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A decellularized flowable placental connective tissue matrix supports cellular functions of human tenocytes in vitro

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Statement of the Problem: Tendon healing is a slow and complex process that cannot restore the structure and function of the native tendon. Flowable connective tissue matrices (CTMs) may promote tendon healing, given their structural and biochemical extracellular matrix components, minimally invasive properties, and capacity to fill irregular spaces. Due to variations in processing procedures, however, not all flowable CTMs are equivalent. The purpose of this study is to evaluate the effects of flowable, placental CTMs on the cellular activities of human tenocytes. Decellularization, the removal of cells, cell fragments, and DNA from CTMs has been shown to reduce the host's inflammatory response. Therefore, the authors hypothesize that a decellularized flowable CTM (DF-CTM) will provide a more cell-friendly matrix to support tenocyte function.

Methodology and Theoretical Orientation: Three human, flowable, placental CTMs were selected for comparison: (1) a minimally manipulated non-viable cellular particulate (MM-CTM); (2) a liquid matrix (L-CTM); and (3) a decellularized flowable CTM (DF-CTM). Outcome variables included tenocyte adhesion, proliferation, migration, phenotype maintenance, and inflammatory response. Adhesion and proliferation were evaluated using cell viability assays and tenocyte migration using a transwell migration assay. Gene expression of tenocyte markers and pro-inflammatory markers were assessed using quantitative polymerase chain reaction. Phenotypic markers included scleraxis (SCX), tenascin-C (TNC), type I collagen (COL1A1), type III collagen (COL3A1), and decorin (DCN). Inflammatory markers included interleukin 8 (CXCL8), tumor necrosis factor (TNF), transforming growth factor beta 1 (TGFβ1) and beta 3 (TGFβ3), and matrix metallopeptidase 1 (MMP1).

Findings: Although MM-CTM supported significantly more tenocyte adhesion than DF-CTM ($p = 0.004$), tenocyte proliferation was significantly higher on DF-CTM than MM-CTM and L-CTM ($p < 0.001$). Unlike MM-CTM, tenocyte migration was higher for DF-CTM than the control ($p = 0.005$). In tenocytes cultured on DF-CTM, gene expressions (SCX, TNC, COL1A1, and COL3A1) significantly increased over time ($p < 0.001$). Conversely, in tenocytes cultured on MM-CTM, gene expressions remained unchanged (SCX and TNC, $p \geq 0.102$) or significantly decreased over time (COL1A1 and COL3A1, $p \leq 0.018$). DCN expression increased over time for both CTMs ($p < 0.001$). Compared with MM-CTM, DF-CTM diminished the effects of TNF-α, significantly reducing the expression of CXCL8 ($p = 0.024$) and MMP1 ($p < 0.001$). Over time, tenocytes cultured on MM-CTM promoted the expression of CXCL8 and MMP1, while DF-CTM promoted the expression of antifibrotic growth factor TGFβ3.

Biography

Anna Gosiewska is a healthcare innovation leader, who is developing cutting edge technologies in tissue engineering and cell therapy and translating them into clinically differentiated products and solutions. Anna joined Celularity Inc., as Vice President of Research & Development (R&D), Degenerative Diseases in 2020. As part of her strategic R&D initiative, she is building a diverse portfolio of scientifically and clinically validated products, uniquely designed to address significant gaps in the treatment of degenerative diseases. These products include placental-derived cell therapies, biomaterials, and bioactives with applications across several therapeutic areas, including orthopedics, soft tissue repair, aesthetics, and ophthalmology.

Anna transitioned to Celularity Inc., from Johnson & Johnson Inc., where her tenure included 25 years of working across three sectors: Medical Devices, Pharmaceuticals, and Consumer Healthcare Industry. She held positions with increasing responsibilities, advancing from Manager of R&D to Director of R&D to Senior Director of R&D/Head of Emerging Science and Innovation. As part of her tenure, Anna led cross-enterprise efforts, focused on emerging technology development, the discovery of novel cell-based technologies, biomaterials, and nanotechnologies, and the development of innovative products to enhance the healing and regeneration of human tissues and organs.

Anna earned her Doctoral degree in Medical Biology and Master of Science degree in Medical Analytics from the Medical University of Bialystok, Poland. She completed her postdoctoral studies at the National Institutes of Health, National Laboratory of Biochemistry in Bethesda, Maryland, studying cell-extracellular matrix interactions.

She has authored many peer-reviewed journal articles, review articles, and book chapters and has 122 issued/pending patent applications, with 48 issued U.S. patents related to stem cells, regenerative biomaterials, and bioactives. Anna is a member of several international scientific societies and serves on the Advisory Board for the Biotechnology at the Middlesex County College in New Jersey.

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