
10
BILLION
AGE ZERO EXOSOMES
RESILIÉLLE

RESILIÉLLE™

WELCOME TO AGE ZERO™

RESILIÉLLE COSMETICS, LLC
MANUFACTURED IN THE USA

For more information, visit our website:
RESILIÉLLE.COM

AMERICA'S EXOSOME EXPERTS

E: Infor@resilielle.com
P: +1 (585) 484-0058

Subsidiary of ATVenture Center LLC

PRODUCT GUIDE

RESILIÉLLE's Age Zero *Exosomes*™ are the world's highest tested and most potent exosome serum that are safe for anyone, regardless of skin type. This best-in-class solution is derived from human 'age zero' perinatal MSCs. Highest potency and purity, with stringent quality testing at every step of the process: isolation, concentration, and storage.

ENHANCE

Age Zero Exosomes can be added to most aesthetic treatments to enhance the rejuvenating effect of the treatment.

RESTORE

When added to treatments Age Zero Exosomes demonstrate skin restoring capabilities and reduce recovery time.

OPTIMIZE

Age Zero Exosomes are particularly effective when applied after the DEP, microneedling, and laser resurfacing treatments.

The Results Are In

In a recent 100-person study, results showed significant improvement in:

TEXTURE	*FIRMNESS*	*PIGMENTATION*	*WRINKLES*	*RADIANCE*
90.3%	*88.0%*	*88.9%*	*86.4%*	*92.6%*

AGE ZERO EXOSOMES 10 BILLION/2.5 mL SALINE

The ideal concentration/volume of pure RESILIÉLLE intended for SKIN | SCALP | HAIR

"Off the shelf" exosomes suspended in saline to maintain ultimate potency, never lyophilized.

AVAILABLE PRODUCT PACKS OF OUR 10 BILLION EXOSOME CONCENTRATION

TRIAL PACK	6 VIAL PACK
SMALL PACK	12 VIAL PACK
LARGE PACK	24 VIAL PACK

Ask us about our Subscription Plans for additional savings.

RESILIÉLLE™

PRODUCT GUIDE

AGE ZERO EXOSOMES™
THE NEW GOLD STANDARD

RESILIÉLLE exosomes are derived from healthy, fresh, human Umbilical Cord Wharton's Jelly Mesenchymal Stromal/Stem Cells.

RESILIÉLLE exosomes are powered by a patent pending Stem Cell technology. Young, healthy donors of umbilical cord WJ-MSCs have been screened and tested negative for communicable diseases, such as HIV I/II, Hepatitis B/C, HTLV I/II, Syphilis, CMV, West Nile, Zika Virus, COVID, and screening for other pathogens per USA FDA 21 CFR 1271HCT/P requirements.

Each **RESILIÉLLE** finished exosome lot is tested for sterility as per <USP 71>, endotoxin as per <USP 85>, bioburden, mycoplasma and infectious diseases at an independent USA certified CLIA lab.

RESILIÉLLE exosomes are characterized quantitatively via NanoSite300 for a full analysis of particle size and concentration, and all functional components present, providing the most comprehensive evaluation of safety and efficacy available anywhere in the world.

RESILIÉLLE exosomes are acellular, preservative-free, and manufactured with Xeno-Free, Serum-free products at **RESILIÉLLE** cGMP facility, registered with FDA HCT/P establishment, and licensed by New York State, as a NYS tissue bank.

RESILIÉLLE exosomes have never been tested on animals.

Product containing, isolated and concentrated, frozen exosomes (not lyophilized) suspended in sterile saline. The Gold Standard.

RESILIÉLLE operates in an ISO 7 Certified Clean Room with ISO 5 Certified BSL2 Hoods. **RESILIÉLLE** ISO 9001: 2015 compliant quality system is best-in-class.

RESILIÉLLE exosomes are manufactured to clinical grade quality standards for topical use only by Dermatologists, Plastic Surgeons, or Aesthetic Professionals.

PRODUCT GUIDE

RESILIÉLLE Storage and Preparation Directions

Unboxing and Storage

One you receive your package you will want to immediately place the product into either a -80 degree Celsius freezer (15 month storage option), a -20 degree Celsius freezer (6-month storage option), or the refrigerator (3-month storage option). Refer to Certificate of Conformity and the product label for expiration date for shelf life reference.

