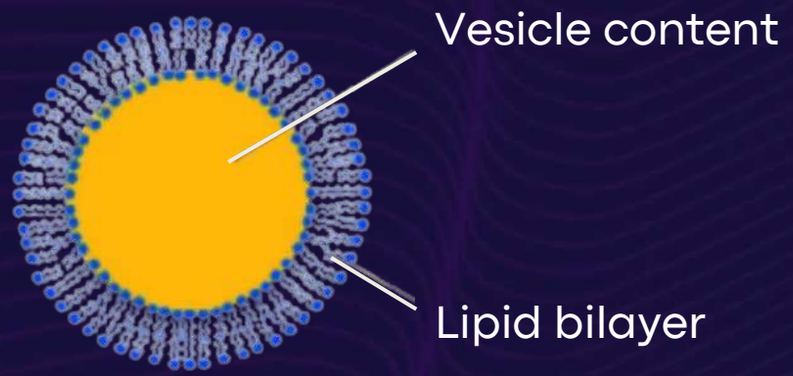

YOUR BODY,
YOUR CURE
The Future of Healthcare
BIOLOGICAL
INNOVATIONS

EXTRACELLULAR VESICLES (EVS)



The extracellular vesicles represent a heterogeneous population of particles bounded by a phospholipid bilayer and are secreted into the extracellular space.

The extracellular vesicles are approximately spherical structures delimited by a lipid bilayer (similar in structure to cell membranes) which contain soluble hydrophilic components in their lumen.

From the cells from which they originate, they draw nucleic acids, proteins and lipids and do NOT have a replicative capacity.

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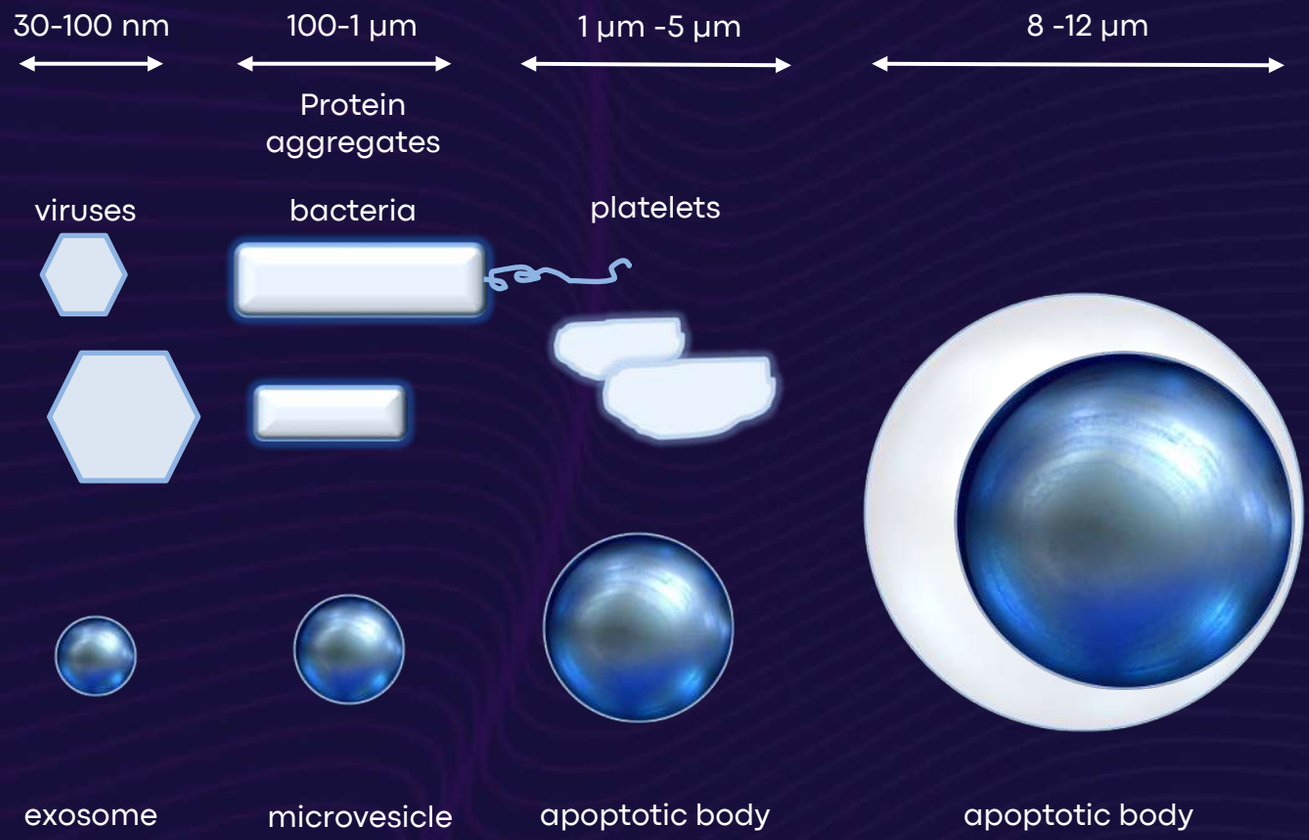
EXTRACELLULAR VESICLES (EVS)



EVS are commonly classified into three subtypes based on their origin, size and biogenesis and are divided into:

- **exosomes (30-100 nm)**
- microvesicles (100 nm - 1µm)
- apoptotic bodies (1-5 µm)

