



Repair
Regrow
Rejuvenate

Stem Cell Exosomes

Xo Glo[®]

Purified MSC Exosomes

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Xo Glo®

XoGlo® is a purified mesenchymal stem cell (MSC)-derived exosome product that contains a multitude of growth factors that can enhance the coordinated cascade of cellular and biochemical events involved in natural wound healing and skin rejuvenation.

The physiologic effects of the exosomal growth factors in **XoGlo®** can be used to rejuvenate collagen in aging and reduce inflammation. **XoGlo®** has the potential to improve skin texture, reduce scarring, stimulate hair growth and shorten recovery time after cosmetic procedures.

XoGlo® is a cell-free isolate of MSC exosomes. This concentrated biologic product is sterile-filtered and re-suspended in [0.9%] normal saline. Each milliliter of **XoGlo®** contains 1 billion MSC exosomes.

	Amniotic Fluid	Bone Marrow	Xo Glo®
Parent Cell	Maternal Epithelial	Hematopoietic	Mesenchymal
Age	Peri-Natal	Adult, Variable	Peri-Natal
Donors	Multiple	Multiple	Single
Mean Size	Not Tested	70 nm	120 nm

Figure 1. Characterization of exosomes from different sources



Figure 2. Second degree burns in patient with Skin Type VI (left). Seven days after treatment with Xo Glo (middle). Sixty days after treatment with Xo Glo (right), with no scarring or abnormal pigmentation

Exosomes

Powerful regenerative messages in extremely small packages...

Exosomes are nano-scale extracellular vesicles – very small packages of signaling information one thousandth the size of a cell. They are produced by virtually every cell type as a means of intercellular communication. This natural paracrine signaling system allows a healthy body to run like a well-oiled machine.

Exosomes contain proteins such as growth factors, enzymes, receptors, transcription factors and matrix proteins that govern cell structure, function and signaling. They also contain messenger RNA (mRNA), the blueprint for protein production, and micro RNA (miRNA), an important intracellular signaling mediator. Having the same type of membrane as their parent cells, **exosomes** protect these exosomal proteins and miRNA from degradation until they are delivered to the target cell.

When **exosomes** deliver their contents to target cells, exosomal proteins can have direct effects on intracellular processes and signaling. **Exosomal** mRNA may be translated by the target cell to produce numerous copies of regenerative protein. Exosomal miRNA influences target cell protein production by interfering with specific endogenous protein production. **Exosomal** signaling can also alter target cell exosome loading for cascading effects and a more sustained effect than the type of proteins in PRP or amniotic fluid alone.

Mesenchymal Stem Cell Exosomes

This very unique type of exosomes are produced by stem cells of the connective tissue lineage – the origin of skin, hair, bone, muscle, cartilage etc. **MSC exosomes** are very different than exosomes found in adult bone marrow, which has a preponderance of hematopoietic stem cell exosomes, or amniotic fluid, which has primarily maternal epithelial cell exosomes. The distinct ability of **MSC exosomes** to induce connective tissue synthesis may be the basis of what has been observed with stem cell therapy.

Advantages of Young Progenitor Cells

As we age, the number and function of the MSCs in our tissues declines sharply. Aged autologous progenitor cells produce about 30% of the cytokines and significantly different miRNAs compared with perinatal MSCs. This substantial difference in secretome confers a significant advantage of peri-natal MSC exosomes over exosomes from aged autologous or allogeneic progenitor cells.

Effects of MSC exosomes on Skin

- * Stimulate fibroblast proliferation and migration;
- * Increase collagen extracellular matrix production/deposition;
- * Regulate tissue remodeling to reduce scarring;
- * Increase the number of hair follicles in the growth phase;
- * Regenerate dermal papilla cells of hair follicle.



Figure 3. Second degree burn treat with Xo Glo (left) one week after injury. Seven days after treatment with Xo Glo (middle). Four weeks after treatment with Xo Glo (right). Courtesy of Gregory Chernoff MD.

Anti-Inflammatory

MSC exosomes down-regulate inflammatory proteins and upregulate anti-inflammatory proteins.



Figure 4. Rosacea (upper), two days after treatment with Xo Glo (lower).

