

Molecular Characterization of Signature Cord™ and Signature Matrix™ Products

Scientific Work and Data Provided by Aidan Research & Consulting, LLC.

INTRODUCTION

Tissues derived from the umbilical cord and amniotic membrane are a source of regenerative cells that secrete molecules that modulate the immune system, stimulate regeneration, reduce inflammation and induce new blood vessel growth [1] [2] [3] [4]. These molecules include: cytokines, chemokines, RNAs and prostanoids. Signature Cord and Signature Matrix tissue products were tested for the presence of these molecules. The products are minimally manipulated and should retain the relevant characteristics of the source tissue.

The content of PGE2 (an immune modulating prostanoid) was tested in this experiment to demonstrate the comparable levels between the final products and fresh tissue samples. In addition, tissue products' cytokines were tested using a third party. They are presented here by relevance in promoting immunosuppression, regeneration and angiogenesis according to published literature [5].

METHODOLOGY

Minimally manipulated umbilical cord and amniotic tissue products manufactured by Signature Biologics, LLC., identified as sellable inventory (Finished Goods), selected at random and stored for at least three months in cryopreservation were used for this study. A total of five (n=5) vials, from five unique lots, of Signature Cord (75 mg per vial) and Signature Matrix (135 mg per vial) were thawed according to manufacturer's instructions for use. The tissues were homogenized and centrifuged to extract the proteins the supernatants, which were stored at -80°C. Aliquots of each of these products were tested for PGE2 by Aidan Research & Consulting (using commercially available ELISA kit) and for cytokines and chemokines by RayBiotech (using the multiplex microchip-based ELISA: Quantibody 440 assay).

RESULTS

1. No significant differences were found in the levels of PGE2 throughout the groups, indicating that the abundance of PGE2 found in native tissue is retained in the final products (Figure 1).
2. The concentrations of cytokines and chemokines are shown in heat map format (Figure 2). The heat maps demonstrate the quantities of anti-inflammatory, tissue regeneration, and angiogenic molecules in the products. They are grouped by relevance according to published literature [5].

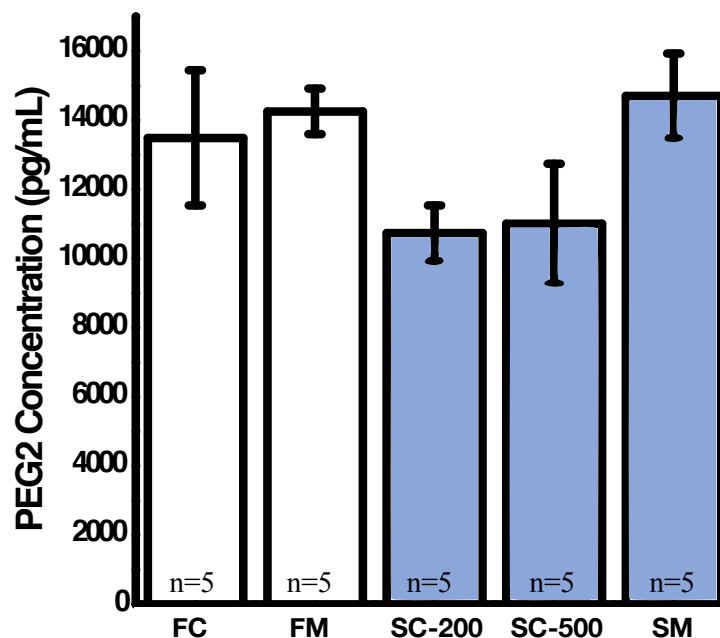


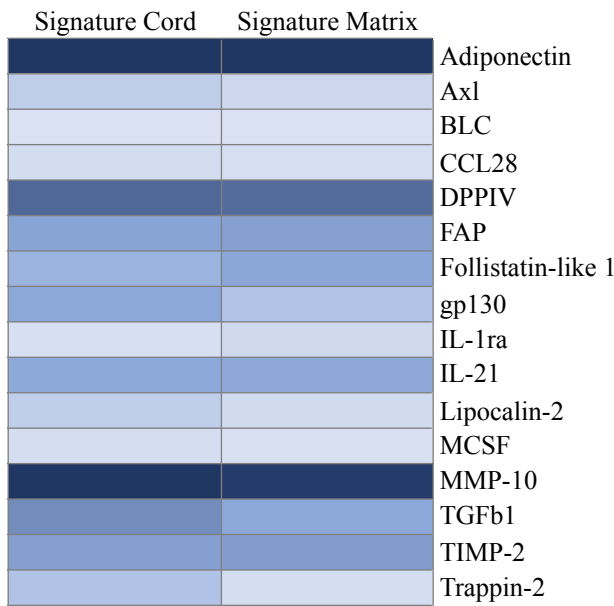
Figure 1. Abundance of PGE2 in placental-derived products and native tissue.