Opening the Vial

Lift the metal tab from the top of the vial and pull down gently. Once you pull down and break the metal seal, it can be carefully disposed of. The rubber stopper can be removed when ready to pull the product into the syringe.

Use

Remove the rubber stopper and draw up the entire content of the vial into a sterile syringe. This can be done with or without a needle. After the treatment is complete you will start at the top of the treated area and place a few drops at a time to flood the treated are slowly.

Massage gently into the skin. Move to your next area and repeat the steps above. Once you have gone over the entire treated area you may go back over the entire area again to deliver the entire contents of the vial per treatment.

PRODUCT GUIDE

RESILIÉLLE Facial Treatment Protocol

(Protocol was used for the 100-Patient Skin Trial)

FACIAL PROTOCOL: EXOSOMES AFTER MICRONEEDLING

Advise the client to perform a double cleanse on the skin prior to treatment.

Use a Skin Cleanser such as, Hibiclens, with 4x4s gauze pads to prepare the skin.

Topical numbing cream should be applied for at least 30 minutes to reduce the risks of discomfort that can result from the microneedling procedure.

Prep the microneedling device according to the manufacturer's recommendations, with a depth no greater than 1.5mm.

Remove the topical numbing cream thoroughly and wipe the skin with the skin cleanser again. Apply glide product of choice. Do not apply the exosomes as the glide agent.

Follow manufacturer's grid pattern. If one was not provided, one can be provided for you.

Watch for clinical endpoint, which in this case is pin-point bleeding. Once you have completed the treatment, wipe the skin again with a gentle toner or water soaked 4X4 gauze pads.

Exosomes should be applied directly after the treatment area is wiped free of the glide and blood.

Each of the participants in the 100-Patient trial received 3 treatments, 30 days apart.

Contact RESILIÉLLE for access to video on patient testimonial and study results 6 months post treatment.

Disclaimer: RESILIÉLLE exosome products are post-care topical cosmetic solutions. The products are not a drug. They are not intended to prevent, treat, or cure diseases or medical conditions. They are not intended to be injected or delivered intravenously.

PRODUCT GUIDE

RESILIÉLLE Hair Treatment Protocol

HAIR PROTOCOL: EXOSOMES AFTER MICRONEEDLING

Advise the client to perform a double cleanse of the hair prior to treatment.

Use a Skin Cleanser such as, Hibiclens, with 4x4s gauze pads to prepare the skin.

Topical numbing cream should be applied for at least 30 minutes to reduce the risks of discomfort that can result from microneedling procedure.

Prep the microneedling device according to the manufacturer's recommendations, with a depth no greater than 0.8mm.

Remove the topical numbing cream thoroughly and wipe the skin with alcohol.

Apply glide product of choice. Do not apply the exosomes as the glide agent.

Follow the manufacturer's grid pattern. If one was not provided a stamping technique may be used by separating the hair one row at a time and stamping or swirling the device in small circles (this technique may cause hair to become tangled or put too much tension on the hair follicle which should be avoided).

Watch for clinical endpoint which in this case is pin-point bleeding. Once you have completed the treatment, wipe the skin again with a gentle toner or water soaked 4X4 gauze pads.

Exosomes should be applied directly after the treatment area is wiped free of glide and blood.

RESILIÉLLE is currently in the process of designing a clinical study for hair rejuvenation and for scar prevention and scar appearance improvement. Contact **RESILIÉLLE** if you want to find out more about how your clinic and patients can participate in groundbreaking studies with cutting edge advanced technology.