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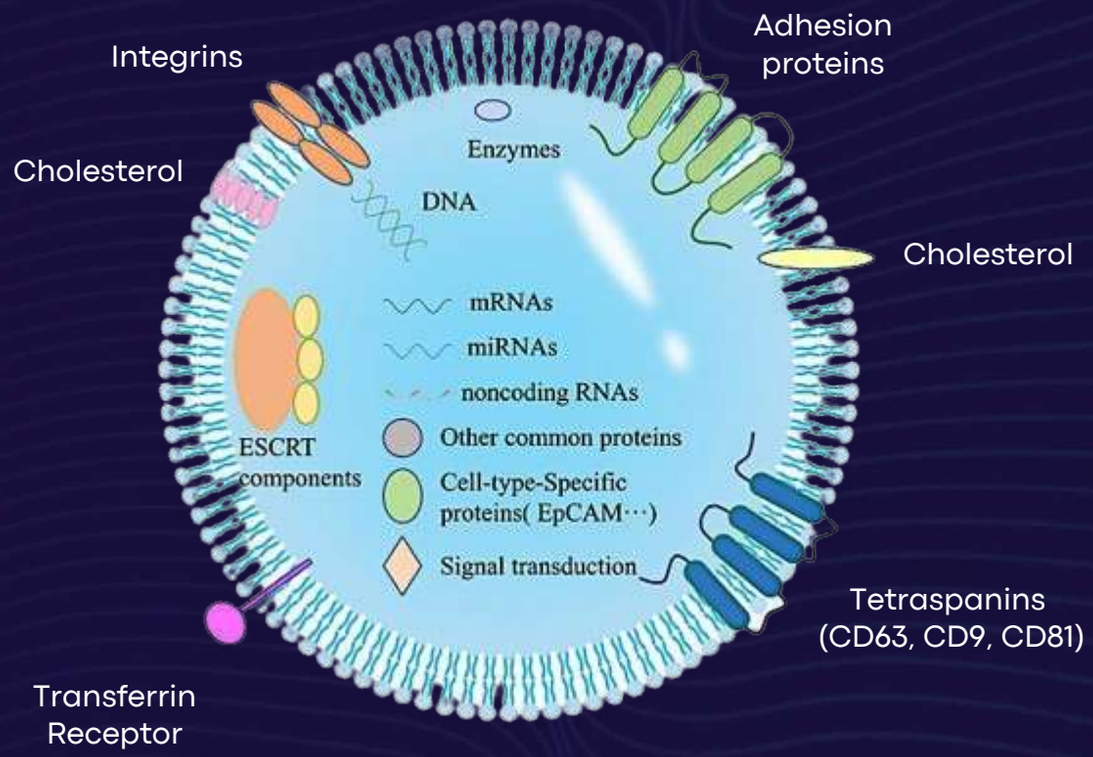
EXOSOME DEFINITION

- Extracellular nanovesicles secreted from almost all types of cells.
- Participate in cell–cell communication via transmitting their cargo, including nucleic acids, proteins, and metabolites to recipient cells.
- Mediators of near and long-distance intercellular communication in health and disease.
- Discovered in biological fluids including blood, urine and cerebrospinal fluid.
- Identified within the tissue matrix, termed Matrix- Bound Nanovesicles (MBV).
- Affect various aspect of cell biology.



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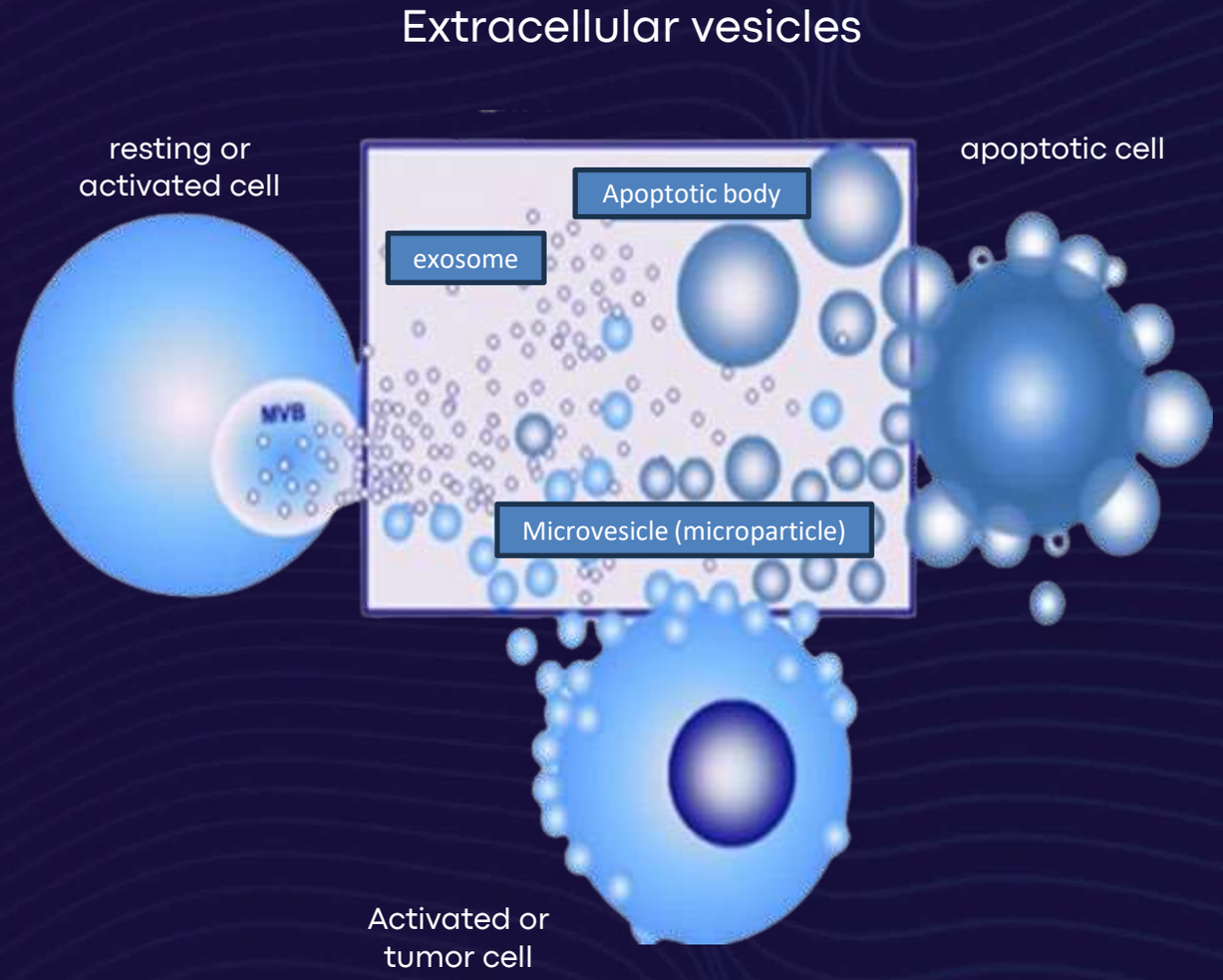
EXOSOME ORIGIN

