BioIntegrate™

GeneXStem™

UMBILICAL CORD TISSUE-BASED SOLUTIONS

GeneXSTEM™ is a minimally manipulated tissue-based product derived from Wharton's Jelly of the umbilical cord for homologous use. GeneXSTEM™ is an exciting alternative regenerative medicine therapy and can be used as options to NSAIDs & steroid injections and help assist with pain in musculoskelatal injuries.

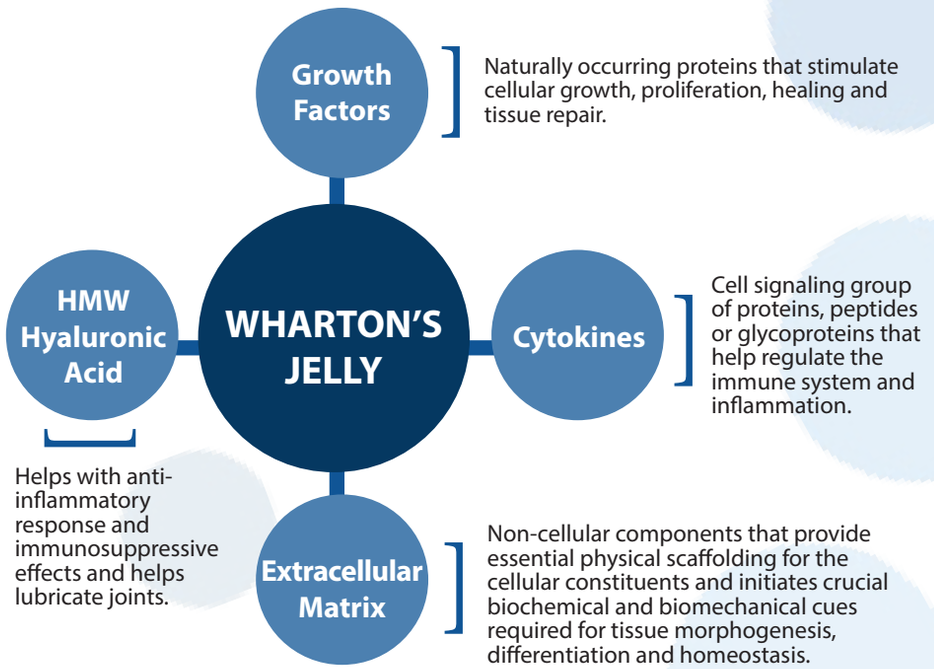
Wharton's Jelly is a gel-like tissue that has unique characteristics of providing structural support, cushioning, and lubrication in the body. Wharton's Jelly may be preferred over other regenerative medicine tissue-types because it contains a higher concentration of long-chain hyaluronic acid, and growth factors; up to 50 times more.

Common Treatment Areas

- **Large joints (Knee, Hip, Shoulder & Ankle)**
- **Chronic partial rotator cuff tears**
- **Persistent partial tendon tears (Tennis Elbow)**
- **Plantar fasciitis / Bone Spurs**
- **Quadriceps and patellar tendon tears**
- **Muscular tears**
- **Meniscus and cartilage tears**
- **Intervertebral disc, SI and spinal facet joints**
- **Osteoarthritis**

WHY WHARTON'S JELLY

WHARTON'S JELLY has a greater abundance of essential regenerative components than other tissue-types, making it an excellent option for regeneration and to help reduce inflammation.



GeneXSTEM™ Product Components[1]

Growth Factors

IGFBP-3 — 24,985.5 pg/ml
Regulates cell growth

IGFBP-4 — 12,302.0 pg/ml
Regulates cell growth

IGFBP-6 — 7,711.1 pg/ml
Regulates cell growth

IGFBP-2 — 6,900.6 pg/ml
Regulates cell growth

FGF-7 — 102.2 pg/ml
Plays important role in regulation of embryonic development, cell proliferation and cell differentiation. Required for normal branching morphogenesis. Possible major paracrine effector of normal epithelial cell proliferation

