

Mingen Xu, Yongnian Yan , Xiaohong Wang.

“Modeling insulin secretion dysfunction in a three-dimensional culture system by cell-assembly techniqu.”Virtual Environments, Human-Computer Interfaces and Measurements Systems, 2009. VECIMS '09. IEEE International Conference on

Here,we engineered an insulin secretion model by cell-assembly technique which can assemble cells into designated places to form complex three-dimensional structures. Adipose-derived stromal cells were assembled and induced differentiation into adipocytes; pancreatic islets were then assembled at designated stations.A perfusion system was used for a time-dependent estimation of insulin response to glucose stimulation. After long-term exposure to high glucose, the insulin secretion peak value of beta-cell in the 3D system decreased and delayed compared with the 2D culture system. These results suggested that adipocytes in 3D structure help beta-cells capture more pathologic features of diabetes. This 3D culture model provides an excellent system to study the insulin secretion kinetics of the beta-cells. This study also demonstrates that the 3D culture system can provide a model for diabetes drug discovery.

Mingen Xu , Xiaohong Wang , Yongnian Yan , Ri Yao , Yakun Ge

“An cell-assembly derived physiological 3D model of the metabolic syndrome, based on adipose-derived stromal cells and a gelatin/alginate/fibrinogen matrix.” Biomaterials 2010:3868-3877

Abstract One of the major obstacles in drug discovery is the lack of in vitro three-dimensional (3D) models that can capture more complex features of a disease. Here we established a in vitro physiological model of the metabolic syndrome (MS) using cell-assembly technique (CAT), which can assemble cells into designated places to form complex 3D structures. Fibrin was employed as an effective material to regulate ADS cell differentiation and self-organization along with other methods. ADS cells differentiated into adipocytes and endothelial cells, meanwhile, the cells were induced to self-organize into an analogous tissue structure. Overall, this study demonstrated that cell differentiation and self-organization can be regulated by techniques combined with CAT. The model presented could result in a better understanding of the pathogenesis of MS and the development of new technologies for drug discovery.

Mingen Xu , Yongnian Yan , Haixia Liu , Rui Yao , Xiaohong Wang
“Controlled Adipose-derived Stromal Cells Differentiation into Adipose and Endothelial Cells in a 3D Structure Established by Cell-assembly Technique”
Journal of Bioactive and Compatible Polymers, 2009:31-47

One of the major obstacles in engineering thick and complex tissues while vascularizing tissues in vitro is to maintain cell viability during tissue growth and structural organization. Adipose-derived stromal (ADS) cells were used to establish a multicellular system through a cell-assembly technique. Attempts were made to control ADS cells differentiation into different targeted cell types according to their positions within an orderly 3D structure. Oil red O staining confirmed that the ADS cells in the structure differentiated into adipocytes with a spherical shape while immunostaining tests confirmed that the endothelial growth factor induced ADS cells on the walls of channels differentiated into mature endothelial cells and then organized into tubular structures throughout the engineered 3D structure.

Mingen Xu , Yanlei Li , Hairui Suo , Yongnian Yan , Li Liu , Qiujun Wang
“Fabricating a pearl/PLGA composite scaffold by the low-temperature deposition manufacturing technique for bone tissue engineering”
Biofabrication. 2010 2(2):025002.

Here we developed a composite scaffold of pearl/poly(lactic-co-glycolic acid) (pearl/PLGA) utilizing the low-temperature deposition manufacturing (LDM). LDM makes it possible to fabricate scaffolds with designed microstructure and macrostructure, while keeping the bioactivity of biomaterials by working at a low temperature. Process optimization was carried out to fabricate a mixture of pearl powder, PLGA and 1,4-dioxane with the designed hierarchical structures, and freeze-dried at a temperature of -40 degrees C. Scaffolds with square and designated bone shape were fabricated by following the 3D model. Marrow stem cells (MSCs) were seeded on the pearl/PLGA scaffold and then cultured in a rotating cell culture system. proper pore size (micropores: <10 microm; macropore: 495 +/- 54 microm) and mechanical property (compressive strength: 0.81 +/- 0.04 MPa; elastic modulus: 23.14 +/- 0.75 MPa). All these results indicate that the pearl/PLGA scaffolds fulfill the basic requirements of bone tissue engineering scaffold.

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Mingen Xu, Yongnian Yan, Renjie Zhang, Ri Yao, Haixia Liu , Xiaohong Wang
“Establishing a multicellular model by three-dimensional cell-assembly technique for metabolic syndrome” Biotechnology, Pharmacology,2008

In this article, we give the first report that establishes an energy metabolic system model using cell-assembly technique which can assemble cells into designated places to form complex three-dimensional structures. Adipose-derived stromal cells were assembled and induced differentiation into adipocytes and endothelial cells; pancreatic islets were then deposited at designated locations and constituted adipoinsular axis with adipocytes. Analysis of the factors involved in energy metabolism showed our system could capture more physiological and pathophysiological features of the in vivo energy metabolism. Drugs known to have effects on MS showed accordant effects in the systems. Construction and study of such multicellular systems could help us better understand pathogenesis of MS, develop new technologies for drug discovery, and foster applications in tissue engineering and metabolomics profiling.