The exosomes originate through the endosomal pathway and are released through the fusion of the multivesicular bodies with the plasma membrane.

The lipid composition of exosomes, which have a low content of phosphatidylserine, differs from that of a microvesicle, while nucleic acids are present in both types of extracellular vesicles.

Exosomes contain RNA, proteins, lipids, and metabolites that reflect the cell type of origin.



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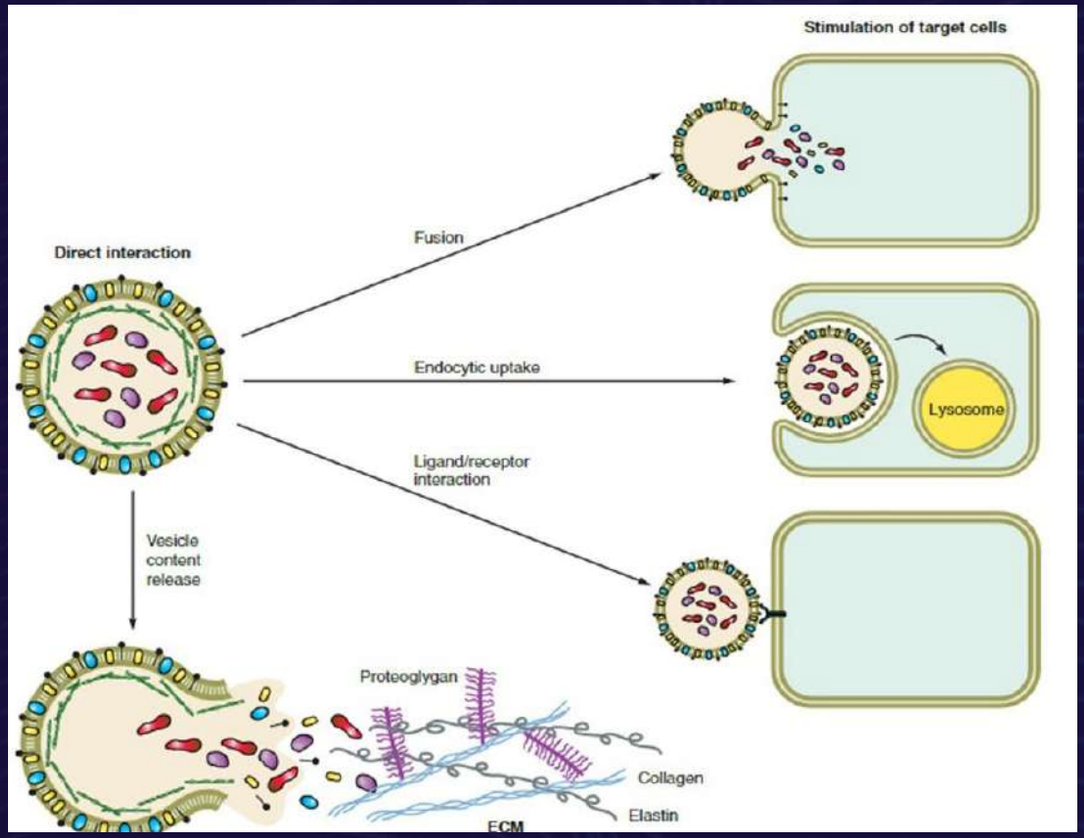
EXOSOME INTERACTION WITH TARGET CELL

The exosomes can interact with the recipient cell through:

- the fusion of the exosomal membrane with that of the target cell;
- undergo phagocytosis through which the exonome is entirely internalized by the target cell;
- communicate with the target cell through receptor-ligand interaction;
- the exosome can release its contents at an extracellular level which will stimulate the target cell;



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EXOSOMES AS A SHUTTLE FOR GENETIC MATERIAL

EXOSOMES CARRY:

- proteins involved in membrane transport and fusion (such as RAB proteins and annexins);
- cytoskeletal proteins;
- adhesion molecules and tetraspanins, membrane-resident;
- cholesterol, ceramide and sphingolipids;
- as well as genetic material;

The exosomes contain **RNA** ((messenger RNA (mRNA), non-coding RNA (ncRNA) and microRNA (miRNA)) and **DNA** (genomic DNA (gDNA) and complementary DNA (cDNA)) and they can transfer genetic information between cells.