EG-VEGF — 32.2 pg/ml
Inhibits Extracellular Matrix degradation

TGFa — 385.9 pg/ml
Promotes cell proliferation, differentiation, and development

IGFBP-1 — 5,211.4 pg/ml
Regulates cell migration and metabolism

VEGF — 15.8 pg/ml
Induces proliferation and migration of vascular endothelial cells, essential for both physiological and pathological angiogenesis. Active in vasculogenesis and endothelial cell growth. Promotes cell migration, inhibits apoptosis and induces permeabilization of blood vessels

PDGF-AA — 31.9 pg/ml
Regulates proliferation and migration of myocytes and supports angiogenesis

VEGF R3 — 16.8 pg/ml
Regulates blood and lymphatic vessel development and homeostasis

B-NGF — 12.8 pg/ml
Regulates growth and the differentiation of sympathetic and certain sensory neurons

EGF R — 14.4 pg/ml
Induces cell proliferation

bFGF — 311.4 pg/ml
Has broad mitogenic and angiogenic activities that have been implicated in diverse biological processes, such as limb and nervous system development, wound healing, and tumor growth

HGF — 266.6 pg/ml
Potent mitogen for mature parenchymal hepatocyte cells, seems to be a hepatotrophic factor, and acts as a growth factor for a broad spectrum of tissues and cell types

Anti-Inflammatory

TNF RI — 191.6 pg/ml
Inhibits TNF-a induced inflammation

TNF RII — 89.9 pg/ml
Inhibits TNF induced apoptosis

IL-1ra — 58.8 pg/ml
Inhibits IL1 -alpha and -beta, inflammation, pain signaling, and tissue degradation

[1] Definitions and descriptions are from the National Center for Biotechnology Information, US National Library of Medicine. Actual results listed are averages from an independent, multi-batch, multi-sample source of GeneXSTEM™: ELISA assay testing conducted by RayBiotech, Inc. Future numbers may vary depending on batch.

Abundance of Growth Factors and Cytokines in GeneXSTEM™

Independent testing on the biologic components of GeneXSTEM™ confirm an abundance of cytokines and growth factors that are known to support the body's natural healing and regenerative processes.[1]

- Helps reduce pain signaling and inflammation [2,3]
- Potential to inhibit tissue degradation stemming from chronic or overproduction of IL-1 alpha [2,3]
- Plethora of growth factors associated with regulation of cell growth and migration that support angiogenesis and morphogenesis [4,5,6]
- Cytokines that play a role in modulating tissue homeostasis, immunomodulation, and signaling that support the natural wound healing cascade [4,5,6,7]

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GSTEM-Compv3 4-19

GeneXSTEM™ Product Components[1]

Wound Healing

GDF-15 — 89.2 pg/ml
Acts as pleiotropic cytokine and involved in stress response program of cells after cellular injury

MCP-1 — 119.0 pg/ml
Chemotactic factor that attracts monocytes and basophils but not neutrophils or eosinophils

G-CSF — 91.6 pg/ml
Controls the production, differentiation, and function of granulocytes

NT-4 — 33.0 pg/ml
Neurotrophins that control survival and differentiation of mammalian neurons

ICAM-1 — 1,554.9 pg/ml
Involved in binding of a cell to another cell or to the extracellular matrix with roles in cell proliferation, differentiation, motility, trafficking, apoptosis and tissue architecture

Regeneration

RANTES — 551.0 pg/ml
Functions as a chemoattractant for blood monocytes, memory T helper cells and eosinophils. It causes the release of histamine from basophils and activates eosinophils

GDNF — 19.5 pg/ml
Enhances survival and morphological differentiation of dopaminergic neurons and increases their high-affinity dopamine uptake

MIP-1d — 44.9 pg/ml
Chemotactic factor that attracts T-cells and monocytes

SCF R — 40.3 pg/ml
Signals mast cell activation in response to antigens. Regulates their subsequent maturation and homing to the residence sites

GH — 31.3 pg/ml
Stimulates both the differentiation and proliferation of myoblasts. It also stimulates amino acid uptake and protein synthesis in muscle and other tissues

IL-16 — 8.7 pg/ml
Stimulates a migratory response in lympocytes, monocytes, and eosinophils

MCSF — 12.2 pg/ml
Regulates survival, proliferation and differentiation of hematopoietic precursor cells (macrophages and monocytes), immunity and inflammatory processes, and the regulation of osteoclast proliferation and differentiation required for normal bone development

IL-6R — 53.3 pg/ml
Regulates cell growth and differentiation and plays an important role in the immune response.