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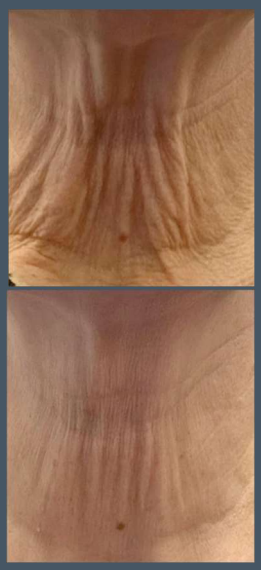
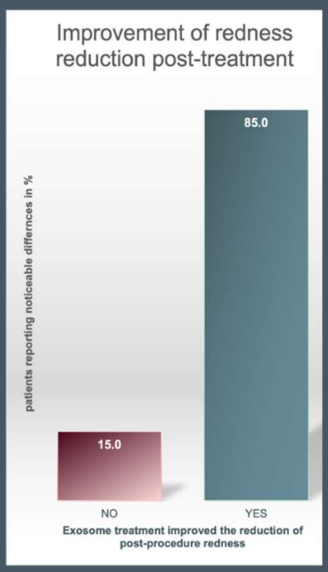
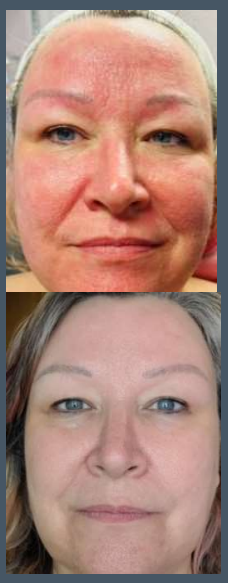
100-PATIENT TRIAL RESULTS & BEFORE/AFTER PHOTOS