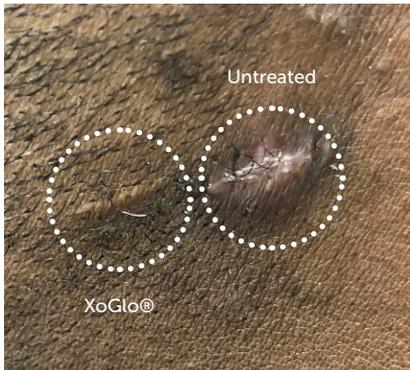


Figure 5. Healed incisions after keloid excisions treated with Xo Glo (left) and untreated (right). Gregory Chernoff MD

Tissue Regeneration & Remodeling

Exosomes derived from mesenchymal stem cells have been shown to reduce apoptosis (programmed cell death), which could lead to less tissue damage in response to disease or injury. MSC Exosomes have the capacity to enhance tissue remodeling by promoting a normal lattice-structure of collagen fibers for reduced scarring and more normal healing.

Regenerative

Exosomes stimulate the proliferation and migration of cells such as fibroblasts, endothelial cells, keratinocytes and specific endogenous progenitor cells. This increases angiogenesis (new blood vessel formation), improves survival of damaged tissues, and reduces scarring.



Figure 6. Healed incision after face lift treated with Xo Glo (lower) and untreated (upper). Gregory Chernoff MD



Xo Glo®

A revolution in regenerative skin therapy. This purified mesenchymal stem cell-derived exosome product delivers regenerative growth factors.

Size	MSC Exosomes
1 mL	1 Billion
2 mL	2 Billion
5 mL	5 Billion



Xo Glo® Pro

The highest concentration of mesenchymal stem cell-derived exosomes. This concentrated product delivers the maximum regenerative effect of MSC exosomes.

Size	MSC Exosomes
1 mL	3 Billion
5 mL	15 Billion

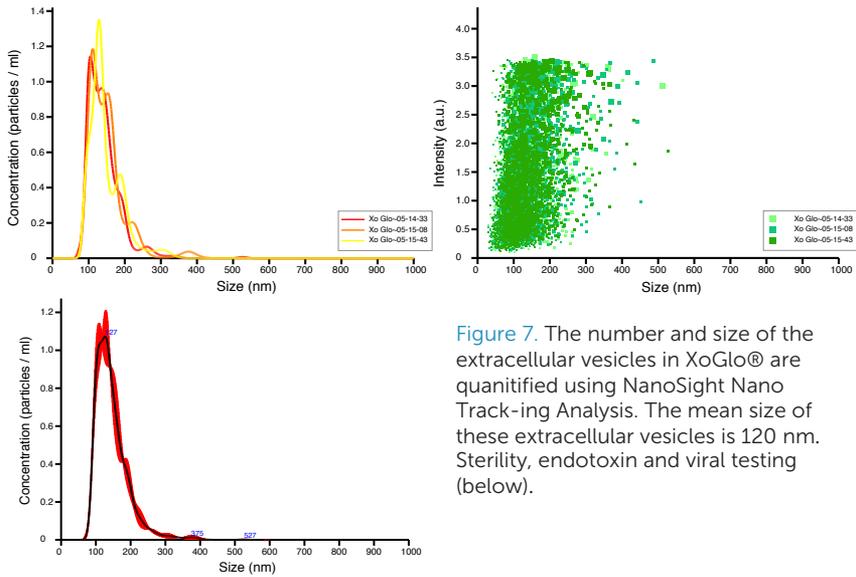


Figure 7. The number and size of the extracellular vesicles in XoGlo® are quantified using NanoSight Nano Track-ing Analysis. The mean size of these extracellular vesicles is 120 nm. Sterility, endotoxin and viral testing (below).

Test	Method	Specification	Result
Sterility	14-Day Sterility per USP <71>	No Growth	No Growth
Sterility	Membrane Filtration per USP <71>	n/a	n/a
Endotoxin	LAL per USP <85>	<0.500 EU/mL	<0.500 EU/mL

Virus Testing			
BKV	PCR Qual	Not Detected	Not Detected
CMV	PCR Qual	Not Detected	Not Detected
EBV	PCR Qual	Not Detected	Not Detected
Hepatitis B	PCR Qual	Not Detected	Not Detected
HBsAg	EIA	Non-Reactive	Non-Reactive
Hepatitis C	qRT-PCR	Not Detected	Not Detected
Hepatitis E	qRT-PCR	Not Detected	Not Detected
HCT	qRT-PCR	Not Detected	Not Detected
HHV6	PCR Qual	Not Detected	Not Detected
HHV7	PCR Qual	Not Detected	Not Detected
HHV8	PCR Qual	Not Detected	Not Detected
HIV-1/2	qRT-PCR	Not Detected	Not Detected
HIV Ab	EIA	Non-Reactive	Non-Reactive
HSV 1/2	PCR Qual	Not Detected	Not Detected
HTLV I/II	qRT-PCR	Not Detected	Not Detected
Norovirus - Genogroup I/II	RT-PCR	Not Detected	Not Detected
Syphilis	EIA	Non-Reactive	Non-Reactive
Zika Virus	RT-PCR	Not Detected	Not Detected
Norovirus - Genogroup I/II	RT-PCR	Not Detected	Not Detected
Syphilis	EIA	Non-Reactive	Non-Reactive
Zika Virus	RT-PCR	Not Detected	Not Detected