IL-1b — 1.3 pg/ml
Mediates inflammatory response, cell proliferation, differentiation, and apoptosis

HMW Hyaluronic Acid

HMW HA — 23,284 ng/ml
Helps lubricate joints and aids with anti-inflammatory response and immunosupppressive effect.

Exosomes

EXOSOMES — 81 billion/ml
Subcellular vesicles that act as intercellular messengers, delivering membrane and cellular proteins, including microRNA, other types of RNA, and mRNA fragments from one cell to another.

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1. Testing and analysis by RayBiotech, Inc. in 2019 with Quantibody ELISA Arrays, the R&D Quantikine Hyaluronan ELISA Arrays and the RayBioTech Quantibody Analysis Tool. Exosome count analysis by The Saban Research institute - CHLA at USC in 2019 using NanoSight Tracking Analysis.
2. Bo Qiu, Ming Gong, Qi-Ting He, and Pang-Hu Zhou, "Controlled Release of Interleukin-1 Receptor Antagonist from Hyaluronic Acid-Chitosan Microspheres Attenuates Interleukin-1β-Induced Inflammation and Apoptosis in Chondrocytes," BioMed Research International, vol. 2016, Article ID 6290957, 12 pages, 2016.
3. Amable PR, Teixeira MVT, Carias RBV, Granjeiro JM, Borojevic R. Protein synthesis and secretion in human mesenchymal cells derived from bone marrow, adipose tissue and Wharton's jelly. Stem Cell Research & Therapy. 2014;5(2):53. doi:10.1186/scrt442.
4. Sobolewski K, Bańkowski E, Chyczewski L, Jaworski S, Collagen and Glycosaminoglycans of Wharton's Jelly. Neonatology 1997;71:11-21
5. Sobolewski, K. et al. Wharton's jelly as a reservoir of peptide growth factors. Placenta , Volume 26 , Issue 10 , 747 – 752
6. Bakhtyar, Nazihah et al. "Exosomes from acellular Wharton's jelly of the human umbilical cord promotes skin wound healing" Stem cell research & therapy vol. 9,1 193. 13 Jul. 2018, doi:10.1186

GeneXStem™

WHARTON'S JELLY: THE IDEAL TISSUE – TYPE

REGENERATIVE MEDICINE THERAPIES COMPARISON

PRODUCTS/ COMPONENTS	PLATELET RICH PLASMA	BONE MARROW ASPIRATE	LIPOASPIRATE	AMNIOTIC FLUID	AMNIOTIC MEMBRANE	UMBILICAL CORD WHARTON'S JELLY
MESENCHYMAL STEM CELLS (MSC)	-	X	XX	-	-	XXX
CYTOKINES	X	X	X	XXX	XXX	XXX
GROWTH FACTORS	XXX	XX	X	XX	XX	XXX
EXTRACELLULAR MATRIX COMPONENTS (ECM)	-	-	-	X	X	XXX
HYALURONIC ACID	-	-	-	X	X	XXX (HMW)

WHARTON'S JELLY has more components than other tissue types making it ideal for regenerative purposes.

Advantages of GeneXSTEM™

1. Less invasive when compared platelet rich plasma (PRP) procedures, bone marrow aspiration, or adipose tissue extraction. No harvesting of tissue is required.
2. Cyropreserved without DMSO, digestive enzymes, or the use of preservative agents.
3. Wharton's Jelly has high concentrations of growth factors and cytokines, which have powerful anti inflammatory properties. The immunologically privileged status of Wharton's Jelly provides the ability to modulate the immunological responses in allogenic settings.
4. GeneXSTEM™ is processed from donated non-embryonic human tissue from full term, c-section deliveries in accordance with the FDA. GeneXSTEM™ is regulated as a human cell, tissue, or cellular or tissue based product (HCT/P) under 21 CFR Part 1271 and Section 361 of the Public Health Service Act. It is not dependent upon the metabolic activity of living cells for its primary function.
5. GeneXSTEM™ products uphold the highest safety measures which exceed those required by AATB and FDA in order to provide a reliable source of products for physicians and patients.