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kimera EXOSOMES

Camp Bowie Wellness Systems, LLC. Your Kimera Representative

XoGlo®

Purified MSC Exosomes

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/regeneration.

The physiologic effects of the exosomal growth factors in **XoGlo®** can be used to stimulate healing of acute and chronic wounds, regenerate collagen in aging and damaged skin and reduce inflammation. **XoGlo®** has the potential to accelerate wound healing, 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

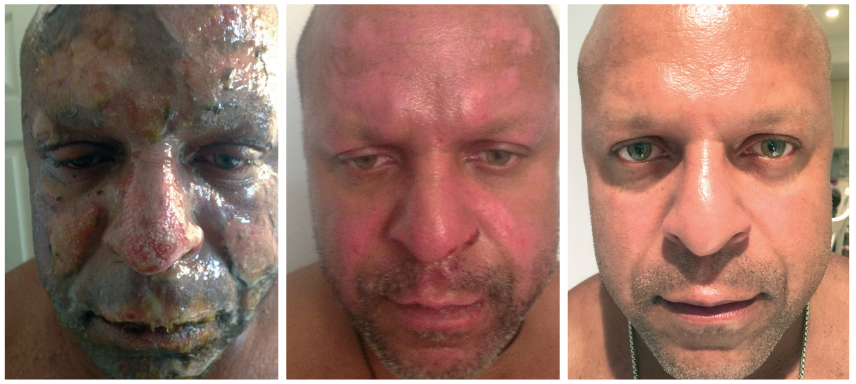

Figure 2. Second degree burns in patient with Skin Type VI (left). Seven days after treatment with Xo Glo (middle). Sixty days after treatment with Xo Glo (right), with no scarring or abnormal pigmentation

Exosomes

Powerful regenerative message 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 many of the remarkable clinical benefits that have 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 peri-natal 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;
* Promote angiogenesis in acute and chronic wounds;
* Increase collagen extracellular matrix production/deposition;
* Modulate inflammation and immune response;
* Regulate tissue remodeling to reduce scarring;
* Increase the number of hair follicles in the growth phase;
* Regenerate dermal papilla cells of hair follicle.

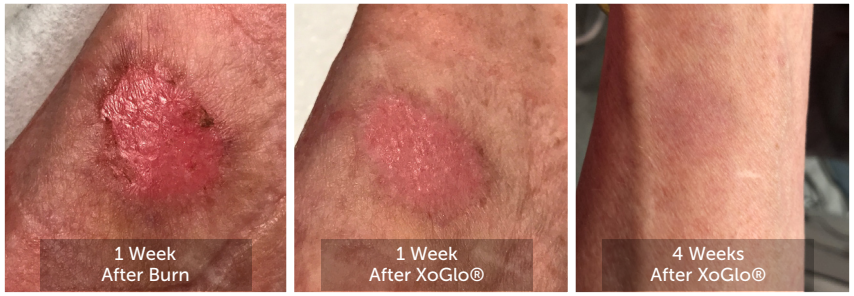

Figure 3. Second degree burn treated with Xo Glo (left) one week after injury. Seven days after treatment with Xo Glo (middle). Four weeks after treatment with Xo Glo (right). Courtesy of Gregory Chernoff MD.

Anti-Inflammatory

By down-regulating inflammatory proteins and upregulating anti-inflammatory proteins, MSC exosomes can reduce inflammation, which is a central mechanism of many autoimmune, inflammatory and degenerative conditions, as well as scarring.

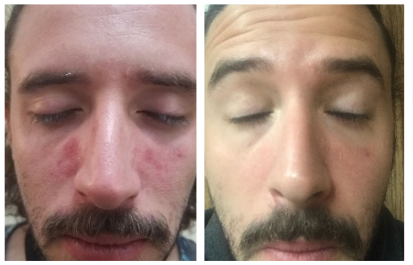

Figure 4. Rosacea (left), two days after treatment with Xo Glo (right).

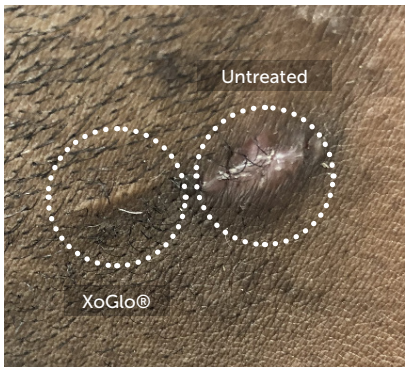

Figure 5. Healed incisions after keloid excisions treated with Xo Glo (left) and untreated (right). Gregory Chernoff MD

Regenerative

Exosomes stimulate the proliferation and migration of cells such as fibroblasts, endothelial cells, keratinocytes and specific endogenous progenitor cells that are involved in healing damaged tissues to increase angiogenesis (new blood vessel formation), improve survival of damaged tissues, accelerate wound healing and skin regeneration, and reduce scarring.

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.