FIRMNESS 88.0%

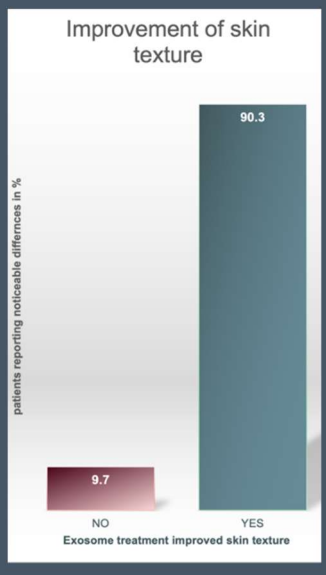


REDNESS 85.0%

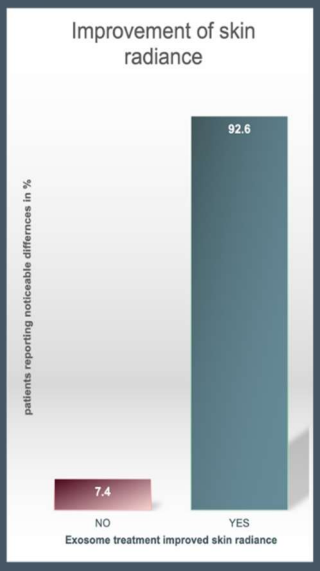




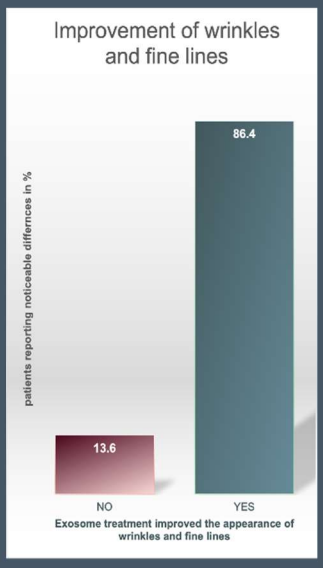
TEXTURE 90.3%

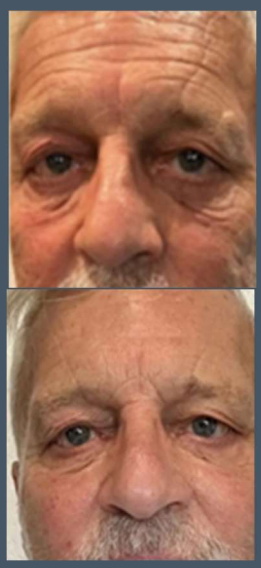


RADIANCE 92.6%

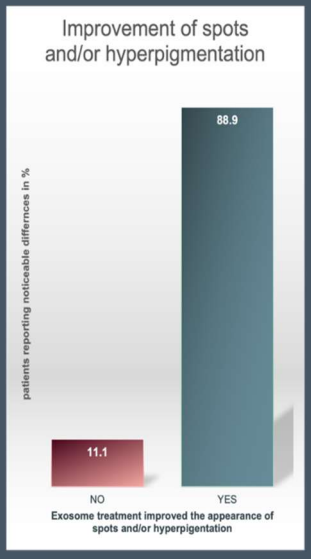


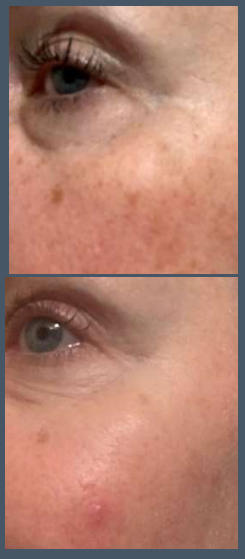
WRINKLES 86.4%





PIGMENT 88.9%





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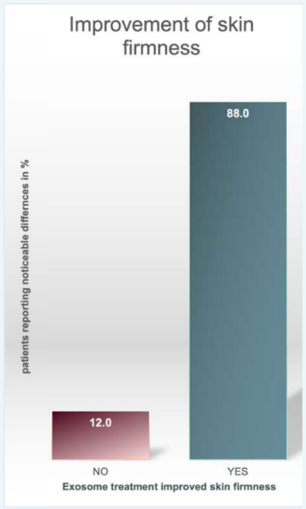
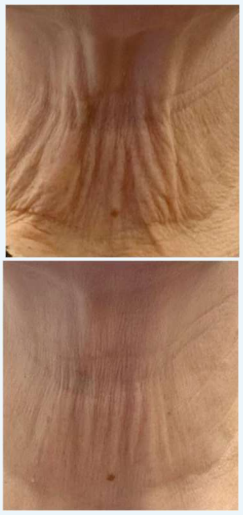
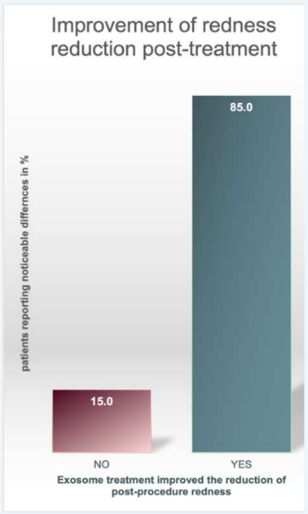
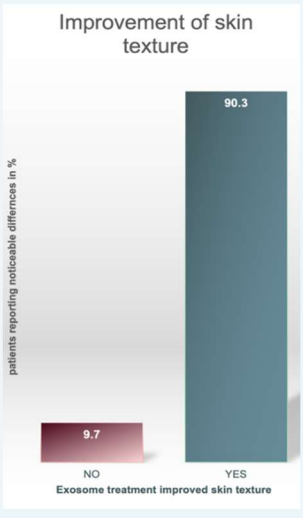




REDNESS 85.0%



TEXTURE 90.3%



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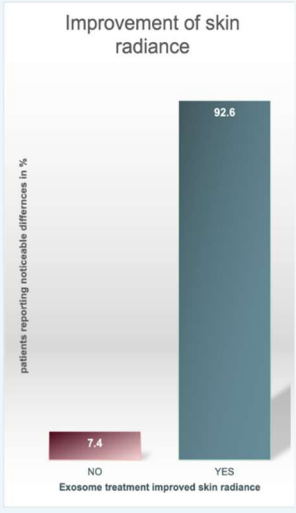

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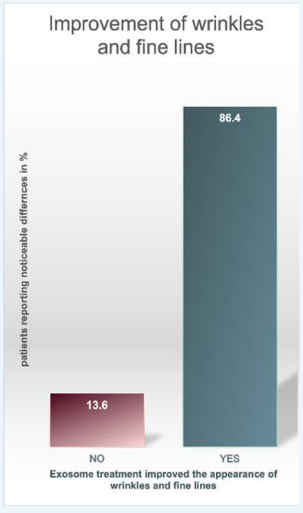

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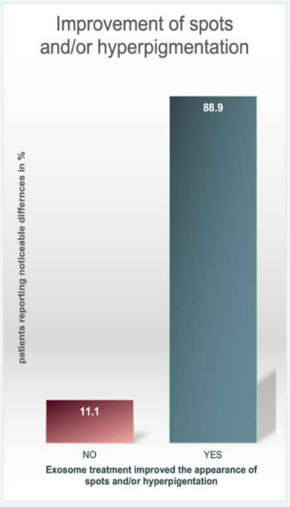

