Engineered cardiac microtissue model reveals no detrimental effect of fibrosis on beating frequency

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ulcers after ESD. In the present study, we evaluated the feasibility of transplantation of autologous ASC sheets for preventing esophageal strictures after ESD in a pig model.

Methodology: ASCs were isolated from subcutaneous fat of pigs and expanded under a culture condition. The surface antigens of expanded ASCs were analyzed by flow cytometry. Furthermore, the capacity of differentiation and proliferation of ASCs were evaluated. ASCs were seeded on temperature-responsive dishes and cultured for 5 days. Then, ASCs sheets were easily harvested upon temperature reduction. To confirm the presence of transplanted ASCs, cell sheets were labeled with a fluorescent dye, PKH26GL, immediately before the transplantation to the esophageal ulcer sites after ESD.

Results: Primarily cultured ASCs expressed the known surface markers specific to ASC (CD29, CD44, CD90, and CD105). Endoscopic transplantation of ASC sheets were performed with a device as reported previously (1). Fluorescence microscopy of frozen sections of transplanted ulcer sites revealed that PKH26GL-positive cells were adhered on the surface of the submucosal layer.


Engineered Cardiac Microtissue Model Reveals No Detrimental Effect of Fibrosis on Beating Frequency

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Cardiac fibrosis is characterized by deterioration of cell and matrix alignment due to extracellular matrix accumulation that may hamper ventricular function. However, it remains unclear how fibrosis affects the microenvironment of the cardiomyocytes and thereby influences tissue contractility on the cellular level.

Here we describe an in vitro cardiac microtissue model composed of a mixture of neonatal mouse cardiomyocytes and cardiac fibroblasts which are seeded in uniaxial and biaxial constraints to induce (an)isotropy. Uniaxial constraints were used to mimic ‘healthy’ aligned organization, while biaxial constraints resulted in ‘diseased’ disorganized matrix. Furthermore, this model allows studying the effect of matrix accumulation by manipulating the collagen concentration.

Disorganization of the matrix had no detrimental effect on the beating frequency and the force generated by the cardiomyocytes, although disarray had a negative effect on the distribution and homogeneity of the contraction. Furthermore, the average dynamic contraction was decreased after increasing the collagen content, while the beating frequency of the microtissues was unaffected.

In this study, cardiac microtissues were used to unravel the effect of matrix disorganization and accumulation on cardiac contractility. Our results indicate that changes in the ECM have no direct influence on the beating frequency, although the dynamic contraction force exerted by the microtissues is affected. Furthermore, the model system presented is suitable for investigating pathophysiological events associated with cardiac fibrosis and may thereby facilitate in the optimization of new therapies.

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Implantable Microenvironments for Studying Human Tumor Metastasis

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The metastatic spread of cancer is responsible for more than 90% of tumor-associated death while remaining a poorly understood aspect in carcinogenesis. Bone marrow, a sponge-like gelatinous tissue found inside of bone cavities, has been observed as a major metastatic site for prominent tumor types. Yet, studying this important interaction is difficult by current methods; there are no good model systems to explore the natural, dynamic course of metastases to the bone marrow. In this presentation, we will introduce a bioengineering strategy to study bone marrow metastases of human tumor cells by applying tissue-engineering principles. We will first discuss the development of humanized marrow implant that is composed of a biomimetic scaffold pre-seeded with human bone marrow stromal cells. This implant can retain and support host and transplanted human bone marrow cells. Multiple genetically-engineered human microenvironments were also achieved in a single host mouse. We will also present a model system to study the spread of human metastasis in a mouse, beginning from an orthotopic tumor, to circulating tumor cells, and finally a metastatic nodule that was captured using our bone marrow implant. This model system was also leveraged as a platform for testing anti-metastatic drug compounds. The presented approach can be readily applied to other types of human cancer types with bone marrow homing prevalence.

Photo-Cross-Linked Amniotic Membranes for Preservation of Limbal Epithelial Progenitor Cells: Ultraviolet Irradiation Dosage Effect

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To avoid potential toxicity induced by chemical cross-linkers, the amniotic membrane (AM) was physically cross-linked by ultraviolet (UV) irradiation to stabilize the tissue collagen matrix. In this study, we investigated the irradiation dosage effect on the biophysical characteristics of tissue matrix and its ability to preserve limbal epithelial progenitor cells. After exposure to different dose levels of UV irradiation (0.9–18.1J/cm2), the AM was investigated by determinations of its cross-linking degree, nanostructure, and biocompatibility. To evaluate the cell stenness, the limbal epithelial cells (LECs) were cultivated on these photo-cross-linked AM substrates for 5 days. The number of cross-links per unit mass of AM significantly increased with increasing irradiation dose. Transmission electron microscopic observations showed that UV irradiation-mediated change in the matrix nanostructure of AM could be attributed to the aggregation of tissue collagen fibrils. The results provide a basis for understanding the relationship between collagen nanofiber size and the number of cross-links generated during AM photo-cross-linking. In vitro and in vivo biocompatibility studies demonstrated that all the physically cross-linked AM materials studied here are not detrimental to corneal cells and tissues. The ABCG2 gene and protein expressions were significantly up-regulated with increasing UV irradiation dosage, suggesting the important roles of cross-linking density and matrix nanostructure in the maintenance of undifferentiated precursor cell phenotype. It is concluded that biophysical characteristics controlled by UV-induced cross-linkage may affect the ability of photo-cross-linked AM to preserve limbal epithelial progenitor cells and its potential application for corneal epithelial tissue engineering.

Peptide-CNT Hydrogels for Tissue Engineering and Cancer tumor Studies

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Self-assembling peptides are promising nanomaterials for tissue engineering and 3D cell culture due to their advantages compared to synthetic or protein-based biomaterials. They are formed from amino acids; can be found throughout the body; at the same time, they can be synthesized with precise control of their chemical composition and form hydrogels with nano-sized fibers/pores upon injection into the body. On the other hand carbon nanotubes as multifunctional