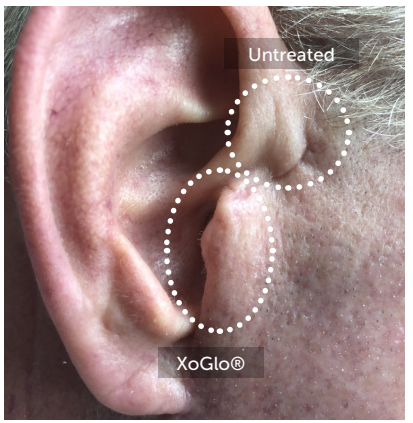

Figure 6. Healed incision after face lift treated with Xo Glo (lower) and untreated (upper). Gregory Chernoff MD

Xo Glo®

A revolution in regenerative skin therapy. This purified mesenchymal stem cell-derived exosome product delivers regenerative growth factors to enhance the cascade of events involved in normal wound healing.

Size	MSC Exosomes
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 for the most difficult wound healing challenges.

Size	MSC Exosomes
1 ml	3 Billion
5 ml	15 Billion

Amnio2X®

Purified amniotic fluid concentrate. Amnio 2X can optimize the results of regenerative skin therapy such as microneedling, scar revision or laser skin resurfacing, and also in musculoskeletal treatments and pain management.

Size	Amniotic Fluid Exosomes
1 ml	300 Billion
2 ml	600 Billion

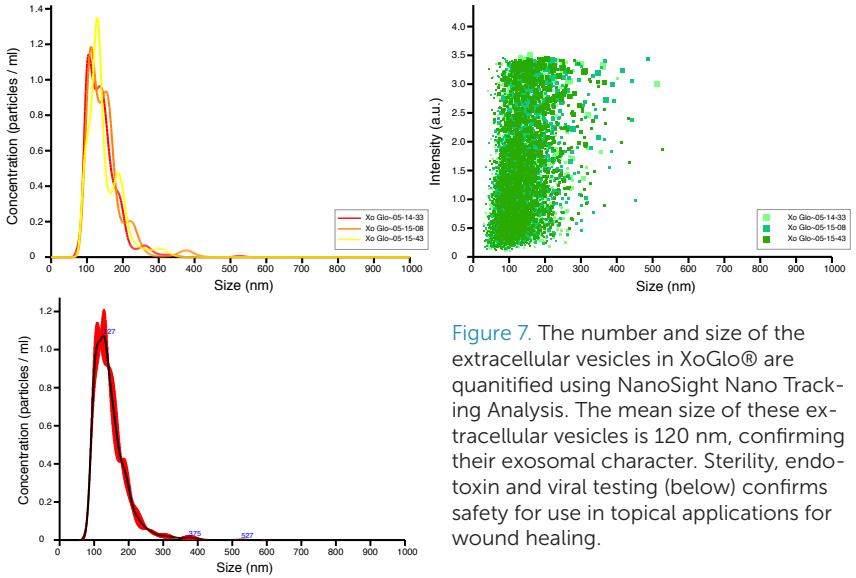

Figure 7. The number and size of the extracellular vesicles in XoGlo® are quanitified using NanoSight Nano Tracking Analysis. The mean size of these extracellular vesicles is 120 nm, confirming their exosomal character. Sterility, endotoxin and viral testing (below) confirms safety for use in topical applications for wound healing.

