the aneurysm. However, the primary mechanisms for recurrence in the endovascular coiling procedures are recanalization of the clot (via enzymatic digestion) and mechanical compactions of coils within the sac (due to blood flow). Enzymatic remodeling reduces the mechanical integrity of the protein network. We propose to deliver a bioactive agent, genipin, locally within the aneurysm sac that will induce covalent crosslinking to stabilize the clot. Genipin is a natural biocompatible crosslinking agent extracted from the Gardenia jasminoides. It is 10,000 times less cytotoxic than its more commonly used counter agent, glutaraldehyde. In our study, we hypothesize genipin-crosslinked fibrin hydrogel networks could improve the performance of haemostatic materials for minimally invasive occlusion of brain aneurysms. The mechanical stability and enzymatic resistance is evaluated through the incorporation of streptokinase, a bacterial enzyme derived from group C(beta)-hemolytic streptococci. Using rheology, our preliminary data depict mechanical stability in the crosslinked system to be significantly higher than in pristine fibrin gels. These observations suggest that genipin could serve as a biologic to improve minimally invasive embolic treatments.

Microengineered Heterospheroids of Pancreatic Islets and Adipose-derived Stem Cells for Effective Cell-based Treatment of Diabetes

Y. Jun[1], S. Lee[1,2];

[1]KU-KIST Graduate School of Converging Science and Technology, Korea University, Seoul, KOREA, REPUBLIC OF, [2]School of Biomedical Engineering, Korea University, Seoul, KOREA, REPUBLIC OF.

Currently, pancreatic islet transplantation is the only curative therapy of type 1 diabetes; however, donor shortages and cellular damage during the isolation critically limit the use of this approach. In this study, we describe a novel method for creating viable and functionally potent islets by co-culturing single islet cells with adipose-derived stem cells (ADSCs) in three-dimensional (3D) environment, and quantitatively demonstrate the positive effect of ADSCs on islet survival *in vitro* and *in vivo*.

Here, mixtures of single islet cells and ADSCs isolated from Sprague-Dawley rats were seeded to PDMS-based concave microwell arrays to have heterospheroids with controlled-size and shape. For *in vivo* tests, we encapsulated spheroids in microfiber and implant them into diabetic mice.

When ADSCs were co-cultured with islets in 3D structure, they segregated from the islets, eventually yielding purified islet spheroids. Thereafter, the ADSC-exposed islet spheroids showed significantly different ultrastructural morphologies, higher viability, and enhanced insulin secretion compared to mono-cultured islet spheroids. Also, they showed increased efficacy of *in vivo* experiments, which revealed that co-culture-transplanted mice maintained their blood glucose levels longer than mono-culture-transplanted mice, and required less islet mass to reverse diabetes.

In conclusion, the initial presence of ADSCs effectively improved islet survival while inhibiting apoptosis and supporting better cell-cell interactions between β cells. Our proposed method could potentially help overcome the problem of cell shortages, and could possibly suggest a future platform for the cell-based treatment of diabetes.

Acknowledgments: This work was supported by National Research Foundation of Korea (No. 2014034805).

Tendon Regeneration Through a Scaffold-free Approach: Development of Tenogenic Magnetic hASCs Sheets

A. I. Gonçalves, M. T. Rodrigues, R. L. Reis, M. E. Gomes;

3B's Research Group, Guimarães, PORTUGAL.

Tendon's regeneration is limited, demanding for cell-based strategies to fully restore their functionality upon injury. The concept of magnetic force-based TE(1), generally using magnetic nanoparticles may enable, for example, stem cell stimulation and/or remote control over TE constructs. Thus, we originally propose the development of magnetic cell sheets (magCSs) with tenogenic capability, aimed at promoting tendon's regeneration.

