

# Maximum Signaling for Maximum Regeneration

## Using Four-Material RICHGEN Flowable Allograft

For homologous use only



RICHGEN Flowable Allograft, composed of four separate materials, is a breakthrough therapy in the field of regenerative medicine. It is available off the shelf as a parenteral preparation and the four materials placenta, amniotic membrane, Wharton's jelly, and amniotic fluid are conveniently in one vial. The proprietary process of RICHGEN preparation preserves a high percentage of key signaling proteins that are involved in repair and regeneration at the site of tissue or bone injury. Thus, RICHGEN accelerates the process of regeneration by stimulating intracellular growth pathways where it is needed most.

### RICHGEN Activity

The RICHGEN preparation has high levels of active signaling proteins, which include exosomes, growth factors, cytokines, chemokines, miRNA, extracellular matrix proteins and mesenchymal stromal cells to name a few. RICHGEN is superior to products that are only single or dual materials or have only multipotent cord blood cells. According to independent, third-party testing of these limited brands show after thaw 0% – 2.4% viability. Additional benefits of RICHGEN include patient comfort, time savings and the reduced risk of adverse reaction at the injury site, due to the well documented low immunogenicity and excellent safety profile of RICHGEN allografts made from fresh, single donor material.

### RICHGEN Superior to Umbilical Cord Blood

RICHGEN allografts are undifferentiated pluripotent cells made from single donor tissue. Umbilical cord blood products are limited to multipotent cells, have red blood cells and other cells with major histocompatibility complex (MHC) proteins and HLA type markers that are known to be involved in immunogenic pathways. Products pre-

pared from cord blood advertise efficacy based only on cell count numbers and do not have the large component of signaling proteins present in RICHGEN that help stimulate regenerative pathways. Cord blood cell products tend to have a higher risk of graft versus host reaction that is not present in RICHGEN. Also cord blood products are usually prepared from multiple donors and do transfer DNA. These products are meant for hematopoietic use only and falsely promoted for many other uses.

### RICHGEN Superior to Aspirate

Autologous adipose and bone marrow aspirate derived cells provide aged, low quality, low count adult cells that lack the highly active signaling proteins present in RICHGEN allografts. Treatment with bone marrow aspirate (BMA) cells have shown marginal improvement in cellular development (with no regeneration and some reports of hip collapses by BMA patients). There is concern that the BMA treatment cellular activity will mainly go to the surgery extraction site and not to the chronic issue that was to be addressed. RICHGEN flowable allograft on the other hand has shown to be useful in bone repair and regeneration without the time-consuming surgery and painful recovery.

### RICHGEN Cellular Signaling Science

Individual signaling messengers present in RICHGEN and their activity is described here. The bone morphogenic proteins (BMP-4, BMP-5, BMP-7) help induce bone repair and can have a beneficial effect in patients with osteoarthritis. The alpha2 macroglobulin enhances anti-inflammatory activity in the joints and may be beneficial for sufferers of rheumatoid arthritis. The collagen substrates I, III, IV, V and VI, fibronectin and laminin enhance wound healing.

RICHGEN products are never centrifuged in order to preserve integrity of components, since centrifugation has been shown to destroy cell structure.

RICHGEN is a naturally wholesome product, carefully processed for maximum efficacy and safety.

RICHGEN has an immunomodulating effect on the macrophages that are released at the site of tissue injury. This effect of RICHGEN on macrophages helps decrease inflammation with rapid removal of cellular debris, and the additional placental allograft components drive development of the intracellular apparatus involved cellular repair that cascade into the specific areas for regeneration.

RICHGEN produces its anti-inflammatory action by modulating M1 and M2 macrophages and this appears to be due to contact with the various growth factors and cytokines in suspension. Amniotic fluid has been identified by several researchers as an untapped source of cells with a broad curative potential that also has immunomodulatory properties. The amniotic fluid also provides several growth factors such as insulin-like growth factor I (IGF-1), fibroblast growth factor (FGF), epidermal growth factor (EGF), platelet-derived growth factor (PDGF) and transforming growth factor beta (TGF-beta) that play a supportive role to the Wharton's jelly extra cellular matrix (ECM) components. The growth factors in amniotic fluid bind with ECM to provide stimulation for the production of large amounts of aminoglycans and collagen that aid in tissue repair.

RICHGEN flowable allograft's bioactive proteins, exosomes, miRNA combined with the presence of the extracellular matrix, laminin, and fibronectin, have been shown in various studies to be effective in a wide array of tissue and bone regenerative applications.

These include:

- Topical wound healing
- Rapid response use in orthopedic pathologies, organ system pathologies, pain / anti-inflammatory control
- Scar management by inhibiting the inflammatory chemotactic pathways
- Providing components for immunomodulation, and scaffolding for generation of healthy tissue & bone, and repair of injured tissue & bone

The patented and patents pending proprietary processing used for RICHGEN flowable allograft products creates maximum signaling for maximum bone and tissue regeneration potential, setting them ahead of single component regenerative grafts. No mixing is required. Additionally, the breakthrough proprietary processing technology only freezes the outer membrane of the cells. The intracellular contents remain intact and non-crystallized resulting in enhanced efficacy and potency of RICHGEN cells when compared to other commercial products.

## RICHGEN Flowable Allografts Are:

- Immunomodulating
- Anti-inflammatory (IL-1RA, IDO, IL-10)
- Anti-microbial (Defensins, N-GAL, LL-37)
- Anti-tumorigenic
- Non-steroidal
- Can be used without limitation, unlike cortisone type products
- No HLA antigen and no host vs. graft reaction

## These Placental Allografts Include:

- Full spectrum of 1500 growth factor proteins (PRP contains only 7 and are centrifuged)
- Cytokines
- Collagen substrates
- Hyaluronic Acid
- miRNA
- Associated exosomes
- Secretomes
- Pluripotent PMSCs (medicinal signaling cells)
- Fibroblasts (bFEF, PDGF) – dermis regeneration
- Keratinocytes
- Endothelial (VEGF, bFGF) – vascularization (SDF-1, IGF-1, epithelial, endothelial, neural) – Regulate MMPs/TIMPs
- CD73, CD90, CD105, CD106, CD146, CD166 and Stro-1

## RICHGEN Is a Reliable Choice

The RICHGEN four-material allografts have an outstanding safety record and makes RICHGEN products a reliable option. The allograft products are tested extensively for bioburden; including endotoxin, viruses, fungus, and yeasts. The allografts have been tested under quality protocols and properly reviewed by independent laboratories to verify the presence of active components that have been listed above.

Finally, RICHGEN is FDA registered. The independent tissue processing lab is FDA compliant, certified and regulated as a human cellular or tissue-based product (HCT/P) under 21 CFR Part 1271 and Section 361 of the Public Health Service Act and ISO 13485. The lab is AATB certified. Manufactured per cGMP and cGTP guidelines.