheumatology, pain management, and regenerative medicine, a large community of clinicians has already built practices around autologous, blood-derived therapy. They have invested in equipment, trained staff, developed protocols, and educated patient populations who accept the model. They have navigated the relevant regulatory framework and built a track record of outcomes.

For these practitioners, CFT is positioned as an evolution rather than a departure:

- Conceptually familiar foundation. PRP and CFT are both autologous, blood-derived, minimally manipulated preparations. Unlike donor cell therapy, gene therapy, or pharmaceutical drugs, CFT is based on the same foundational model that PRP physicians already work within.
- Familiar clinical thinking. Patient selection, informed consent, safety monitoring, and follow-up overlap closely with existing PRP practice. The clinical decision-making is the same shape.
- Workflow integration with planning. CFT requires coordination with a centralised manufacturing facility rather than clinic-based centrifugation. That is a real workflow change, not a trivial one. It introduces shipping, scheduling, and traceability considerations that physicians and their teams need to plan for. In return, it offers a defined product specification, batch traceability, and the ability to deliver multiple infusions across a treatment course from a single draw.
- Regulatory familiarity. Physicians and compliance staff who already navigate autologous, blood-derived practice will recognise the structural similarities. As Section 6 sets out, neither PRP nor CFT sits inside the Section 361 HCT/P framework, and CFT's regulatory position is preparation-specific and use-specific. The point of the comparison is the shared autologous, blood-derived foundation, not a transferred classification.
- Premium positioning within the practice. Physicians offering both therapies can present CFT as a premium option within the autologous regenerative toolkit: the same foundational biology, with broader factor diversity and broader biological exposure. PRP remains available for focal use contexts where local injection is the right delivery mode.

CFT is therefore framed as an upward step within an existing practice rather than a category switch. For patients already comfortable with blood-derived therapy through PRP, the conversation is evolutionary: the same foundation, with a more sophisticated biological signal.

8. Market Context: Standard and Premium Tiers

The PRP market has demonstrated, at scale, that physicians and patients adopt and pay for autologous, blood-derived regenerative therapy. Industry analyses place the global PRP market at roughly USD 0.6 to 0.75 billion in 2025, growing at an estimated 10 to 15 percent a year toward USD 1.3 to 1.7 billion by 2030. Absolute figures differ across firms; the consistent point is that PRP is a real, expanding clinical category with an established physician and patient base, supported by a clear regulatory framework.

Many mature medical markets settle into a stratified structure of standard and premium offerings. Orthopaedic implants are tiered. Diagnostic imaging is tiered. Cosmetic and aesthetic procedures are tiered. Regenerative medicine is following the same pattern. PRP is positioned as the standard, accessible, proven autologous tier. CFT is positioned as the premium tier above it: the same foundation, with broader factor diversity, EV enrichment, intravenous delivery, controlled manufacturing, and multi-dose protocol support.

This stratification allows PRP and CFT to coexist according to the patient's needs rather than competing head-to-head for the same patient. Individuals considering a focal, accessible autologous procedure can stay with PRP. Individuals considering broader biological signalling support, multi-site coverage, or a more standardised manufacturing model can graduate to CFT. Physicians offering both can segment their practice along clinical indication and patient preference. The market logic is additive rather than substitutive.

9. Honest Limitations and What This Paper Does Not Claim

The case for CFT as a premium tier above PRP rests on the underlying biology and on operational characteristics of the preparation, supported by analogous cell-free secretome literature. It does not yet rest on a comprehensive set of head-to-head human comparative trials between CFT and PRP. That distinction matters.

Several limitations should be stated openly. First, proteomic and EV characterisation of CFT preparations is ongoing; specific numeric claims about factor counts or EV concentrations should be tied to the analytical method that generated them. Second, while preclinical and translational evidence supports the mechanistic rationale, direct comparative clinical trials of CFT against PRP for specific indications are limited and represent the appropriate next step. Third, CFT's regulatory position is preparation-specific and use-specific, depending on the source material, processing steps, final composition, route of administration, claims and intended use; qualified counsel should review the position for any specific clinical setting. Fourth, individual responses vary, and the appropriate treatment choice for any patient is a clinical conversation, not a brochure-level comparison.

This paper does not claim that CFT treats, cures, or prevents any disease. It does not claim that PRP is obsolete; PRP remains a valuable, well-established tool with a strong evidence base in defined indications. It does not claim equivalence between CFT and any other regenerative product line; the comparison here is specifically between PRP and CFT as autologous, blood-derived options. And it does not substitute for case-by-case regulatory or clinical judgement.

10. Conclusion: A Natural Upgrade Path

PRP has earned its position as the world's most widely adopted autologous regenerative therapy. Two decades of clinical use, a substantial published literature, and a mature physician and patient base attest to a real impact on regenerative medicine. PRP demonstrated that physicians and patients will adopt autologous, blood-derived procedures in defined clinical contexts, and that the model can be supported by an established evidence base.

PRP's inherent biological and operational constraints are also clear: a short signalling window driven by platelet alpha-granule release, a narrow factor profile relative to the wider regenerative cytokine pool, local-injection-only delivery, single-use per blood draw, and considerable clinic-to-clinic variability in preparation. These are not failures; they are the boundaries of what platelets in a centrifuged plasma fraction can do.

Cell-Free Therapy is designed to operate at that frontier. By briefly stressing cells from the patient's own blood and harvesting their cell-free secretome, CFT is positioned as a broader and more standardised biological signal, delivered through a route and a manufacturing model that differ from PRP. It is not a revolution; it is a natural progression within the autologous, blood-derived paradigm that PRP established.