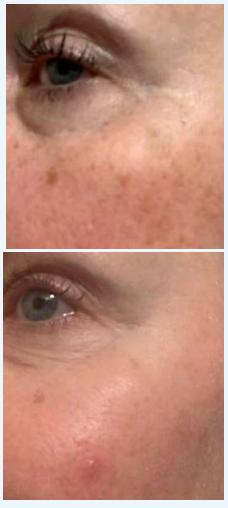

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Age Zero™

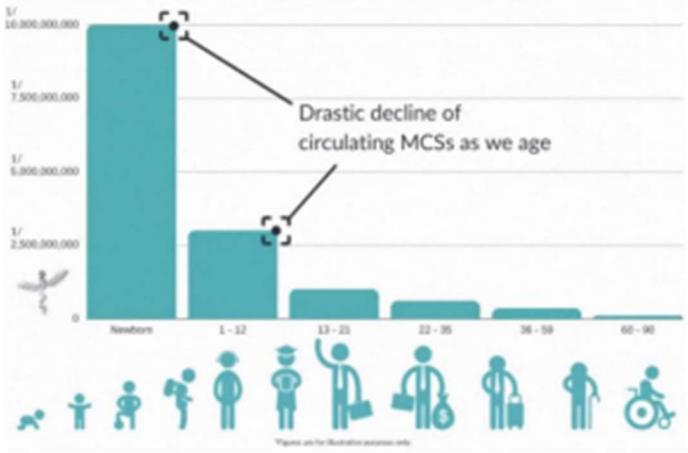
What does 'age zero' mean?

"Age zero" in the context of stem cells or exosomes, particularly those derived from Wharton's Jelly of the human umbilical cord (hUC-WJ), refers to the notion that these cells are *as young as human cells can be*. The term emphasizes the idea that these cells have *not undergone the aging processes* that most other cells in the body have. Stem cells from this source, and the exosomes derived from them, have the potential to be *especially potent* for therapeutic uses and rejuvenation because of their pristine, youthful state. Think of stem cells from hUC-WJ like a *brand-new* car *straight from the factory*, having *none of the wear and tear* that older cars (or cells) might have.

Or, imagine your body's cells as a continuously playing movie. As time goes on, the quality of the movie deteriorates: colors fade, the sound gets distorted, and there might be glitches. This deterioration can be likened to the aging process in our cells. Now, stem cell or stem-cell derived exosomes aim to rewind that movie back to the beginning, or to a point where the quality was at its best. This 'rewinding' can potentially restore the functions of our cells back to a more youthful state. Exosomes, which are tiny vesicles released by cells, including stem cells, that these cells use to communicate, can be involved in this process by delivering the necessary 'instructions' and factors to assist in the rejuvenation. They carry proteins, lipids, and nucleic acids to other cells. Exosomes derived from "age zero" stem cells would also carry their pristine, youthful characteristic, potentially making them more effective in therapeutic and rejuvenation applications.

Why is 'age zero' important?

We all know of and experience the process of aging. With age, over time, things do no longer regenerate as they used to, we lose energy, activities that were easy and fun become more strenuous, recovery times get longer. If we want to counteract these and other signs of aging, we resort to the most powerful source to help with it: stem cells. Stem cells are the building blocks of life, they have the capacity to self-renew (virtually indefinitely) or to specialize into other cell types. The most commonly used sources for stem cells are bone marrow, adipose tissue and perinatal tissues (umbilical cord, placenta). All these SCs are called 'adult' stem cells. Among them, SCs harvested from perinatal tissues are obviously the 'youngest' ones (i.e. age zero), and therefore the most potent.



Circulating MSCs rapidly decline with age, resulting in longer repair and recovery times. As we age, we are more prone to disease and degeneration.

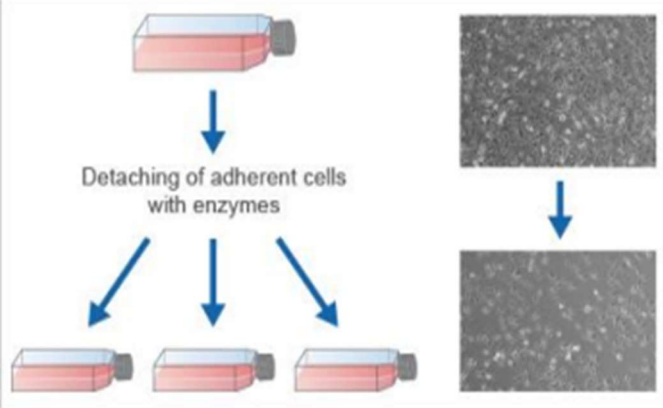
This explains why adult adipose and adult bone marrow-derived MSCs are less potent than 'zero aged' hWJ-MSCs

The graph above illustrates the difference between age-zero SCs/exosomes and those derived from other sources, later in life. Even if you perceive a healthy 20-30 year old in the prime of their life, they have only a fraction of their original SCs left, and those are 20- 30 years old. While SCs are theoretically regraded immortal, the truth is that their quality lessens with age, also because we are subjected to environmental factors that are

detrimental to our health, also, because we might not live healthy lives, or because we have accrued maladies or suffered diseases that affect our overall health.