Growth Factor (pg/ml)		XoGlo (5 ml)	XoGlo Pro	Amnio2X
AR	Androgen receptor	80	240	23.2
BDNF	Brain-derived neurotrophic factor	2	6	34
bFGF	basic fibroblast growth factor	21	63	5.6
BMP-4	Bone morphogenetic protein-4	0	0	0
BMP-5	Bone morphogenetic protein-5	18817.5	56452.5	847.70
BMP-7	Bone morphogenetic protein-7	0	0	527.7
b-NGF	Nerve growth factor	0	0	0
EGF	Epidermal growth factor	19	57	53
EGFR	Epidermal growth factor receptor	277	831	824.8
EG-VEGF	Endocrine gland-derived VEGF	0	0	1421.5
FGF-4	Fibroblast growth factor-4	0	0	0
FGF-7	Fibroblast growth factor-7	79	237	9.9
GDF-15	Growth/differentiation factor-15	29005.5	87016.5	2642.4
GDNF	Glial cell-derived neurotrophic factor	70.5	211.5	8.30
GH	Growth hormone	1020.5	3061.5	128
HB-EGF	Heparin-binding EGF-like growth factor	0	0	0
HGF	Hepatocyte growth factor	808.5	2425.5	3015.6
IGFBP-1	IGF binding protein-1	894.5	2683.5	16644
IGFBP-2	IGF binding protein-2	8755.5	26266.5	5,898.70
IGFBP-3	IGF binding protein-3	27222.5	81667.5	277,006.20
IGFBP-4	IGF binding protein-4	0	0	13579.5
IGFBP-6	IGF binding protein-6	1338	4014	80901.4
IGF-1	Insulin-like growth factor 1	0	0	0
Insulin	Insulin	2465.5	7396.5	370.1
MCSF R	Macrophage colony-stimulating factor	121	363	9933.3
NGF R	Nerve growth factor receptor	16	48	110.4
NT-3	Neurotrophin-3	22.5	67.5	0
NT-4	Neurotrophin-4	0	0	0
OPG	Osteoprotegerin	34088.5	102265.5	43.90
PDGF-AA	Platelet-Derived Growth Factor	182	546	440.7
PIGF	Placental growth factor	364.5	1093.5	13.3
SCF	Stem Cell Factor	600	1800	9.7
SCF R	Stem Cell Factor Receptor	71	213	342.4
TGF α	Transforming growth factor alpha	0	0	0
TGF β 1	Transforming growth factor beta 1	0	0	941.7
TGF β 3	Transforming growth factor beta 3	1702.5	5107.5	0
VEGF	Vascular endothelial growth factor	914	2742	5.1
VEGF R2	Vascular endothelial growth factor receptor 2	0	0	33.1
VEGF R3	Vascular endothelial growth factor receptor 3	68	204	23.2

Growth Factor Functions

Activated by binding testosterone and dihydrotestosterone and translocating into the nucleus

Member of the neurotrophin family of growth factors, which are related to the canonical nerve growth factor

Broad mitogenic and cell survival activities, embryonic development, cell growth, morphogenesis, tissue repair

Bone and cartilage development, specifically tooth and limb development and fracture repair

Promotes dendritic growth in cultured sympathetic neurons

Transformation of mesenchymal cells into bone and cartilage

Regulation of growth, maintenance, proliferation, and survival of certain target neurons

Epithelial cell proliferation and differentiation

Receptor for members of the epidermal growth factor family (EGF family)

Involved in normal and pathological reproductive processes

Embryonic development, cell growth, morphogenesis, tissue repair, tumor growth and invasion

Potent mitogen that regulates epithelial cell migration and differentiation

Involved with regulation of inflammation, apoptosis, cell repair and cell growth

Potently promotes the survival of many types of neurons

Stimulates growth, cell reproduction, and cell regeneration

Unique receptor for diphtheria toxin and functions in juxtacrine signaling in cells

Growth, motility, morphogenesis of epithelial cells, endothelial cells, hemopoietic progenitor cells & T cells

Regulates metabolic and vascular homeostasis

Regulation of cell proliferation, migration, and adhesion

Main IGF transport protein in the bloodstream

Prolongs the half-life of the IGF and consistently inhibits several cancer cells in vivo and in vitro