No significant differences were observed among groups: Fresh Cord (FC), Fresh Amniotic Membrane (FM), Signature Cord Micro (SC-200), Signature Cord (SC-500) and Signature Matrix (SM) concentration determined using PGE2 ELISA.

Molecular Characterization of Signature Cord™ and Signature Matrix™ Products

Figure 2 – Heat Maps of Important Cytokines

A) Anti-Inflammatory & Immunomodulatory



B) Tissue Regeneration & Angiogenesis

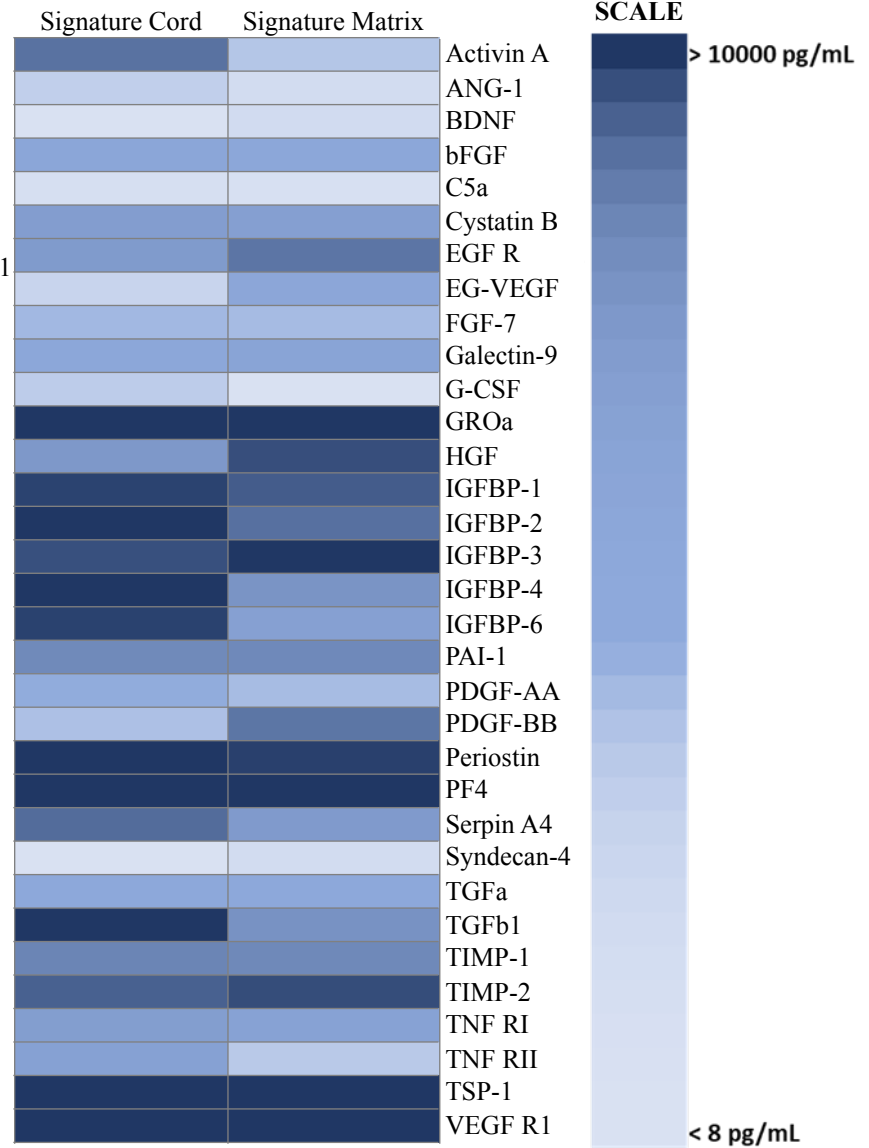


Figure 2. Heat maps representing cytokine and chemokine concentrations in Signature Cord (n=5) and Signature Matrix (n=5) placental-derived products.

Concentrations of A) Anti-inflammatory & immunomodulatory molecules and B) Tissue regeneration & angiogenic molecules.

REFERENCES

1. Atala, A., et al., Editors, 2018, *Perinatal Stem Cells*. Academic Press: Boston. p. iv.
2. Kyurkchiev, D., et al. (2014). Secretion of immunoregulatory cytokines by mesenchymal stem cells. *World J Stem Cells*. **6**(5): 552-70.
3. Weiss, M.L., et al. (2008). Immune properties of human umbilical cord Wharton's jelly-derived cells. *Stem Cells*. **26**(11): 2865-74.
4. Sane, M. S., et al. (2018). Cytokines in umbilical cord blood-derived cellular product: a mechanistic insight into bone repair. *Regen Med* **13**(8): 881-898.
5. Sakaguchi, K., et al. (2017). Periodontal tissue regeneration using the cytokine cocktail mimicking secretomes in the conditioned media from human mesenchymal stem cells. *Biochem Biophys Res Commun*. **484**(1): 100-106.