Age-zero WJ-MSCs however, ***just 'finished building a human being'***, and the exosomes derived from them are experts in cell-cell signaling and repair to get this amazing job done. Consequently, they are ***the most specialized and most potent helpers to achieve rejuvenation*** that can be found anywhere.

Low passage



When the cells have grown for several days into a dense monolayer, they will be taken off with help of enzymes and passaged onto several new flasks. This constitutes ***one*** **passage**. This process gets repeated with the aim to largely increase cell numbers.

What does "low passage" mean and why is it important?

A 'passage' is the transfer of cells from one culture flask to the next. When culturing SCs to increase their numbers, they are first seeded e.g., in just one flask. After letting them grow to confluency, the cells are taken off the flask and split onto several new flasks with fresh medium to expand them further. Such a split or transfer is called a 'passage'.

It is critical to limit the numbers of passages. Why? The longer we keep the stem cells in culture, the higher the risk for contaminations, spontaneous mutations, or differentiation – which means that the cells are no longer useful for our purposes or could even harbor health risks.
The International Society for Stem Cell Research (ISSCR) recommended a ***low passage*** *limit of just* ***4 passages***, so to afford obtaining enough cells while minimizing the risk that is inherent to extended culturing. The by the scientific community agreed-upon limit of 4 passages warrants that the cells harvested and used are exact replicas of the ones originally harvested from the umbilical cord.

Noteworthy: most competitors do not do that, because extended culturing of one cell line is way cheaper than processing a fresh new umbilical cord every time. Plus, they typically only validated their original cell line, if that, but not after thawing and growing them again and again. Some are known to use 1,500 passage or more – at that point, these have likely long since differentiated and are no longer stem cells and also feature a high probability of mutations.
Since the age zero characteristic is obviously desired and important to generate the most potent products for rejuvenation, Resiliélle strictly adheres to a ***low passage protocol*** *of never more than* ***4*** *passages*.

Immunoprivilege

The term "immunoprivileged" refers to the unique properties of WJ-MSCs that allow them to evade the immune system or modulate its response. This makes them a compelling option for therapies because of they typically do

not run the risk of potential rejection when using them, and another reason why we use SCs from a perinatal source: *The concept of "immunoprivilege" is crucial for pregnancies because it helps ensure that the maternal immune system doesn't reject the developing fetus, which is, in essence, a semi-allograft (it possesses antigens from both the mother and the father)*.

Here's why WJ-MSCs are considered immunoprivileged:

1. **Low Immunogenicity**: WJ-MSCs have been found to express lower levels of major histocompatibility complex (MHC) class I molecules and usually do not express MHC class II molecules. This reduced expression makes them less recognizable to the recipient's immune system, thereby reducing the likelihood of an immune attack.
2. **Immunomodulation**: WJ-MSCs can modulate the immune response. They secrete factors that can suppress the proliferation and function of various immune cells, such as T cells, B cells, and natural killer cells. They can also promote the generation of regulatory T cells, which play a role in controlling the immune response.
3. **Trophic Support**: Beyond immunomodulation, WJ-MSCs secrete various growth factors, cytokines, and other molecules that support tissue regeneration and repair. Their paracrine (cell-to-cell communication) functions can support endogenous healing mechanisms, which is crucial for regenerative medicine or rejuvenation.

These properties make WJ-MSCs attractive candidates for therapy in a variety of conditions. The immunoprivileged status allows for the allogeneic use of WJ-MSCs (using cells from a donor rather than the patient) without the need for intense immunosuppression.

Exosomes cargo

Exosomes derived from human umbilical cord Wharton's Jelly mesenchymal stromal/stem cells (hWJ-MSCs) carry a diverse cargo of biomolecules, including proteins, lipids, and nucleic acids such as mRNA and non-coding RNAs. These components play essential roles in cell-to-cell communication, tissue repair, and regeneration. The detailed cargo of exosomes from hWJ-MSCs may vary depending on the specific cell source, isolation method, and culture conditions.

