(2.O6) DEVELOPMENT AND IN VITRO DEGRADATION OF PLA/PEG/CaP GLASS BIODEGRADABLE SCAFFOLDS BY RAPID PROTOTYPING

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Introduction. Rapid prototyping allows the development of temporary 3D scaffolds with optimal architecture, providing an adequate support for cell in-growth, differentiation and ultimately tissue regeneration. Particularly, a nozzle-deposition system integrated with pumping technology is a versatile tool that uses a CAD/CAM approach to build complex, reproducible 3D structures. In this study, polylactic acid (PLA) and polyethylene glycol (PEG) were combined with soluble CaP glass particles and processed by RP to obtain fully biodegradable structures with superior mechanical properties and bioactivity. The aim of this work was the development, characterization and in vitro degradation study of biodegradable PLA/PEG and PLA/PEG/CaP glass 3D scaffolds.

Materials and Methods. A blend of 95% Poly(95L/5DL)lactic-acid and 5% PEG (Mw=400) in chloroform (5%w/v) was prepared. In the case of the composite, CaP glass particles (<40um) in the system 44.5P2O5-44.5CaO-6Na2O-5TiO2 were also added (50% w/w). Scaffolds with orthogonal and orthogonal-displaced geometries were fabricated. The in vitro degradation behaviour of the structures was evaluated by immersing the scaffolds in SBF at 37°C for 8 weeks. Differential scanning calorimetry, scanning electron microscopy (SEM), mechanical compression test, micro-computed tomography, and ionic (Ca2+) release were evaluated after different degradation times. Biological evaluation was also carried out.

Results. Well defined structures with 65% porosity were obtained. Initial compression tests showed that both geometry and glass particles affected the scaffolds mechanical properties. Weight loss measurements and SEM images (Fig.1) indicated that scaffolds were slowly degraded loosing up to 7% of their initial weight and increasing their surface microporosity. Nevertheless, mechanical properties slightly decreased preserving the scaffolds stability. Glass particles added an interesting bioactive effect by releasing Ca to the medium. Indeed, the addition of CaP-glass positively affected cell behaviour.

Conclusion. The combination of RP and PLA/PEG/CaPglass turned into promising fully degradable, mechanically stable, bioactive and biocompatible composite scaffolds for TE.

Keywords. biofabrication, rapid prototyping, biomaterials, biodegradable scaffolds, bone, regenerative therapies

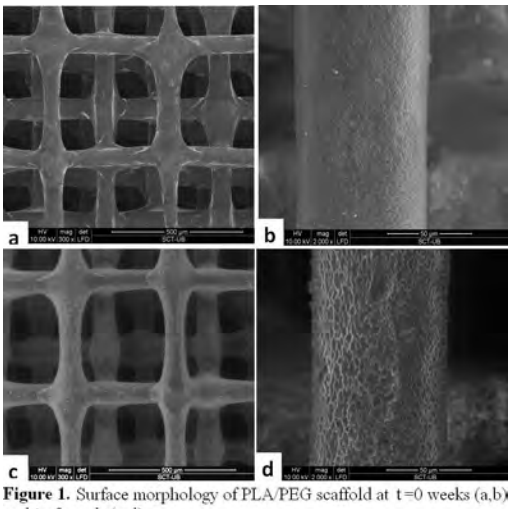

Figure 1. Surface morphology of PLA/PEG scaffold at t=0 weeks (a,b) and t =5 weeks(c,d)

(2.O7) MICROWELL SCAFFOLDS FOR EXTRAHEPATIC ISLET OF LANGERHANS TRANSPLANTATION IN TYPE 1 DIABETES

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Introduction. The conventional therapy for type 1 diabetes is insulin administration. Despite this, some patients are poorly controlled and suffer from hypoglycemia and long-term complications. For these patients, allogeneic islet transplantation into the liver has become an alternative therapy[1]. Patients benefit from this therapy due to near normalization of blood glucose levels without an increased risk of hypoglycemia. However, islet graft function in the liver tends to decline over years indicating that the liver is not an optimal transplantation site[2]. In order to develop alternative transplantation sites with better long-term outcome, we have developed a new microwell scaffold platform.

Materials and Methods. Microwell scaffolds were prepared from dense solution-cast and porous electrospun 4000PEOT30PBT70 block-copolymer films using microthermoforming. Polymer wettability and scaffold topology were assessed by captive bubble contact angle measurements and scanning electron microscopy (SEM), respectively. Furthermore, constructs were characterized for their permeability for the nutrient glucose. To determine the applicability of the constructs for islet transplantation, the morphology and function of human islets after 7 days of culturing were studied by SEM, histological analysis and glucose challenge tests.

Results. We fabricated reproducible dense and porous films, the latter with a fiber-diameter of 1.71±0.42µm. The polymer films were hydrophilic (contact angle <40°) . Diffusion tests revealed that the electrospun scaffolds were permeable for glucose (flux: 0.0018±0.0002 gm-2s-1). Based on SEM and histological analysis there were no indications for islet spreading or outgrowth of islet stromal cells. Function tests revealed that human islets remained responsive to glucose challenge after 7 days of

culturing in the constructs (figure 1). Currently, first in vivo trials are performed.