Ting Zhang , Yongnian Yan , Xiaohong Wang , Zhuo Xiong , Feng Lin
“Three-dimensional Gelatin and Gelatin/Hyaluronan Hydrogel Structures for Traumatic Brain Injury”
Journal of Bioactive and Compatible Polymers, 2007;19-29

Brain tissue engineering has now emerged as one of the most promising treatments for the traumatic brain injury. In this article, two groups of three-dimensional (3D) hydrogel structures composed of gelatin and gelatin/hyaluronan have been formed using our 3D cell assembly technique for in vivo study in rats, in order to investigate their effects in reparation of injury in the central nervous system (CNS). After 4, 8, 10, and 13 weeks of implantation, sections of brains were processed with NISSL staining for observing the immigration of host neural cells into the implanted materials and the degradation property of the materials. The results showed that simplex gelatin and gelatin/hyaluronan (20:1) with 3D structures both have good biocompatibility with brain tissue while gelatin/hyaluronan has a better contiguity with the surrounding tissue. Through our primary study, it seems that 3D gelatin/hyaluronan structures may be useful in brain tissue repair.

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Wei Xu , Xiaohong Wang , Yongnian Yan , Wei Zheng , Zhuo Xiong , Feng Lin
“Rapid Prototyping Three-Dimensional Cell/Gelatin/Fibrinogen Constructs for Medical Regeneration”

Journal of Bioactive and Compatible Polymers, 2007:363-377

There is a need for rapid fabrication of tissue or organs with well-defined structures and functions in regenerative medicine. Two patterns of cell/matrix constructs containing hepatic cells, gelatin and fibrinogen were successfully created by automated rapid prototyping techniques and stabilized with thrombin. No apparent cell damage was found during the process. Mechanical characterization demonstrated that a 1:1 ratio gelatin/fibrin mixture had the greatest elasticity modulus and compressive strength. Microscopic and histological observations showed that hepatic cells were embedded in the gelatin/fibrinogen matrix and were proliferating. Immunostaining and biochemical analysis indicated that the embedded hepatocytes secreted albumin. Fibrin appears to be a favorable component for a gelatin based cell assembly matrix in that it is bioresorbable, easily manipulated, and supports in vitro cell functions.

Xiaohong Wang , Shaochun Sui , Yongnian Yan , Renji Zhang
“Design and Fabrication of PLGA Sandwiched Cell/Fibrin Constructs for Complex Organ Regeneration”

Journal of Bioactive and Compatible Polymers,2010:229-240

A poly(DL-lactic-co-glycolic acid) (PLGA) sandwich fibrinogen/ adipose stem cell (ADSC) construct was fabricated to generate smooth muscle tissue. The mechanical properties and ADSC compatibility of PLGA, poly(ethylene glycol-1,6-hexamethyl diisocyanate-caprolactone) i.e. polyurethane (PU), gelatin, alginate, and fibrin composites were evaluated for vascular smooth muscle tissue generation. Synthetic PLGA and PU combined with natural gelatin, alginate, and fibrin for strength and cell compatibility were found to be effective. A trilayer construct was designed and built with a microporous inner PLGA layer to provide nutrient, oxygen, and metabolite transfer while the outer PLGA layer with no pores prevented leakage during in vitro culture and in vivo implantation. The fibrin layer suitably accommodated ADSC growth, migration, proliferation, and differentiation inside the construct. This design has the potential for wide use in tissue engineering and complex organ construction.

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HaiXia Liu , ShengJie Li , YongNian Yan , XiaoHong Wang , Feng Lin , RenJi Zhang
“**A liver analog construct for use as an alcoholic liver disease model**” Chinese
Science Bulletin, 2012:955-958

The construction of an in vitro liver analog is likely to be of great use for the study of alcoholic liver disease (ALD) and other hepatic disorders. Preliminary results indicate that multi-cell assembling technology can produce two hybrid cell-matrix spatial distributions according to predesigned digital models; therefore, it is possible to fabricate a liver-like construct that can mimic the structure and main components of the natural liver. After in vitro culture, a liver analog was formed. Employing the rat liver analog constructs cultured in vitro for several days for the study of ALD by adding alcohol, MDA and NO concentration were altered and controlled by adding vitamin E and vitamin C. ALD is considered an important factor in liver cancer where the pathogenesis is complex but the mechanism is still not well understood. Previous research of pathogenesis and drug prevention in ALD was based on animal models, such as baboons or rats, with particular limitations. Therefore, multi-cell assembling technology used to construct human liver analogs that contain various human liver cells is likely to be useful for studying ALD pathogenesis and related drug research.

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