Promotion of apoptosis in some cells and inhibition of angiogenesis, act as a tumour suppressor

Important role in childhood growth, anabolic effects in adults

Stimulate glucose uptake by cells

Causes hematopoietic stem cells to differentiate into macrophages or other related cell type

Regulation of insulin-dependent glucose uptake, mediates survival & death of neural cells, circadian oscillation

Supports survival and differentiation of existing neurons, encourages growth and differentiation of new neurons

Proliferation and differentiation of periodontal ligament cells; induce cell migration in melanoma

Inhibits osteoclastogenesis and bone resorption

Potent mitogen for cells of mesenchymal origin, including fibroblasts, smooth muscle cells and glial cells

Pro-angiogenic factor

Involved in hematopoiesis, spermatogenesis, and melanogenesis

Plays a role in cell survival, proliferation, and differentiation

Activates a signaling pathway for cell proliferation, differentiation and development.

Control of cell growth, cell proliferation, cell differentiation, and apoptosis

Cell adhesion, ECM formation, migration of epidermal & dermal cells, M2 macrophage & T reg polarization

Stimulates the formation of blood vessels

Regulates endothelial migration and proliferation

Mediates lymphangiogenesis

Immune Factor (pg/ml)		XoGlo (5 ml)	XoGlo Pro	Amnio2X
BLC	B lymphocyte chemokine/CXCL13	0	0	164.7
Eotaxin	Eotaxin	211.5	634.5	15
Eotaxin-2	Eotaxin-2	24	72	8.7
G-CSF	Granulocyte-colony stimulating factor	15.5	46.5	192.4
GM-CSF	Granulocyte-macrophage CSF	44.5	133.5	1.6
I-309	I-309	48.5	145.5	21.2
ICAM-1	Intercellular Adhesion Molecule 1	18894	56682	63,072.10
IFN- γ	Interferon gamma	0	0	16.5
IL-1 α	Interleukin 1 alpha	3827.5	11482.5	23.4
IL-1 β	Interleukin 1 beta	147.5	442.5	3.8
IL-1ra	Interleukin 1 receptor antagonist	2074	6222	972.1
IL-2	Interleukin 2	0	0	3
IL-4	Interleukin 4	20	60	2.3
IL-5	Interleukin 5	0	0	4.1
IL-6	Interleukin 6	7735.5	23206.5	90.40
IL-6R	Interleukin 6 receptor	51	153	692.3
IL-7	Interleukin 7	150	450	0
IL-8	Interleukin-8	697	2091	14
IL-10	Interleukin-10	34	102	3.1
IL-11	Interleukin-11	9832	29496	348.00
IL-12p40	Interleukin-12p40	217	651	9.5
IL-12p70	Interleukin-12p70	17	51	1.1
IL-13	Interleukin 13	34.5	103.5	1.3
IL-15	Interleukin 15	36	108	2.1
IL-16	Interleukin 16	645	1935	7
IL-17	Interleukin 17	18	54	1.3
MCP-1	Monocyte chemotactic protein-1	10147	30441	273.40
MCSF	Macrophage colony-stimulating factor	136.5	409.5	5.4
MIG	Mitogen-inducible gene 6	61	183	1
MIP-1 α	Macrophage inflammatory protein 1 alpha	41.5	124.5	5.5
MIP-1 β	Macrophage inflammatory protein 1 beta	787.5	2362.5	17.4
MIP-1 δ	Macrophage inflammatory protein 1 delta	0	0	1493.8
PDGF-BB	Platelet-derived growth factor	4832.5	14497.5	2
RANTES	RANTES/CCL5	8188.5	24565.5	56.40
TIMP-1	Tissue inhibitor of metalloprotease-1	108565.5	325696.5	4,743.20
TIMP-2	Tissue inhibitor of metalloprotease-2	147236.5	441709.5	10,784.70
TNF α	Tumor necrosis factor alpha	131.5	394.5	21.20
TNF β	Tumor necrosis factor beta	0	0	0.00
TNF RI	Tumor necrosis factor receptor I	2168	6504	7,808.60
TNF RII	Tumor necrosis factor receptor II	0	0	12635.3

Immune Factor Functions

Chemotactic for B cells

Stimulates migration of eosinophils from the small blood vessels in the lungs

Stimulates the migration of human eosinophil and basophil leukocytes.