THE GENETIC MATERIAL:

- mRNAs / miRNAs can be transferred and influence the transcription profile.
- Donor cell-derived cDNAs (e.g. for c-Myc) can be delivered to the recipient cytoplasm or be generated from reverse transcribed mRNAs.
- Retrotransposons and other DNA elements of the microvesicle can integrate into the recipient genome

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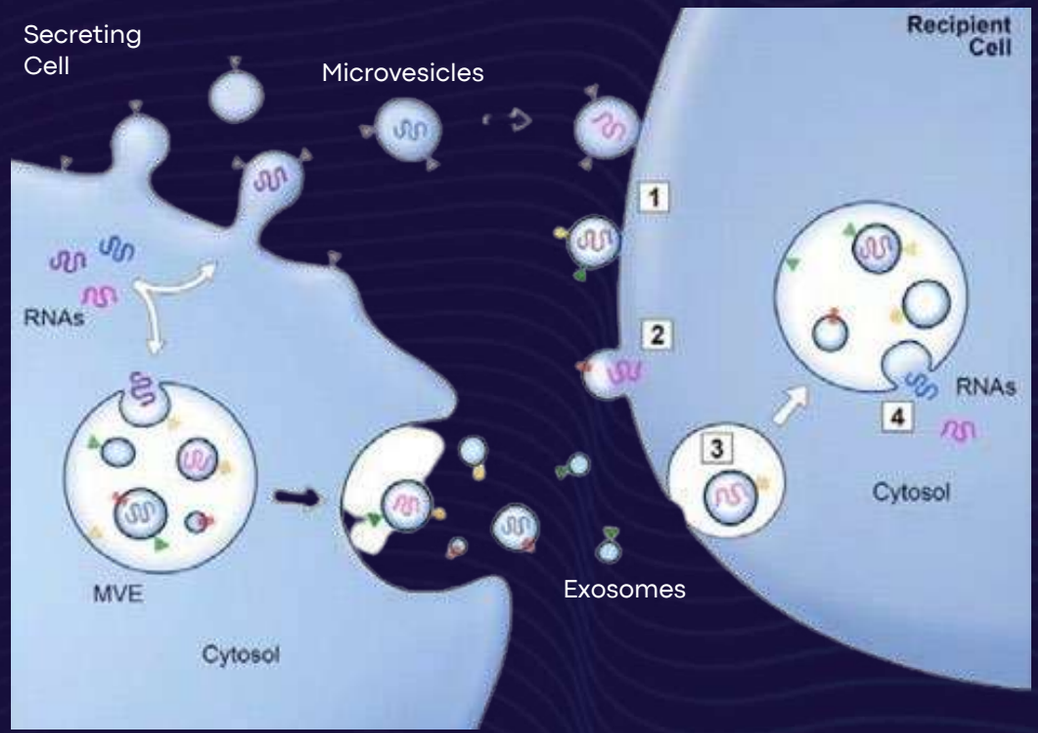
EXOSOMES AS A SHUTTLE FOR GENETIC MATERIAL

Once released into the extracellular environment from the secreting cell, exosomes can anchor themselves to the plasma membrane of the target cell.

The binding vesicles can either fuse directly with the plasma membrane or be endocytosed.

The endocytic vesicles can subsequently fuse with the delimiting membrane of an endocytic compartment. Both pathways give rise to the delivery of proteins and RNA to the membrane or cytosol of the target cell.



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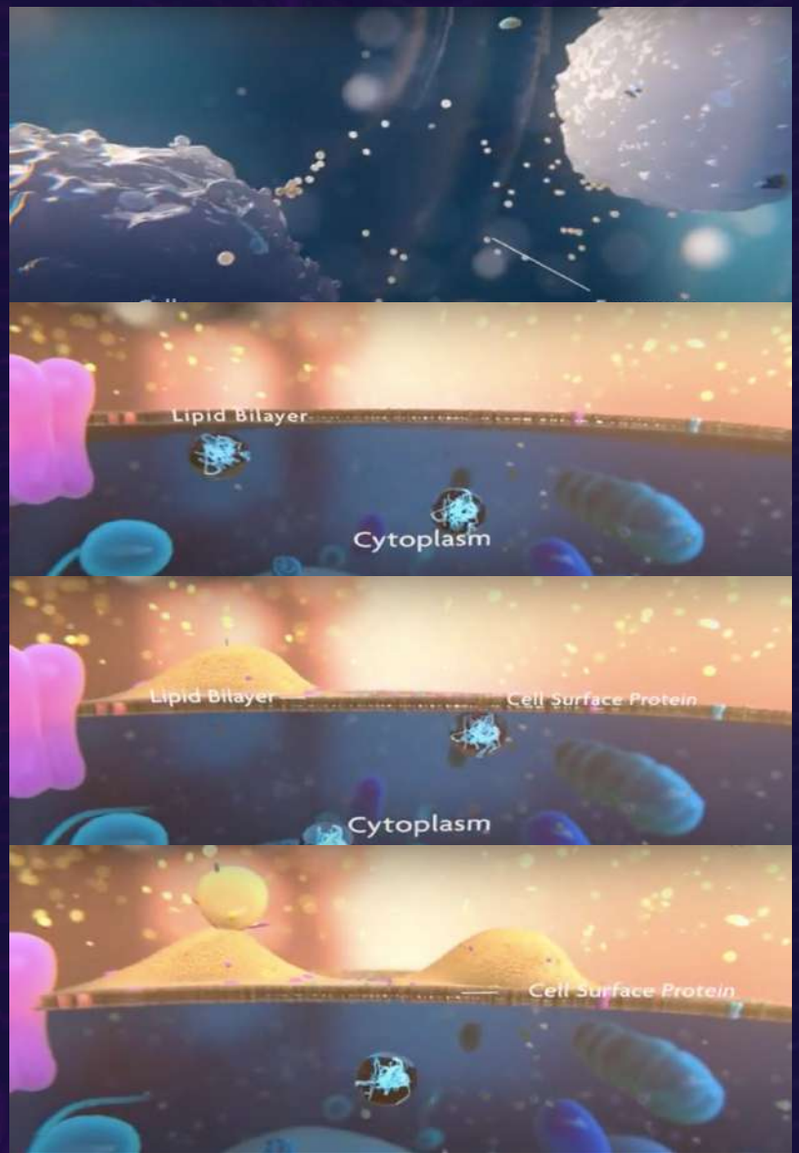
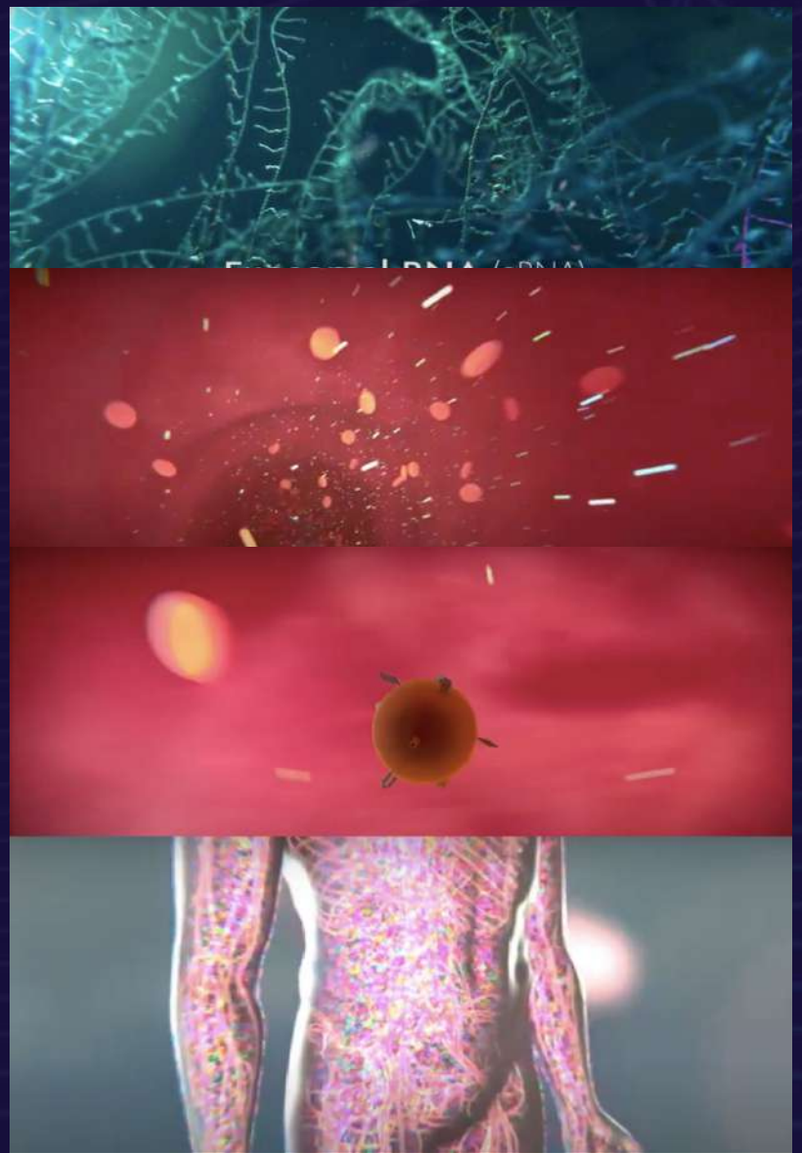
MECHANISM OF ACTION





