corresponding regulatory framework, and practical considerations for products in development from the perspective of the medical centers.

Development of Scalable Scaffolds, Biomaterials, Matrices

J. Johnson;

Chief Scientific Officer, Columbus, OH.

Focus is shifting to the mass production of tissue engineered scaffolds and products under appropriate regulatory requirements. The scale-up of this translational process will help bring regenerative medicine into the mainstream of clinical practice, but it also drives renewed focus on how earlier research may better enable future therapeutic applications. Manufacturing costs and sourcing of raw materials should be factored into the product development strategy as a critical step towards commercialization. Nanofiber Solutions, Inc. is a regenerative medicine company developing a new class of implants with unrivaled performance for the $20B soft tissue repair and organ regeneration market. Our nanofiber technology is used to build scaffolds that are critical in the development of life-saving tissue engineered implants. We manufacture the world's first nanofiber tracheal implant which has been used successfully in four European surgeries and are rapidly expanding our product offerings and patent estate based on this proven scaffold technology.

Industrialization and Manufacture of Cells, Growth Factors

J. Rowley;

Chief Executive & Technology Officer, RoosterBio, Inc., Fredrick, MD.

Why Manufacturing Matters: How Today's Cell Therapy Bio-Manufacturing Innovations are Laying the Foundation for a Sustainable Tissue Engineering Revolution. Technology is rapidly moving toward the integration of biologics into products like cell therapies, engineered tissues, bio-robotics, implantable devices, 3D printing, food, clothing, and even toys. This coming decade will see the incorporation of living cells into all these platforms and others not yet imagined. To expedite this biologics revolution, inventors, developers and suppliers will require a limitless, standardized, low-cost supply of cells - and today's cell therapy biomanufacturing innovations are laying the groundwork to make this a reality.

Session: The Past, Present and Future in Functional Tendon Repair and Regeneration

Date and Time: Friday, September 11, 2015, 9:15 AM - 10:45 AM

Harnessing Endogenous Stem/Progenitor Cells for Tendon Regeneration

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Tendon and ligament injuries frequently result in scar-like tissue with poor restoration of biological structure and mechanical properties. In additional to surgical grafting by autologous or allogeneic tissues, previous experimental work has attempted to improve tendon/ligament healing using growth factors, stem/progenitor cells and biomaterials. However, these tissue-engineered grafts have encountered difficulties in clinical translation. Here we identified a rare population ($\sim$0.8% of total tendon cells) of tendon stem/progenitor cells (TSCs) with a perivascular origin, consistent to the previous reports. The perivascular TSCs (PTSCs) were highly clonogenic and multipotent. Interestingly, the PTSCs are selectively enriched up to $\sim$20 fold by treatment with connective tissue growth factor (CTGF). In addition, CTGF-treated PTSCs readily differentiated into tenocyte-like cells as evidenced by significant increases in tendon related gene expressions as compared to the other tendon cells. In a patellar tendon (PT) full-transection model, the number of PTSCs drastically increased in the early phase of CTGF-delivered tendon healing ($2 \sim 7$ days) in contrast to control. The PTSCs then underwent differentiation into SCX+/COL-I+tenocyte-like cells in the later healing phase (>7 days) in the CTGF-delivered tendon that consequently led to scar-less tendon healing, featured by highly organized collagen fibrils, normal level of cellularity and mechanical properties. Initial signaling study using siRNA knockdown showed that CTGF-induced proliferation and tenogenic differentiation of PTSCs were regulated via FAK and ERK1/2 signaling pathways. Our approach for tendon regeneration by harnessing regenerative capacity of host stem/progenitor cells requires no cell transplantation, and may offer an alternative approach for endogenous regeneration.

Advancing Tendon Regeneration through the Development of Bio-stimulating Tissue Engineering Approaches

M. Gomes[1,2];

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Tendon tissue engineering (TE) requires tailoring scaffolds designs and properties to the anatomical and functional requirements of tendons located in different regions of the body. Cell sourcing is also of utmost importance as tendon cells are scarce. Recently, we have found that it is possible to direct the tenogenic differentiation of Amniotic fluid and Adipose tissue derived stem cells (hAFSCs and hASCs), and also that there are hASCs subpopulations that might be more prone to tenogenic differentiation. Nevertheless, biochemical stimulation may not be enough to develop functional TE substitutes for a tissue that is known to be highly dependent on mechanical loading.

These findings trigger our interest on *in vitro* biomechanically-stimulating culture environments that can be achieved modulating the scaffold architecture and composition and the stem cells. Particularly, the incorporation of magnetic nanoparticles (MNPs) within 3D constructs constitutes a novel and attractive strategy towards the development of magnetically-responsive system that may eventually combine therapeutic and diagnostic functionalities. An additional advantage is that cells naturally respond to magnetic forces, and consequently, the application of a magnetic field may enhance cell biological performance, and ultimately stimulate cell proliferation and differentiation. This work reports on recent studies concerning the development of specific scaffolds architectures based on various polymers, doped with MNPs and fabricated by either rapid prototyping technologies or electrospinning, enabling responsive systems for culturing stem cells, stimulating their tenogenic differentiation.

Assessment of Tenogenic Induction by Extracellular Tendon Matrix and Cyclic Stretching

J. Burk[1], A. Aldag[1], W. Brehm[1], S. Heller[2], B. Pfeiffer[1], C. Kasper[3];

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Treatment of tendon injuries with multipotent mesenchymal stromal cells (MSC) led to encouraging results in animals. However, there is still only limited understanding of the mechanisms underlying the beneficial effects of locally applied MSC on tendon healing.

Tenogenic differentiation induced by the natural tendon environment, accompanied by synthesis of important matrix components, could be part of the complex mechanisms.

The aim of this study was to investigate this hypothesis using a new *in vitro* model system, which allowed combining the use of tendon matrix scaffolds and the application of cyclic strain, imitating crucial natural stimuli.

Adipose-derived MSC from equine donors were seeded on decellularized tendon scaffolds and once subjected to mechanical stimulation with increasing stress-rest-periods. 4, 8 and 24 h post stimulation, samples were assessed regarding their morphology, cell alignment, and integration and expression of musculoskeletal markers.