Conclusion. This study reports on the development of a novel microwell scaffold platform for extrahepatic islet of Langerhans transplantation. Alternative transplantation sites using biomaterial scaffolds may improve islet transplantation outcome.

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[2]E.A.Ryan et al.Diabetes,54,2060-2069(2005)

Keywords. Islet transplantation, Biomaterial, Scaffold, Diabetes

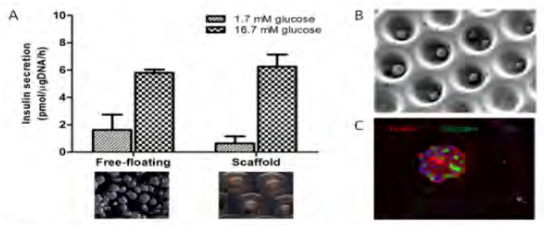

Figure 1 A) Glucose stimulated insulin release of free-floating and scaffold cultured human islets. Islets were subjected to 1 hour sequential incubations in 1.7mM glucose and 16.7mM glucose. Scaffold cultured islets showed a glucose stimulation profile similar to free-floating control islets, B) SEM image of human islets in the construct indicating that scaffold cultured islets preserve their rounded morphology, C) Immunofluorescence revealed insulin (red) and glucagon (green) expression throughout the human islet cultured in the construct (construct is indicated by arrow). Data were obtained after 7 days of culturing.

(2.O8) MICROFLUIDICS FABRICATION OF SELF-ASSEMBLED POLYSACCHARIDE - PEPTIDE MICROCAPSULES FOR CELL THERAPY

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Self-assembling is an appealing methodology for the bottom-up fabrication of new biomaterials that can be used for the controlled growth of cell populations for cell therapies or to promote regenerative processes in vivo. Peptides are excellent structural units to form complex nanostructures that can recreate some of the architectural features of the natural extracellular matrix, as they can self-assemble into fibril nanostructures. We report here a mild cell encapsulation method based on triggering the self-assembly of a multidomain peptide in presence of xanthan gum polysaccharide, which has been investigated in our group as artificial matrix for the encapsulation of chondrocytic cell. The self-assembling peptide K2(QL)6K2 has a central block of glutamine-leucine (QL) repeats, and two flanking positively charged lysine (K) to bind to the negatively charged xanthan. Using a microfluidic device we were able to produce microcapsules with homogenous size (diameter of 300 mm) by forming a water-in-oil multiphase. This technology allows a control over the properties of the microcapsules in terms of size and morphology, being a low stress inducing method suited for cell encapsulation. The properties and performance of xanthan-peptide microcapsules were optimized by changing peptide/polysaccharide ratio and their effects on the microcapsules permeability and mechanical stability were analyzed. Moreover, the effect of microcapsule formulation on viability and proliferation of encapsulated chondrogenic cells were also investigated. The encapsulated ATDC5 cells were metabolically active, showing an increased viability and proliferation over 21 days of in vitro culture demonstrating the long-term stability of the developed microcapsules and their ability to support and enhance the survival of encapsulated cells over prolonged time. Combining self-assembling materials with microfluidics processing proved to be innovative approach to fabricate suitable matrices for cell encapsulation and delivery.

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Keywords. Peptide self-assembly; Xanthan gum; Microfluidics. Cell encapsulation, Microcapsules

(2.O9) FABRICATION OF A CUSTOMIZED TISSUE ENGINEERING SCAFFOLD FOR BREAST RECONSTRUCTION

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Introduction. Mastectomy can be necessary in breast cancer therapy. To improve the patient's quality of life, plastic surgeons often reconstruct the breast. The state-of–the-art procedure is the transplantation of free fat grafts from the belly to the breast. Disadvantages are long operation times and risk of hematoma, infections or donor site defects. A tissue engineered and vascularized adipose construct could overcome these disadvantages and could mimic the natural breast in respect of shape, ptosis and touch. Tissue engineering scaffolds are needed to shape the breast and support fat formation. Here we demonstrate a method that is close to clinical reality, using CAD/CAM technologies.

Materials and Methods. The body of a young female patient is scanned with a 3D laser scanner from three different angles. These scan images are digitally merged and converted to a 3D model of the patient's body. This 3D model is imported into CAD software. Software algorithms are used to mirror the healthy breast and to adapt this designed breast to the predicted thorax shape, so that the scaffold fits to the recipient area of the removed breast. Furthermore, CAD date are transferred to rapid prototyping commands (STL language) and used to fabricate a full-size breast scaffold with fused deposition modeling.

Results and Conclusion. In conclusion, geometrically complex scaffolds can be manufactured individually and customized with 3D laser scanning, CAD modeling and rapid prototyping.

Keywords. breast reconstruction, customization, clinical setting, rapid prototyping, CAD, CAM