However, some key components typically found within these exosomes include:

1. **Proteins:** Exosomes derived from hWJ-MSCs are enriched in proteins involved in various cellular processes such as cell adhesion, migration, proliferation, differentiation, and immunomodulation. Some of the most important proteins found in these exosomes include:
    - **Tetraspanins** (CD9, CD63, CD81): Tetraspanins are a family of proteins that play a crucial role in exosome biogenesis and cargo sorting. They also serve as exosome markers and are involved in cell adhesion and signal transduction.
    - **Heat shock proteins** (HSP60, HSP70, HSP90): Heat shock proteins are molecular chaperones that facilitate protein folding, stability, and degradation. They play a role in cellular stress responses and can modulate immune responses.
    - **Cytoskeletal proteins** (Actin, Tubulin): These proteins are involved in maintaining exosome structure and integrity. They also play a role in cellular processes like cell adhesion, migration, and invasion.
    - **Extracellular matrix protein**s (Collagens, Fibronectin, Laminin): These proteins contribute to the structural support and organization of tissues. They are involved in cell adhesion, migration, and differentiation, playing crucial roles in tissue repair and regeneration.
    - **Growth factors** (TGF-β, VEGF, FGF, EGF, PDGF, IGF): Growth factors are essential signaling molecules that regulate cellular processes such as proliferation, migration, and differentiation. They play a critical role in tissue repair, angiogenesis, and wound healing.
        - Transforming Growth Factor-beta (TGF-β): TGF-β is a multifunctional growth factor that regulates cell proliferation, differentiation, migration, and apoptosis. It also plays a critical role in immunomodulation and extracellular matrix remodeling.
        - Vascular Endothelial Growth Factor (VEGF): VEGF is a potent angiogenic factor that promotes the growth of new blood vessels, enhances endothelial cell proliferation, migration, and survival. It is essential for wound healing and tissue regeneration.
        - Fibroblast Growth Factors (FGFs): FGFs are a family of growth factors involved in various biological processes, including cell proliferation, differentiation, migration, and angiogenesis. They can promote wound healing, tissue repair, and regeneration.
        - Epidermal Growth Factor (EGF): EGF stimulates cell growth, proliferation, and differentiation. It plays a significant role in wound healing, tissue repair, and skin regeneration.
        - Platelet-Derived Growth Factor (PDGF): PDGF is a potent mitogen for cells of mesenchymal origin, such as fibroblasts, smooth muscle cells, and glial cells. It is involved in cell proliferation, migration, and differentiation, as well as wound healing and tissue repair.

- Insulin-like Growth Factor (IGF): IGFs are growth factors that regulate cell growth, proliferation, differentiation, and survival. They play essential roles in tissue regeneration, wound healing, and cellular metabolism.

- **Cytokines** and **chemokines** (IL-6, IL-8, IL-10, MCP-1, TNF-α, SDF-1, RANTES MIP-1α, MIP-1β): These proteins are involved in modulating immune responses, inflammation, and cell recruitment. They can influence tissue repair, regeneration, and immune regulation. Some of the most important cytokines and chemokines found in these exosomes include:
    - Interleukin-6 (IL-6): IL-6 is a pleiotropic cytokine with both pro- and anti-inflammatory functions. It plays a role in immune regulation, acute-phase responses, and hematopoiesis.
    - Interleukin-8 (IL-8): IL-8, also known as CXCL8, is a chemokine that acts as a potent chemoattractant for neutrophils and other immune cells. It plays a role in inflammation, angiogenesis, and wound healing.
    - Interleukin-10 (IL-10): IL-10 is an anti-inflammatory cytokine that downregulates the expression of pro-inflammatory cytokines, such as IL-1, IL-6, and TNF-α. It plays a crucial role in modulating the immune response and preventing excessive inflammation.
    - Monocyte Chemoattractant Protein-1 (MCP-1/CCL2): MCP-1 is a chemokine that attracts monocytes, memory T cells, and dendritic cells to sites of inflammation and tissue injury. It plays a role in immune cell recruitment, inflammation, and tissue repair.
    - Tumor Necrosis Factor-alpha (TNF-α): TNF-α is a pro-inflammatory cytokine involved in immune cell activation, inflammation, and apoptosis. It can be present in hWJ-MSC-derived exosomes but in lower amounts compared to other cytokines, as hWJ-MSCs are known for their immunomodulatory
    - Stromal Cell-Derived Factor-1 (SDF-1/CXCL12): SDF-1 is a chemokine that attracts various immune cells, including T cells, B cells, monocytes, and hematopoietic stem cells. It is involved in immune cell trafficking, tissue repair, and angiogenesis.
    - Regulated upon Activation, Normal T cell Expressed, and Secreted (RANTES/CCL5): RANTES is a chemokine that attracts T cells, monocytes, eosinophils, and basophils. It plays a role in immune cell recruitment, inflammation, and the immune response to pathogens.
    - Macrophage Inflammatory Protein-1 alpha (MIP-1α/CCL3) and Macrophage Inflammatory Protein-1 beta (MIP-1β/CCL4): These chemokines attract and activate various immune cells, including monocytes, macrophages, and T cells. They are involved in immune cell recruitment, inflammation, and the immune response to pathogens.