Stimulates bone marrow to produce granulocytes and stem cells and release them into circulation

Stimulates stem cells to produce granulocytes (neutrophils, eosinophils, and basophils) and monocytes

Binds to and activates endothelial cell functions and acts as an angiogenic molecule in vivo

Role in inflammation and regulation of vascular permeability

Antiviral activity, potent macrophage activator, antiproliferative effects on transformed cells

Production of inflammation, as well as the promotion of fever and sepsis

Important mediator of the inflammatory response, cell proliferation, differentiation, apoptosis

Natural inhibitor of the pro-inflammatory effect of IL1 β

Regulates the activities of white blood cells (leukocytes)

Induces differentiation of naive helper T cells (Th0 cells) to Th2 cells.

Stimulates B cell growth, increases IgA secretion, key mediator in eosinophil activation

Both a pro-inflammatory cytokine and anti-inflammatory myokine; induces the acute phase response

Regulates the immune response, hematopoiesis, the acute phase response and inflammation

T-cell development and survival, homeostasis of mature T-cells

Attracts and activates neutrophils in inflammatory region

Inhibits the activity of Th1 cells, NK cells, and macrophages

Hematopoietic cytokine with thrombopoietic activity

Chemoattractant for macrophages, promotes the migration of bacterially stimulated dendritic cells

Differentiation of naive T cells into Th1 cells, stimulates T cells & production of IFN- γ and TNF- α

Central regulator in IgE synthesis, mediator of allergic inflammation and asthma

Regulates activation and proliferation of T and natural killer (NK) cells

Chemoattractant, modulator of T cell activation, and inhibitor of HIV replication

Pro-inflammatory cytokine

Recruitment of monocytes to sites of injury and infection

Hematopoietic growth factor that regulates the proliferation, differentiation and activation of monocytes

Triggers antitumor effect and attenuates progesterone resistance in endometrial carcinoma cells

Proinflammatory activities in vitro including leukocyte chemotaxis

Chemoattractant for natural killer cells, monocytes

Chemotactic for neutrophils, monocytes, and lymphocytes

proliferation & migration of fibroblasts, osteoblasts, tenocytes, etc; blood vessel formation

Homing and migration of effector and memory T cells during acute infections

Regulates matrix metalloproteinases (MMPs), and disintegrin-metalloproteinases (ADAMs and ADAMTSs)

Suppresses proliferation response to angiogenic factors, inhibits protease activity; remodelling of ECM

Systemic inflammation and acute phase reaction

Target cell killing or growth stimulation, adhesion molecule (ICAM-1) expression & induction of differentiation

Initiates the subsequent cascade of caspases (aspartate-specific cysteine proteases) mediating apoptosis

Activation and proliferative expansion of immunosuppressive Tregs, tolerogenic DCs and MDSCs

FAQ

What is an exosome?

Exosomes are extracellular vesicles ranging between 30-150 nm that are produced by virtually every cell type as a means of intercellular communication. They contain proteins (growth factors), mRNA (blueprint for protein production) and micro RNA (on-off switch for specific protein production), all contained within a membrane similar to their parent cells that protects exosomal proteins and RNA from degradation until they are delivered to the target cell.

Does the parent cell type of the exosome matter?

Yes, the cargo of the exosomes varies significantly according to the specific parent cell type. In this case, these MSC exosomes carry the developmental message of perinatal mesenchymal stem cells, which are progenitor cells of the connective tissue lineage, meaning that they are involved in development of tissues like skin, hair, bones, muscle and cartilage.

How does Xo Glo compare to amniotic fluid?

Amniotic fluid has a significantly different protein profile than Xo Glo and lacks key proteins like TGF- β 3, which is an important modulator of inflammation and immune function. Also, the exosomes present in amniotic fluid are primarily of maternal epithelial cell origin, which means that their cargo is substantially different than that of an MSC exosome.

How does Xo Glo compare to “stem cell” products often referred to as umbilical cord blood, Wharton’s jelly or biologic allograft?

After thawing these frozen “stem cell” products, the viability of these allogeneic cells approaches zero, meaning that their effects are dependent on the growth factors and the low concentration of exosomes present in the product. Unlike Xo Glo, which has a very high concentration of MSC exosomes, these growth factors are not protected by the liposomal membrane.

How does this compare to bone-marrow derived exosome products?

Bone-marrow derived exosomes originate primarily from hematopoietic stem cells (HSCs) rather than mesenchymal stem cells, which are the source of the exosomes in Xo Glo®. These HSCs are progenitor cells of the blood cell lineage, not the connective tissue lineage, and so their exosomal cargo is much different from that of MSC exosomes. The very low numbers of MSCs that are present in adult bone marrow also differ significantly from peri-natal MSCs in their exosome production, because of the specific microenvironment in which these cells reside, as well as the age of the cells.



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Distributed by
Refine USA
340 3rd Avenue South
Jacksonville Beach, FL
refineusa.com | 866-590-5533

