BIOPRINTING CARTILAGE GRAFTS

Marcy Zenobi-Wong

ETH Zürich, Zurich, Switzerland

Bioprinting is an emerging technology for the fabrication of patient-specific, anatomically-complex tissues and organs. A novel bioink was developed based on two unmodified regulatory-compliant polysaccharides, gellan and alginate, which undergoes cell friendly gelation in the presence of cations. Rheological properties of the bioink revealed optimal shear thinning and shear recovery properties for high fidelity bioprinting. Tensile testing of bioprinted dumbbell-shaped specimens revealed a strong, ductile material. To make the bioink tissue-specific and bioactive, extracellular matrix particles can be added, or the polymers can be sulfated for growth factor binding affinity. As proof of concept, clinical product BioCartilage® (cartilage extracellular matrix particles) and bovine chondrocytes were added to the bioink. 3D auricular, nasal, meniscal and vertebral disc grafts were printed based on computer tomography (CT) data or generic 3D models. The bioink containing BioCartilage supported proliferation of chondrocytes and, in the presence of transforming growth factor beta-3 (TGF-β3), supported strong deposition of cartilage matrix proteins. A clinically-compliant bioprinting method is presented which yields patient-specific cartilage grafts with good mechanical and biological properties. The versatile method can be used with any type of tissue particles to create tissue-specific and bioactive scaffolds.

3D CELL AND TISSUE CULTURING UNDER PERFUSION

David Wendt

Cellec Biotek AG, Basel, Switzerland

The in vitro culture of primary cells typically involves monolayer expansion on tissue culture plastic (e.g., on Petri dishes) and serial replating of the cells onto new dishes upon confluence. This technique fails to recapitulate a physiological environment and is associated with a loss of characteristics and functionality of the expanded cell progeny. Cell culture in a 3D setting (e.g., within the pores of 3D scaffolds), which in turn requires the use of perfusion-based bioreactor systems to maintain suitable mass transfer rates, has the potential to recapitulate features of a

physiological and pathological environment and thereby support cell functionality. This presentation will highlight the use of bioreactor-based 3D culture systems for applications including: (i) the expansion of progenitor cells while preserving their native properties ('niche' concept), (ii) the co-culture of different cell types, including those of the inflammatory/immune system, as well as (iii) the expansion of primary tumors and cell lines. These advanced 3D cell culture systems can represent organotypic tissue models based on human cells to investigate processes involved in tissue regeneration or disease modeling and treatment. The generated knowledge will be relevant to identify new strategies or compounds to instruct in situ regeneration, as well as to restore pathologic conditions.

BIOREACTOR-BASED CARTILAGE ENGINEERING

David Wendt

Departments of Biomedicine and Surgery, University Hospital Basel, Basel, Switzerland

Autologous Chondrocyte Implantation (ACI) and the second generation Matrix-assisted ACI (MACI) have long been established in the clinic for the repair of cartilage injuries. However, as these products are manufactured with minimal in vitro pre-cultivation times, they contain little to no extracellular matrix and therefore lack the complex biological and mechanical signals which can be delivered by a more physiological mature tissue graft. Our laboratory has recently conducted a clinical trial based on mature cartilaginous engineered tissues for treatment of cartilage lesions, demonstrating the safety and feasibility of the tissue grafts. However, the manufacturing processes used to produce the engineered grafts were based on traditional bench-top manual culture methods, requiring a large number of labor-intensive manipulations, which ultimately pose challenges towards regulatory compliance, process up-scaling, and long-term cost-effectiveness. As an alternative, bioreactor-based manufacturing systems, which automate and control the various bioprocesses, have the potential to overcome the limitations associated with conventional manufacturing methods. Robust and streamlined bioreactor-based processes, as described in this presentation, will be key for the future manufacturing of cartilage grafts for clinical applications, as they facilitate the establishment of simple, compact, and closed manufacturing systems, with minimal user intervention required, lower operating costs, and increased compliance to safety guidelines.