For physicians who have built practices around PRP, CFT is positioned as a transparent upgrade path: the same autologous foundation and familiar blood-derived clinical logic, but with a broader factor profile, an enriched EV fraction, protocol-controlled IV delivery, controlled laboratory manufacturing, and multi-dose protocol support. For patients already comfortable with blood-derived therapy through PRP experience, CFT is the next chapter in a familiar story. The foundation has been laid by PRP. CFT is designed to build on it.

11. References

1. Marx, R. E. (2004). Platelet-rich plasma: evidence to support its use. Journal of Oral and Maxillofacial Surgery, 62(4), 489-496. [Link]

2. Anitua, E., Sanchez, M., Orive, G., & Andia, I. (2008). Delivering growth factors for therapeutics. Trends in Pharmacological Sciences, 29(1), 37-41. [Link]

3. Andia, I., & Maffulli, N. (2013). Platelet-rich plasma for managing pain and inflammation in osteoarthritis. Nature Reviews Rheumatology, 9(12), 721-730. [Link]

4. Filardo, G., Di Matteo, B., Kon, E., Merli, G., & Marcacci, M. (2018). Platelet-rich plasma in tendon-related disorders: results and indications. Knee Surgery, Sports Traumatology, Arthroscopy, 26(7), 1984-1999. [Link]

5. Everts, P., Onishi, K., Jayaram, P., Lana, J. F., & Mautner, K. (2020). Platelet-rich plasma: new performance understandings and therapeutic considerations in 2020. International Journal of Molecular Sciences, 21(20), 7794. [Link]

6. Grand View Research. (2024). Platelet Rich Plasma (PRP) Market Size, Share & Trends Analysis Report. Industry research publication, San Francisco, CA. [Link]

7. Vizoso, F. J., Eiro, N., Cid, S., Schneider, J., & Perez-Fernandez, R. (2017). Mesenchymal stem cell secretome: toward cell-free therapeutic strategies in regenerative medicine. International Journal of Molecular Sciences, 18(9), 1852. [Link]

8. Phinney, D. G., & Pittenger, M. F. (2017). Concise review: MSC-derived exosomes for cell-free therapy. Stem Cells, 35(4), 851-858. [Link]

9. Lichtenauer, M., Mildner, M., Hoetzenecker, K., Hacker, S., Niederreiter, B., Werba, G., et al. (2011). Secretome of apoptotic peripheral blood cells (APOSEC) confers cytoprotection to cardiomyocytes and inhibits tissue remodelling after acute myocardial infarction. Basic Research in Cardiology, 106(6), 1283-1297. [Link]

10. Welsh, J. A., Goberdhan, D. C. I., O'Driscoll, L., Buzas, E. I., Blenkiron, C., Bussolati, B., et al. (2024). Minimal information for studies of extracellular vesicles (MISEV2023): from basic to advanced approaches. Journal of Extracellular Vesicles, 13(2), e12404. [Link]

11. Yanez-Mo, M., Siljander, P. R., Andreu, Z., Bedina Zavec, A., Borras, F. E., Buzas, E. I., et al. (2015). Biological properties of extracellular vesicles and their physiological functions. Journal of Extracellular Vesicles, 4, 27066. [Link]

12. Tao, S. C., Yuan, T., Zhang, Y. L., Yin, W. J., Guo, S. C., & Zhang, C. Q. (2017). Exosomes derived from miR-140-5p-overexpressing human synovial mesenchymal stem cells enhance cartilage tissue regeneration and prevent osteoarthritis of the knee in a rat model. Theranostics, 7(1), 180-195. [Link]

13. Thery, C., Witwer, K. W., Aikawa, E., Alcaraz, M. J., Anderson, J. D., Andriantsitohaina, R., et al. (2018). Minimal information for studies of extracellular vesicles 2018 (MISEV2018). Journal of Extracellular Vesicles, 7(1), 1535750. [Link]

14. U.S. Food and Drug Administration. (2020). Regulatory considerations for human cells, tissues, and cellular and tissue-based products: minimal manipulation and homologous use. Guidance for Industry and FDA Staff. Reference is also relevant to the position that PRP is not an HCT/P under 21 CFR Part 1271. [Link]

15. U.S. Food and Drug Administration. Code of Federal Regulations Title 21, Part 1271, Human cells, tissues, and cellular and tissue-based products. [Link]

16. Pachito, D. V., Bagattini, Â. M., de Almeida, A. M., Mendrone-Júnior, A., & Riera, R. (2020). Technical procedures for preparation and administration of platelet-rich plasma and related products: a scoping review. Frontiers in Cell and Developmental Biology, 8, 598816. [Link]

17. U.S. Food and Drug Administration. (2019). Public Safety Notification on Exosome Products. Center for Biologics Evaluation and Research, 12 December 2019. [Link]

18. U.S. Food and Drug Administration. (2021). Public Safety Alert Due to Marketing of Unapproved Stem Cell and Exosome Products. [Link]

19. U.S. Code of Federal Regulations. (current). Title 21, Section 801.4, Meaning of intended uses. Reference for the principle that intended use can be reflected in labeling, advertising, and other written or oral statements. [Link]

Disclaimer: Individual results vary. Cell-Free Therapy is not intended to diagnose, treat, cure, or prevent any disease. The information in this paper is provided for educational purposes and does not constitute medical, legal, or regulatory advice. CFT supports the body's normal biological function through autologous, cell-free biological preparations.

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