A Tenomodulin (TNMD+) subpopulation was sorted from human adipose stem cells (hASCs), using TNMD-coated immunomagnetic beads(2) and used as cell source for the development of magCSs. Briefly, cells were labeled with iron oxide composite particles (Micromod) and cultured for 7 days in α-MEM medium with or without magnetic stimulation provided by a magnetic device (nanoTherics). CSs were retrieved from the plates using magnet attraction as contiguous sheets of cells within its own deposited ECM.

CSs were evaluated by confocal microscopy, flow cytometry and immunocytochemistry for tendon related markers, and prussian blue staining. Cell metabolic activity and proliferation was also assessed by MTS and DNA assays. Moreover, the genetic expression of collagen I, III, and tenascinC was quantified by real time RT-PCR.

Preliminary results suggest that magnetic actuation improves cell proliferation and influences the synthesis of tendon ECM proteins in comparison to magCSs under static conditions. Ongoing studies on mechanical properties will provide information on the functionality of magCSs versus non-magnetic as tissue-like substitutes for tendon TE.

(1) Ito, A., *et al.* TE.10:873, 2004.
(2) Mihaila, SM., *et al.* TE PartA.19.1-2:235, 2012.

Acknowledgments: NOVOMAR Project (0687_NOVOMAR_1_P) cofinanced by FEDER; EC project POLARIS (REGPOT-CT2012-316331) and project RL3 -TECT -NORTE-07-0124-FEDER-000020 cofinanced by ON.2 (NSRF), through ERDF.

Extracellular Matrix-based Device for Reconstruction of the Temporomandibulat Joint Meniscus

B. N. Brown[1], W. L. Chung[1], J. Cheetham[2], A. J. Almarza[3], S. F. Badylak[4];

[1]Bioengineering, University of Pittsburgh, Pittsburgh, PA, [2]Clinical Sciences, Cornell University, Ithaca, NY, [3]Oral Biology, University of Pittsburgh, Pittsburgh, PA, [4]Surgery, University of Pittsburgh, Pittsburgh, PA.

Currently, no consistently effective option exists to replace a temporomandibular joint (TMJ) disc. The present study examined the use of an extracellular matrix (ECM) device as an inductive template for reconstruction of the TMJ disc in a porcine model, considered the ''gold-standard'' for TMJ disc research. The device was implanted following bilateral discectomy, leaving the contralateral side empty (control). Animals (n = 60) were sacrificed at 2, 4, 12, and 24 weeks and remodeling was assessed by gross morphologic and histologic examination, MRI imaging, and biomechanical analysis (tension and compression). All results were compared to native disc as a control.

The ECM device was remodeled and replaced by a structure highly resembling native tissue by 4 weeks post-implantation in greater than 50% of animals. Immunolabeling showed that mononuclear macrophages and perivascular progenitor cells mediate the early stages (2–4 weeks) of tissue remodeling. The histologic appearance of the remodeled implant at later times (>4 weeks) was characterized by dense, aligned fibrocartilage containing spindle-shaped cells within the area of articulation. Formation of peripheral muscular and tendinous attachments resembling those in native tissue was also observed. MRI confirmed these results. The biomechanical properties of the remodeling tissue approached that of native tissue over the course of remodeling. Protection of condylar surfaces in ECM implanted animals was observed regardless of ECM-mediated formation of new TMJ disc tissue.

This device fills a clinical need for which there are currently no effective treatments and may represent a simple and effective ''off-the-shelf'' solution for reconstruction of the TMJ disc.

Silk Based Antibacterial Nanofibers

S. Calamak[1,2], E. A. Aksoy[1,3], **K. Ulubayram**[1,2,3];

[1]Department of Basic Pharmaceutical Sciences, Faculty of Pharmacy, Hacettepe University, Ankara, TURKEY, [2]Nanotechnology and Nanomedicine Division, Institute for Graduate Studies in Science and Engineering, Hacettepe University, Ankara, TURKEY, [3]Polymer Science and Technology Division, Institute for Graduate Studies in Science and Engineering, Hacettepe University, Ankara, TURKEY.