2. **Nucleic acids**: The exosomes contain various types of nucleic acids, including mRNA and non-coding RNAs like microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs). These RNA molecules play vital roles in gene regulation, cellular differentiation, and tissue regeneration. Some of the most important nucleic acids found in these exosomes include:

    - **microRNAs** (miRNAs): miRNAs are small non-coding RNAs (~22 nucleotides long) that play crucial roles in post-transcriptional gene regulation. They can modulate various cellular processes, such as proliferation, differentiation, migration, apoptosis, and immune responses.

Specific miRNAs found in hWJ-MSC-derived exosomes may differ depending on the source and experimental conditions, but some examples include miR-21, miR-146a, miR-155, and miR-let-7 family members.

- **Long non-coding RNAs** (lncRNAs): lncRNAs are a class of non-coding RNAs longer than 200 nucleotides. They have diverse roles in gene regulation, epigenetic control, chromatin remodeling, and transcriptional regulation. Some important lncRNAs identified in hWJ-MSC-derived exosomes include MALAT1, HOTAIR, and TUG1.
- **Circular RNAs** (circRNAs): circRNAs are a class of non-coding RNAs characterized by their circular structure. They can act as miRNA sponges, modulate transcription and splicing, and interact with RNA-binding proteins. Although their presence and roles in hWJ-MSC-derived exosomes are not well-established, they might be important players in gene regulation and cellular communication.
- **Messenger RNAs** (mRNAs): Exosomes derived from hWJ-MSCs can also contain mRNAs that encode proteins involved in various cellular processes, such as cell adhesion, migration, proliferation, differentiation, and immunomodulation. The transfer of these mRNAs to recipient cells can contribute to the functional effects of hWJ-MSC-derived exosomes in tissue repair and regeneration.

3. **Lipids**: Exosomes derived from hWJ-MSCs have a lipid bilayer membrane composed of various lipids such as phospholipids, sphingolipids, and cholesterol. These lipids contribute to the stability structure, and biological functions of exosomes. Some of the most important lipids found in these exosomes include:
    - **Phospholipids**: Phospholipids are the primary lipid components of exosome membranes. They form a lipid bilayer that provides structure and stability to the exosomes. Phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), and phosphatidylinositol (PI) are some of the most common phospholipids found in exosomes.
    - **Sphingolipids**: Sphingolipids are a class of lipids that play essential roles in exosome biogenesis, membrane microdomain organization, and cellular signaling. Some important sphingolipids found in exosomes include sphingomyelin (SM) and ceramide.
    - **Cholesterol**: Cholesterol is a sterol that helps maintain exosome membrane fluidity and integrity. It is involved in the formation of lipid rafts, which are membrane microdomains enriched in certain lipids and proteins and play a role in exosome biogenesis and cargo sorting.
    - **Glycosphingolipids**: Glycosphingolipids are a type of sphingolipids with one or more sugar moieties attached. They are involved in cell recognition, adhesion, and signaling. Gangliosides, such as GM1, GM2, and GM3, are examples of glycosphingolipids found in exosomes.
    - **Phosphatidic acid** (PA): PA is a phospholipid involved in membrane curvature and fusion events. It has been implicated in exosome biogenesis and can regulate the activity of proteins involved in vesicle trafficking.