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

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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.