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	Growth Factor Functions
AR	Androgen receptor	80	240	23.2	Activated by binding testosterone and dihydrotestosterone and translocating into the nucleus
BDNF	Brain-derived neurotrophic factor	2	6	34	Member of the neurotrophin family of growth factors, which are related to the canonical nerve growth factor
bFGF	basic fibroblast growth factor	21	63	5.6	Broad mitogenic and cell survival activities, embryonic development, cell growth, morphogenesis, tissue repair
BMP-4	Bone morphogenetic protein-4	0	0	0	Bone and cartilage development, specifically tooth and limb development and fracture repair
BMP-5	Bone morphogenetic protein-5	18817.5	56452.5	847.70	Promotes dendritic growth in cultured sympathetic neurons
BMP-7	Bone morphogenetic protein-7	0	0	527.7	Transformation of mesenchymal cells into bone and cartilage
b-NGF	Nerve growth factor	0	0	0	Regulation of growth, maintenance, proliferation, and survival of certain target neurons
EGF	Epidermal growth factor	19	57	53	Epithelial cell proliferation and differentiation
EGFR	Epidermal growth factor receptor	277	831	824.8	Receptor for members of the epidermal growth factor family (EGF family)
EG-VEGF	Endocrine gland-derived VEGF	0	0	1421.5	Involved in normal and pathological reproductive processes
FGF-4	Fibroblast growth factor-4	0	0	0	Embryonic development, cell growth, morphogenesis, tissue repair, tumor growth and invasion
FGF-7	Fibroblast growth factor-7	79	237	9.9	Potent mitogen that regulates epithelial cell migration and differentiation
GDF-15	Growth/differentiation factor-15	29005.5	87016.5	2642.4	Involved with regulation of inflammation, apoptosis, cell repair and cell growth
GDNF	Glial cell-derived neurotrophic factor	70.5	211.5	8.30	Potently promotes the survival of many types of neurons
GH	Growth hormone	1020.5	3061.5	128	Stimulates growth, cell reproduction, and cell regeneration
HB-EGF	Heparin-binding EGF-like growth factor	0	0	0	Unique receptor for diphtheria toxin and functions in juxtacrine signaling in cells
HGF	Hepatocyte growth factor	808.5	2425.5	3015.6	Growth, motility, morphogenesis of epithelial cells, endothelial cells, hemopoietic progenitor cells & T cells
IGFBP-1	IGF binding protein-1	894.5	2683.5	16644	Regulates metabolic and vascular homeostasis
IGFBP-2	IGF binding protein-2	8755.5	26266.5	5,898.70	Regulation of cell proliferation, migration, and adhesion
IGFBP-3	IGF binding protein-3	27222.5	81667.5	277,006.20	Main IGF transport protein in the bloodstream
IGFBP-4	IGF binding protein-4	0	0	13579.5	Prolongs the half-life of the IGF and consistently inhibits several cancer cells in vivo and in vitro
IGFBP-6	IGF binding protein-6	1338	4014	80901.4	Promotion of apoptosis in some cells and inhibition of angiogenesis, act as a tumour suppressor
IGF-1	Insulin-like growth factor 1	0	0	0	Important role in childhood growth, anabolic effects in adults
Insulin	Insulin	2465.5	7396.5	370.1	Stimulate glucose uptake by cells
MCSF R	Macrophage colony-stimulating factor	121	363	9933.3	Causes hematopoietic stem cells to differentiate into macrophages or other related cell type
NGF R	Nerve growth factor receptor	16	48	110.4	Regulation of insulin-dependent glucose uptake, mediates survival & death of neural cells, circadian oscillation
NT-3	Neurotrophin-3	22.5	67.5	0	Supports survival and differentiation of existing neurons, encourages growth and differentiation of new neurons
NT-4	Neurotrophin-4	0	0	0	Proliferation and differentiation of periodontal ligament cells; induce cell migration in melanoma
OPG	Osteoprotegerin	34088.5	102265.5	43.90	Inhibits osteoclastogenesis and bone resorption
PDGF-AA	Platelet-Derived Growth Factor	182	546	440.7	Potent mitogen for cells of mesenchymal origin, including fibroblasts, smooth muscle cells and glial cells
PIGF	Placental growth factor	364.5	1093.5	13.3	Pro-angiogenic factor
SCF	Stem Cell Factor	600	1800	9.7	Involved in hematopoiesis, spermatogenesis, and melanogenesis
SCF R	Stem Cell Factor Receptor	71	213	342.4	Plays a role in cell survival, proliferation, and differentiation
TGFa	Transforming growth factor alpha	0	0	0	Activates a signaling pathway for cell proliferation, differentiation and development.
TGF ⊠1	Transforming growth factor beta 1	0	0	941.7	Control of cell growth, cell proliferation, cell differentiation, and apoptosis
TGF ⊠3	Transforming growth factor beta 3	1702.5	5107.5	0	Cell adhesion, ECM formation, migration of epidermal & dermal cells, M2 macrophage & T reg polarization
VEGF	Vascular endothelial growth factor	914	2742	5.1	Stimulates the formation of blood vessels
VEGF R2	Vascular endothelial growth factor receptor 2	0	0	33.1	Regulates endothelial migration and proliferation
VEGF R3	Vascular endothelial growth factor receptor 3	68	204	23.2	Mediates lymphangiogenesis

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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-☒	Interferon gamma	0	0	16.5
IL-1☒	Interleukin 1 alpha	3827.5	11482.5	23.4
IL-1☒	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☒	Macrophage inflammatory protein 1 alpha	41.5	124.5	5.5
MIP-1☒	Macrophage inflammatory protein 1 beta	787.5	2362.5	17.4
MIP-1☒	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
TMP-2	Tissue inhibitor of metalloprotease-2	147236.5	441709.5	10,784.70
TNFa	Tumor necrosis factor alpha	131.5	394.5	21.20
TNFb	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 IL1β
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

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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 peri-natal 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-β3, which is an important modulator of inflammation and immune function. Also, the exosomes present in amniotic fluid are primarly 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 being frozen for storage, the number of viable cells in these stem cell products, is very low. Also, any viable allogeneic cells only survive for a very short period time, during which they act by releasing exosomes, meaning that the effects of these products are dependent on the growth factors and the low concentration of exosomes present. Xo Glo® has billions of peri-natal MSC exosomes, and these exosomes remain viable after frozen storage, Also unlike Xo Glo, the growth factors in these products are not protected from degradation by a 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 microevironment in which these cells reside, as well as the age of the cells.

Contact us with your questions: at www.campbowiehealth.com