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MEDIATORS OF CELLULAR COMMUNICATION

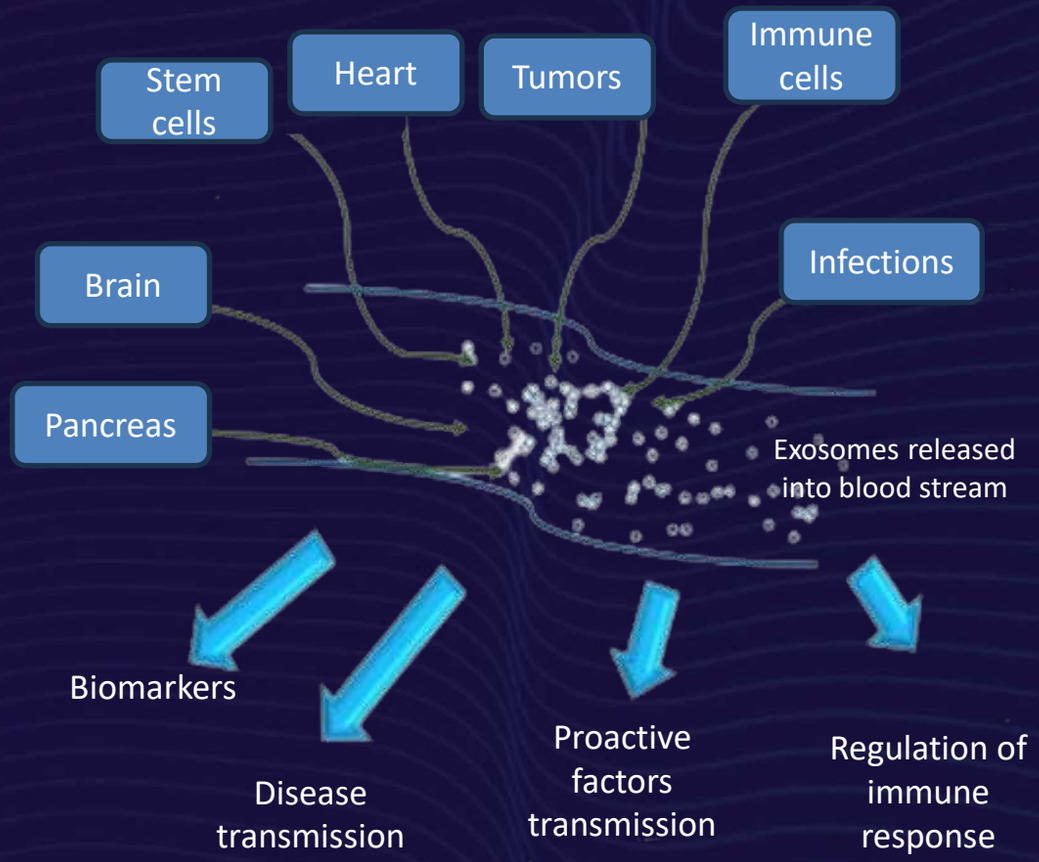
Exosomes are of fundamental importance in conveying critical intercellular messages both in physiological and pathological processes.

