Pleanary sessions

PL1.1

Lgr5 Stem Cell-based organoids in human disease

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The intestinal epithelium is the most rapidly self-renewing tissue in adult mammals. We originally defined Lgr5 as a Wnt target gene transcribed in colon cancer cells. Two knock-in alleles revealed exclusive expression of Lgr5 in cycling columnar cells at the crypt base. Using lineage tracing experiments in adult mice we found that these Lgr5+ve crypt base columnar cells (CBC) generated all epithelial lineages throughout life implying that they represent the stem cell of the small intestine and colon. Lgr5 was subsequently found to represent an exquisitely specific and almost 'generic' marker for stem cells including in hair follicles kidney liver mammary gland inner ear tongue and stomach epithelium.
Single sorted Lgr5+ve stem cells can initiate ever-expanding crypt-villus organoids or so called 'mini-guts' in 3D culture. The technology is based on the observation that Lgr5 is the receptor for a potent stem cell growth factor R-spondin. Similar 3D cultures systems have been developed for the Lgr5+ve stem cells of human stomach liver pancreas prostate and kidney. Using CRISPR/Cas9 technology genes can be efficiently modified in organoids of various origins.

PL2.1

Biofabricating the interface between biology and electronics

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Advances in biology and microelectronics transformed our lives over the last 50 years and there remains considerable opportunity to create synergies between these two fields. For instance the effective interfacing of biological and electronic systems could enable remarkable capabilities for sensing (disease diagnosis and monitoring) energy harvesting (biofuel cells) and medicine (neuroprosthetics). Through a network of local and international collaborations we are examining two challenges to bio-device integration – constructing the physical interface and establishing communication across this interface. In both cases we are applying the materials and mechanisms from biology to address these challenges.
To construct a bio-device interface we employ stimuli-responsive hydrogel-forming biopolymers that can be triggered to self-assemble at electrode addresses in response to electrode-imposed signals. The hydrogel films assembled at the electrode can be bio-functionalized to offer cellular functions or modified with proteins to offer molecular functions. Communication across this interface is achieved through redox. Specifically a redox-active (but non-conducting) film is fabricated to accept redox information from biology and transmit this information to the electronics. These studies demonstrate that biology offers unique materials and mechanisms for the “fusion” of biology and electronics.

PL3.1

Cellular building blocks for 3D tissue fabrication

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Several MEMS/Microfluidic-based approaches for the rapid construction of large-scale 3D tissue that mimic microscopic tissue structures in vivo will be presented. We demonstrated a bottom-up tissue construction method using different types of cellular modules that serve as building blocks for thick and dense 3D tissues (eg. cell beads and cell fibers).
To prepare the cellular beads we used an axisymmetric flow focusing device (AFFD) that allows us to encapsulate cells within monodisperse collagen beads. By putting these cellular microcapsules in a 3D chamber and incubating them we built a complicated and milli-sized 3D structure.
As the fiber-shaped cellular building units a cell- encapsulating core-shell hydrogel fiber was produced in a double coaxial laminar flow microfluidic device. The cells cultured in the fiber show excellent intrinsic functions. When with myocytes endothelial and nerve cells they showed the contractile motion of the myocyte cell fiber the tube formation of the endothelial cell fibers and the synaptic connections of the nerve cell fiber respectively. By using microfluidic handling higher-order assembly of fiber-shaped 3D cellular constructs can be performed. In particular mechanical weaving of cell fibers with our lab-made microfluidic weaving machine provides a woven "cell fabric" composed of three different cell fibers within 3 h in a culture medium. As the practical application the fiber encapsulating beta-cells is used for the implantation of diabetic mice and succeeded in normalizing the blood glucose level.

PL4.1

Direct tissue engineering approaches for regenerative biology and medicine

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The ability to manipulate and distribute living mammalian cells with control presents fascinating possibilities for a plethora of applications in our healthcare. These imply several possibilities in tissue engineering and regenerative biology/medicine to those of a therapeutic nature. The physical sciences are increasingly playing a pivotal role in this endeavour by both advancing existing cell engineering technology and pioneering new protocols for the creation of biologically viable structures. The talk will briefly introduce leading technologies1 which have been fully validated from a physical chemical and biological stand point for completely demonstrating their inertness for directly handling the most intricate advanced material known to humankind. Hence each protocol's advantages and disadvantages will be clearly identified whilst recognizing their future biological and engineering challenges. Although several technologies will be discussed the talk will focus of bio-electrosprays2 and cell electrospinning3 which have truly pushed back the frontiers of tissue engineering and regenerative medicine previously hither to unachieved by any of its competing technologies in the toolbox. In conclusion a few selected biotechnological applications will be presented where these protocols could undergo focused exploration. Successful development of these bio-protocols sees the emergence of unique future platform strategies within both a laboratory and a clinical environment having far-reaching consequences for our healthcare.

1. D. Poncelet P. de Vos N. Suter and S.N. Jayasinghe Bio-electrospraying and cell electrospinning: progress and platform opportunities for basic biology and the clinical sciences Advanced Healthcare Materials 1(2012)27-34.
2. S.N. Jayasinghe A.N. Qureshi and P.A.M. Eagles Electrohydrodynamic jet processing: An advanced electric-field-driven jetting phenomenon for processing living cells Small 2(2006)216-219.
3. A. Townsend-Nicholson and S.N. Jayasinghe Cell Electrospinning: a unique biotechnique for encapsulating living organisms for generating active biological microthreads/scaffolds Biomacromolecules 7(2006)3364-3369.

PL5.1

Cartilage engineering research and its application

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Cartilage defect repair has always been a challenge in clinical treatment. Our lab devoted to fundamental and application oriented research focusing on cartilage regeneration and repair and achieved some important progresses: ① established chondrogenic induction system which could promote stem cell chondrogenesis for cartilage regeneration by mimicking the chondrogenic micro environment which may help to address the issue of seed cell source; ② established in vitro 3D cartilage regeneration technology and established shape control technology for the in vitro regenerated cartilage by combining with CAD-CAM related techniques;③ developed bioreactor to be used specially for cartilage regeneration and promoted mechanical properties of the in vitro regenerated cartilage;④ established and successfully repaired cartilage defect models (such as articular joint defect meniscus defect etc.) in big animals;⑤ successfully conducted clinical trials for articular joint repair based on stem cell and in vitro regenerated cartilage. ⑥ recently achieved important breakthrough on in vitro regeneration of human ear shaped cartilage which has been clinically translated to treat patient with microtia. These works addressed fundamental issues of cartilage engineering and played important roles in promoting clinical translation of this technology.