S9

生物制造分会场

深圳大中华喜来登酒店

主席：杜亚楠

主席：席建忠

2022年3月27日 星期日 09:00-17:33
深圳大中华喜来登酒店-元3+4

时间	演讲题目	演讲者姓名和单位
09:00-09:25	Cell Identity Conversion and Liver Regeneration	**惠利健** 中国科学院分子细胞科学卓越创新中心
09:25-09:50	微纳静电生物打印：调控细胞 / 组织生长新途径	**贺健康** 西安交通大学
09:50-10:15	A novel 3D microscaffold promoted the generation of hematopoietic stem/progenitor cells from human pluripotent stem cells	**那 洁** 清华大学
10:15-10:40	Systemic immune responses to irradiated tumours via the transport of antigens to the tumour periphery by injected flagellate bacteria	**吴锦慧** 南京大学
10:55-11:20	基于核酸链置换的基因精准分析	**齐 浩** 天津大学
11:20-11:45	基于液滴微流控的模块化组织 3D 打印技术	**王华楠** 大连理工大学
11:45-12:10	微组织工程革新生物制造和再生医学	**杜亚楠** 清华大学
13:30-13:50	构建透明化肝癌模型评估多种化疗栓塞制剂	**郭琼玉** 南方科技大学
13:50-14:10	Accelerate wound healing by microscale gel array patch encapsulating defined SDF-1α gradient	**许 振** 深圳大学
14:10-14:30	3D printed hydrogel scaffolds with macro pores and interconnected microchannel networks for tissue engineering vascularization	**罗永祥** 深圳大学
14:30-14:50	Surface-anchored framework for generating RhD-epitope stealth red blood cells	**王 本** 浙江大学
14:50-15:10	A novel electrospray system for cell encapsulation with high-throughput	**范泽军** 清华大学
15:10-15:30	基于 DLP-3D 打印的工艺研发及高精度微流控芯片的高通量制造与运用	**罗志明** 深圳大学
15:45-15:57	Dynamic and High Throughput Multi-spheroid Organoid-chip for Effective and Accurate Drug Screening	**朱宇瑄** 浙江大学
15:57-16:09	Application of Heart-on-a-chip with computer vision in drug toxicity detection	**赵 吉** 天津工业大学
16:09-16:21	In vitro micro-tissue model reconstructs expansion pattern in liver fibrosis progression and reveals cell communication through mechanical cues	**周 律** 清华大学
16:21-16:33	TGase-mediated matrix crosslinking is a marker of liver fibrosis and regulates cell behavior in hepatic microenvironment	**吕 丞** 清华大学
16:33-16:45	ECM-degradable endothelial cells for liver fibrosis treatment	**赵 鹏** 清华大学
16:45-16:57	三维蛋白支架对细胞生长状态的影响及应用研究	**邹晓敏** 深圳大学
16:57-17:09	Electrohydrodynamic printing of 3D vascularized multidirectionally-aligned cardiac tissue constructs for enhanced cardiac infarction repair	**韩 康** 西安交通大学
17:09-17:21	Engineering vascular model reveals mechanism of hepatic vascular microenvironment response to hydrostatic pressure in liver fibrosis progression	**龙 艺** 清华大学
17:21-17:33	开发一种可折叠的两亲性的透明高分子薄膜植片用于治疗大泡性角膜病变	**李俊阳** 清华大学

上午 25 分钟的口头报告包含 20 分钟报告 +5 分钟提问；下午 20 分钟的口头报告包含 17 分钟报告 +3 分钟提问，12 分钟的口头报告包含 10 分钟报告 +2 分钟提问。

Cell Identity Conversion and Liver Regeneration

Lijian Hui
State Key Laboratory of Cell Biology, Shanghai Institute of Biochemistry and Cell Biology, Center for Excellence in Molecular Cell Science, Chinese Academy of Sciences, Shanghai, China
Email：huilab@sibcb.ac.cn

Objective： To understand the mechanistic regulation underlying cell plasticity during liver regeneration and tumorigenesis of normal cells is a long-term interest of our lab.

Methods： Recently, taken hepatocytes as the experimental system, our lab has initiated studies on cell lineage conversion for regeneration, namely transdifferentiation and dedifferentiation in vitro and in vivo. Striving to understand these two seemingly different phenomena, we find ourselves in querying the essential scientific question: How is cell identity maintained through preventing the conversion of terminally differentiated cells to other cell types, including cell lineage conversion and transformation to tumor cells; or in a reversed term, how is the cell plasticity regulated?

Results： In vivo cellular reprogramming after injury can regenerate injured tissue and restore function. Li et al. show that Arid1a regulates liver regeneration by promoting a permissive chromatin state in hepatocytes, which renders them competent to respond to injury associated regenerative signals and facilitates expression of liver-progenitor like cell genes.