Exosomes participate in cell–cell communication, cell maintenance, inflammation, stimulating immune responses and antibacterial effects.

Secreted exosomes are primarily made of DNA, RNA, lipids, metabolites, and cytosolic and cell-surface proteins which are all indicative of cells they originate from.

Subsequently, exosomes are released into the extracellular space where they are taken up by other cells.

Exosomes serve as an additional mediator of intercellular communication, facilitating both short and long-distance communication between cells and tissues.



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EXOSOME MSCs INTERACTION

For many years, efforts to identify the active therapeutic factor in the MSCs secretome have focused on growth factors, cytokines and chemokines(**paracrine effects**).

In recent years, exosomes have been increasingly reported as the principal therapeutic agent in MSC secretion that underpins the regenerative and immunomodulatory capabilities of MSCs in tissue repair.

It is becoming widely known that exosomes are as effective as cell therapies for tissue regeneration for diseases such as stroke, heart failure, arthritis and tissue regeneration.

Although it has been reported that the RNA cargo IN exosome varies according to the tissue sources of MSC exosomes.

Most of (Stem) cell secretome is provided through exosomes.

The intercellular communication in terms of both paracrine and autocrine pathway is mainly fashioned through signalling molecules packaged within exosomes.

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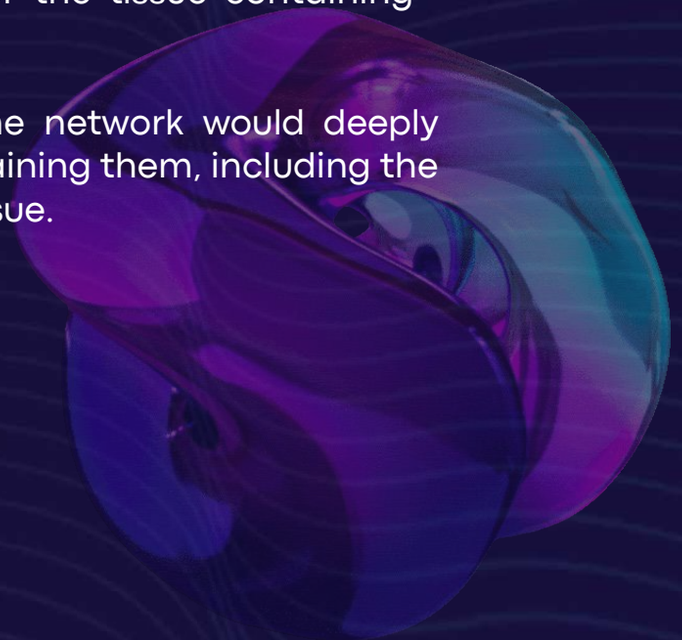
EXOSOME MSCs INTERACTION

When taken up by (Stem) Cells these molecules are released into the cellular interior acting in a modality we have referred to as intracrine fashion, encompassing small peptides, transcription factors, miRNA, long chain RNA, and even DNA quadruplex, imparting features of feed-forward signalling, long term potentiation and memory.

These intracrine, exosome-related dynamics greatly impact on stem cell dynamics, in terms of potency and rescuing potential.

A major problem hampering the enhancement of the self-healing potential brought about by MSC transplantation is the separation from MSCs or the tissue containing them, and the exosomal network associated with these cells.

Unplugging these preparations from their associated exosome network would deeply impair crucial features of the transplanted MSCs or tissues containing them, including the homing, the engraftment and the interplay with the recipient tissue.



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ISOLATION METHODS

The use of exosomes in the clinical setting is restricted due to the lack of standardization in exosome isolation and analysis methods.

Exosomes were originally isolated by ultracentrifugation-based methods, and while these methods remain the gold standard, other methods have been developed to address the challenges associated with ultracentrifugation.

- Ultrafiltration Exosome Isolation
- Sequential Filtration
- Size Exclusion Chromatography (SEC)
- Flow Field-Flow Fractionation (FFFF)
- Hydrostatic Filtration Dialysis (HFD)

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OUR SOLUTION: AUTOLOGIX

AutologIX is a medical device class IIa containing ProtSmart 6 and 2x IDRIA G.

It's a selective concentrator of plasma through an innovative technology of ultrafiltration.

AutologIX is designed to collect and hyper-concentrate autologous exosomes from peripheral blood to be used in the field of regenerative medicine.

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AUTOLOGIX CONCEPT

FILTRATION CUT OFF ⊥15.000 KDA WITH AVERAGE PERFUSION DIAMETER < 5NM

Exosomes Ultrafiltrator

Thanks to its selective ability to concentrate and ultrafilter, water and fragments of salt ions are pushed out in the bag while exosomes, proteins and cells are collected internally into the tubes.