By using directly reprogrammed human hepatocytes (hiHeps) and inactivation of p53 and RB, Sun et al. established organoids possessing liver architecture and function. HiHep organoids were genetically engineered to model the initial alterations in human liver cancers. Bona fide hepatocellular carcinomas were developed by overexpressing c-Myc. Excessive mitochondrion–endoplasmic reticulum coupling induced by c-Myc facilitated hepatocellular carcinoma initiation and seemed to be a target of preventive treatment. Furthermore, through the analysis of human intra-hepatic cholangiocarcinoma-enriched mutations, we demonstrate that the RAS-induced lineage conversion from hepatocytes to intra-hepatic cholangiocarcinoma cells can be prevented by the combined inhibition of Notch and JAK–STAT.

Conclusion： In this talk, I will present our latest findings to demonstrate a role of hepatocyte reprogramming in liver regeneration and tumorigenesis.

微纳静电生物打印：调控细胞 / 组织生长新途径

贺健康
西安交通大学
Email：jiankanghe@mail.xjtu.edu.cn

目的：自然组织与器官细胞外基质通常由特定排布规律的微纳米胶原纤维结构组成，体外精确制造这些微结构环境对调节细胞分化生长与功能化活性组织构建具有重要意义。近年来，生物打印技术由于在三维结构可控制造方面的巨大优势被广泛应用于人工组织与器官制造研究，但由于现有生物打印的尺寸精度普遍较低（>200 μm），从而难以精确模拟体内组织细胞生长的三维微纳结构环境。为此，本文介绍了一种基于电流体动力学原理的微纳静电生物打印新方法。

方法：微纳静电生物打印是通过采用静电场力代替传统机械挤出力，使打印单根纤维尺寸远小于喷头直径，从而实现可降解生物材料纤维与活性细胞 / 水凝胶单丝的高精度可控沉积与叠加。研究了工艺参数如电压、接受距离、流量等对打印纤维线宽的影响规律，阐明了静电打印过程中电场强度随着打印高度的衰减规律与静电排斥机制，发明了高活性、高精度的活性细胞静电打印新技术，探索了微纳静电生物打印技术在调控细胞三维定向生长与功能化心肌组织体外制造方面的应用。

结果：研制了具有原位监测功能的微纳静电生物打印系统，主要包括高压电源、注射泵、打印喷头、收集基板和高分辨率移动台等模块；实现了最大结构高度为 10.01 ±0.18 mm、平均纤维线宽为 18.3 ± 1.5 μm 的三维生物纤维结构的精确打印，成功构建了三维分层定向、高频跳动的活性类心肌组织；提出了采用绝缘接收基底代替传统半导体或导电基底并将打印距离从现在的毫米级缩小至 50-100 μm 的静电打印新策略，从而保证可控稳定打印的同时将细胞静电打印过程中的电流从毫安级（>0.5 mA）大幅减小至微安级（<10 μA），实现了高活性（>96%）、高精度（<50 μm）的细胞静电打印。

结论：微纳静电生物打印技术突破了现有生物挤出打印尺寸严重依赖喷头直径的限制，将生物打印纤维尺寸大幅缩减至微米 / 亚微米尺度，为可控制造与天然细胞外基质纤维或活细胞尺度相似的微结构环境提供了新途径。

A novel 3D microscaffold promoted the generation of hematopoietic stem/progenitor cells from human pluripotent stem cells

Jie Na
Tsinghua University
Email：jie.na@tsinghua.edu.cn

Objective: Embryonic primitive and definitive hematopoiesis are essential for the development and maintenance of the blood system. During embryo development, hematopoietic stem/progenitor cells (HSPCs) are derived from a special type of endothelial cells (ECs), termed hemogenic endothelial cells (HECs), at several locations in the embryo. As HSPCs have significant value in regenerative medicine. The aim of our study is to establish an efficient system to generate HECs and HSPCs from human pluripotent stem cells (hPSCs).

Methods: we established a novel 3D platform, that mimics the microenvironment of primitive hematopoiesis, such as at the yolk sac and aorta-gonad-mesonephros (AGM) region, and use it to differentiate HECs and HSPCs from hPSCs.

Results: We found that the 3D microscaffold greatly promoted the formation of HECs and HSPCs from hPSCs. Moreover, cells in the 3D microscaffold are capable to modify the biomaterial to mimick the in vivo niche structure. Single-cell RNA-seq analysis revealed that HSPCs generated in the 3D microenvironment better resembled human embryonic hematopoietic stem cells in vivo. Moreover, the 3D microscaffold also form a protective niche and facilitated the larger scale production of HECs and HSPCs.

Conclusion: Our study improve the quality and quantity of HEC and HSPC derived from hPSCs and help to meet the growing need for off-the-shelf HSPCs for drug development, cell therapy and regenerative medicine.

Systemic immune responses to irradiated tumours via the transport of antigens to the tumour periphery by injected flagellate bacteria

Jinhui Wu
Nanjing University
Email：wuj@nju.edu.cn

Objective: The immune system has been identified to be able to cure cancers. Among these strategies, the most promising method is to stimulate immune response by novel tumour antigens to eliminate systemic tumour. However, the intrinsic inhibitory immune microenvironment of tumour inhibits the uptake and presentation of these new antigens, which in turn leads to inhibition of immune response.

Methods: We employed the movable Nano-bacteria to capture tumour antigens and actively deliver them out of immunosuppressive microenvironment for better immune activation.

Results: Results showed that through this way, a 36-fold increase of OVA- specific DC activation can be achieved. Systemic antitumour effects were observed in four tumour-bearing mice models and over than 60% survival rate in tumour-metastasis mice model (v.s. 20%) were observed. Moreover, the cured mice (tumour free) were not observed to have tumour recurrence within 265 days and were able to resist further multiple tumour inoculations. Furthermore, the antitumour effects can be abrogated by CD8 blocking, indicating the systemic tumour regression was caused by the adoptive immune response.

Conclusion: In conclusion, to solve the problem that the in-situ antigen cannot initiate the immunity in tumour suppressing microenvironment, we have innovatively proposed a method of transporting the antigens into tumour marginal tissue microenvironment and then activating the DCs.This method is simple and effective, and does not need to regulate the immune microenvironment, providing a new idea and direction for personalized in-situ vaccine.

基于核酸链置换的基因精准分析

齐浩
天津大学
Email：haoq@tju.edu.cn

目的：核酸分子间识别的高度序列依赖性已经成为有力可靠的生物工程工具之一，这里我们通过设计链置换分子探针，针对低浓度、单碱基位点，实现恒温、精准的片段化核酸序列分析。

方法：核酸分子链置换反应被广泛应用到诸多的分子生物技术，基于现有的计算机辅助分子结构算法，仅通过核酸序列已经可以实现高精准度的结构以及核酸分子间相互作用的预测。基于高精度的核酸行为模拟计算，在核酸接合反应（ligation）中，我们引入了具有 Toehold 设计的核酸分子探针，通过 Toehold 诱导实现热动力平衡驱动的核酸接合反应复合体形成，通过探针的热动力性能的调控实现了对于单碱基变异序列高效识别的核酸结合反应。

结果：通过简单的 Toehold 核酸探针设计与添加，我们在经典的模板依赖性核酸接合反应中实现了多个全新的可调节分子功能，首先与现有的反应机理相比，Toehold 探针实现了目标模版的循环，这也是首次报到的人工设计的可循环核酸接合反应，极大地提高接合反应效率，可以实现高探针 / 模板分子比例下的核酸接合反应，并且可以有效地防止探针间的多倍体链接。因此，我们实现了具有单碱基区分能力的核酸接合反应，并且实现了 DNA 探针对于 RNA 或者 DNA 目标序列上的单碱基变异的高效识别。在恒温操作下，我们证明了对于来自外周血的高度片段化肿瘤 DNA 分子诊断，以及病毒核酸序列的高灵敏度检测分型。

结论：与现有的技术相比，Toehold 核酸探针介导的接合反应可以实现在较小目标序列范围内实现特定序列的单碱基变异的精准检测，对于肿瘤的液体活检、病毒快速分型都具有极大的应用前景。

基于液滴微流控的模块化组织 3D 打印技术

王华楠
大连理工大学
Email：huananwang@dlut.edu.cn

目的：本研究提出以微凝胶（Microgels）组装的颗粒水凝胶（Granular hydrogels）作为 3D 生物打印墨水，基于液滴微流控（Droplet microfluidics）技术精准设计制造载单细胞微凝胶载体作为基本模块，通过微颗粒组装和 3D 打印技术结合突破单细胞精度的仿生组织体外精准构建。

方法：通过微流芯片设计、乳液体系设计、新型温敏表面活性剂合成等技术研发，以突破细胞包裹微凝胶的连续、高通量制备技术。通过流体力学模拟优化集合复杂多通道芯片制造，以实现高通量微凝胶载体的制备。开展水凝胶基质的设计优化和单细胞可控组装，以满足细胞微环境的重塑和仿生，从而调控干细胞增殖分化等功能。通过多场耦合交联凝胶网络设计，以赋予颗粒基凝胶打印成形性和结构稳定性，以实现工程化组织的精准构建。

结果：成功开发出乳化 - 破乳一体化芯片、温控乳化 - 破乳一步法、双乳液液滴模板法等多种载细胞微凝胶制备技术，实现连续、快速、一步法的微凝胶载体制备，不仅实现单细胞水平的细胞封装，同时又保持封装细胞的存活和功能。进一步利用流体模拟技术结合复杂多层芯片制造工艺，成功开发出大批量制备载单细胞凝胶微载体的新型高通量芯片，单细胞微载体生产率比现有液滴微流控技术提高了两个数量级（>10ml/hr）。开发出一种由明胶和透明质酸复合的、光触发亚胺交联的新型微凝胶制备材料，解决了自由基引发聚合的微凝胶载体制备时因氧阻聚导致的网络分布不均匀、力学强度差的难题；成功开发可多场交联的颗粒凝胶作为打印墨水，赋予了颗粒凝胶剪切变稀和自愈合特性及打印成形性，通过体外细胞实验和体内动物模型，证实打印的组织工程支架显著促进干细胞的成骨分化和骨组织再生。

结论：本研究从生物微制造技术和微环境仿生材料设计两方面出发，为单细胞精度的工程化类组织体外精准制造提供了新策略，并在单细胞水平开展干细胞微环境研究，为 3D 生物打印技术的再生医学应用开辟了新方向。