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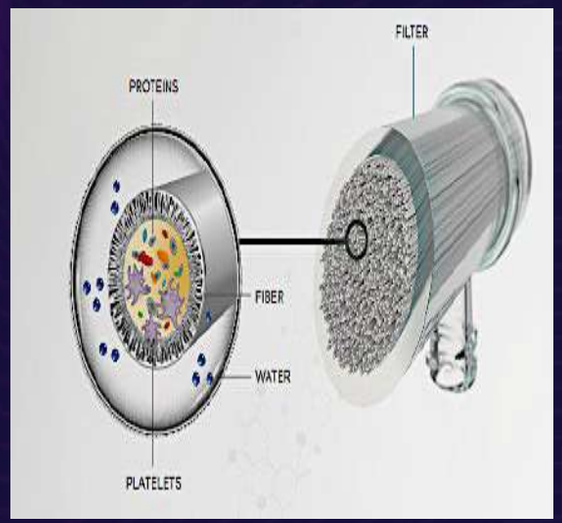
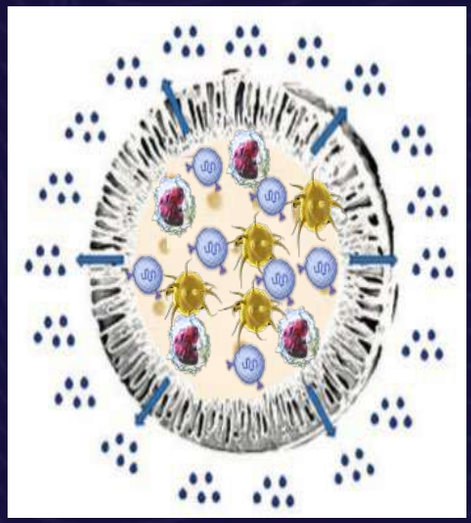
AUTOLOGIX CONCEPT

EXOSOMES ARE TYPICALLY 30–150 NM IN DIAMETER





All the exosomes, cells and cytokines are forced by the pressure of the syringes through the hundreds of hollows of ProtSmart 6 and at the end of the procedure they are all recovered in the syringe.

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AUTOLOGIX CONCEPT

During the centrifugation step of PRP, exosomes are released from the cells and remain suspended in the plasma.

The principle is total restitution and integrum of all the cells, cytokines and exosomes of the patient.

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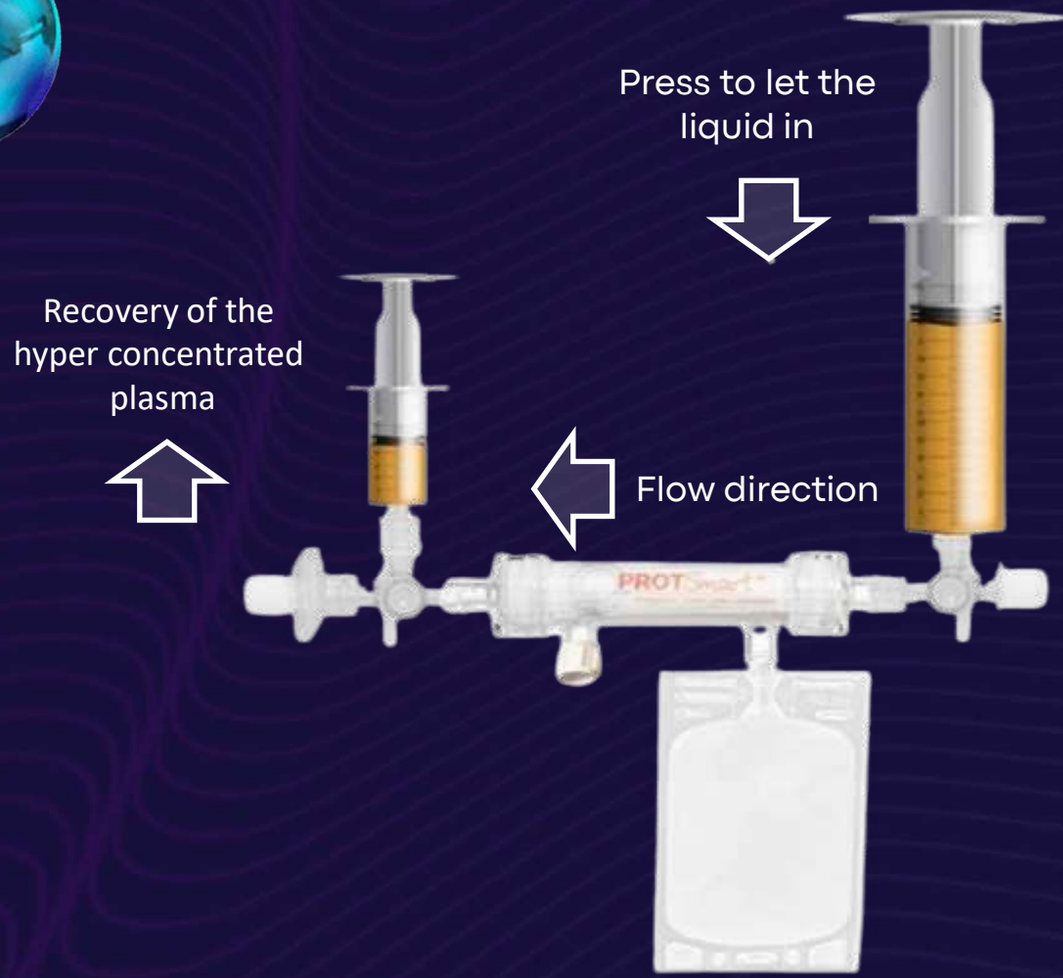
AUTOLOGIX CONCEPT



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AUTOLOGIX CONCEPT

All exosomes, cells and the plasmatic proteins are concentrated from Blood Plasma with ProtSmart6 ultra concentrator and eliminate the plasmatic water to have a hyper concentrated final product.

Recommendation:
26 to 30 ml of Blood Plasma to process with ProtSmart 6.

The final product will be 6-7 ml.

Single 8-minute spin(1500 rgf)..

Accelerated healing

Reduced inflammation

Personalized treatment

Pain relief

Minimally invasive

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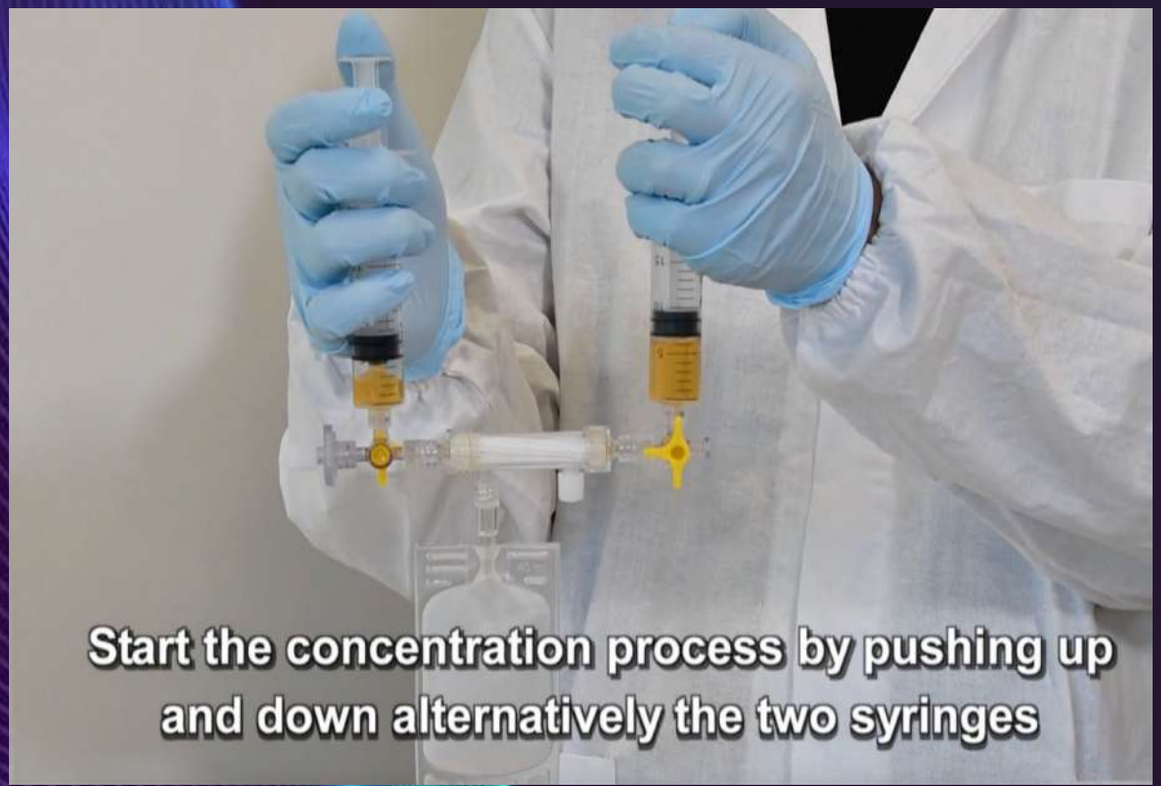
HOW IT WORKS



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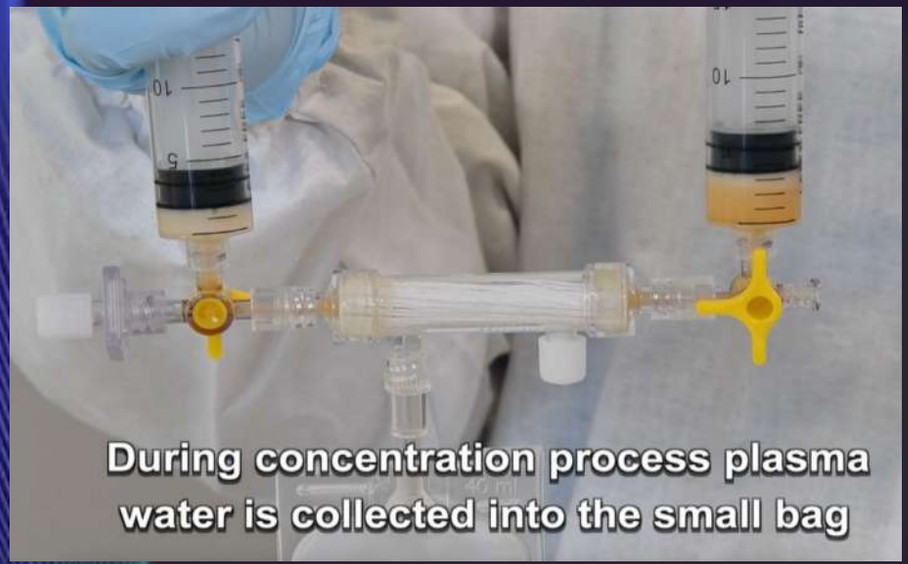
HOW IT WORKS



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AUTOLOGIX INDICATIONS

Musculoskeletal injuries
Autologous platelet exosomes therapy may be beneficial for treating musculoskeletal injuries, such as tendonitis, ligament injuries, and muscle strains. The therapy can stimulate tissue repair and regeneration, reducing inflammation and promoting healing.

Skin rejuvenation
Autologous platelet exosomes therapy may promote skin rejuvenation by stimulating the production of collagen and elastin, reducing the appearance of fine lines and wrinkles, and improving skin texture and tone.

Hair loss
Autologous platelet exosomes therapy may be beneficial for promoting hair growth and improving hair quality. The therapy can stimulate hair follicle stem cells, promoting hair growth and thickening.

Pain management
Autologous platelet exosomes therapy may help alleviate pain associated with various conditions, such as osteoarthritis, tendinopathy, and sports injuries. The therapy can reduce inflammation and promote tissue repair, which can help relieve pain.

Dermatological conditions
Autologous platelet exosomes therapy may be beneficial for treating various dermatological conditions, such as acne, psoriasis, and eczema. The therapy can reduce inflammation and promote tissue regeneration, improving skin health and function.

Wound healing
Autologous platelet exosomes therapy may accelerate the wound healing process by promoting tissue regeneration and reducing inflammation. The therapy can stimulate the growth of new blood vessels, improving oxygen and nutrient delivery to the wound site.

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