Studies on various culture systems for chondrocytes and osteoblasts

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt förvar i Hörsal E, Humanisthuset, onsdagen den 27 september, kl. 09:00.
Avhandlingen kommer att förvaras på engelska.

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Osteoarthritis and osteochondral defects are ailments that are increasing in frequency as the lifespan of the population increases and sedentary lifestyle becomes more common. Osteoarthritis is an inflammatory disease that causes the progressive degeneration of the articular surface and the underlying bone. Accidents and injuries can cause osteochondral defects similar to osteoarthritis. In both cases the structure of the articular cartilage fails, leading to pain and disability. Articular cartilage has a naturally poor ability to regenerate since there is no vasculature and it is aneural. The sparse chondrocytes mainly act to maintain the healthy extracellular matrix. Once the defect is severe enough, a surgical intervention becomes necessary. For small defects and young patients, a cell-based treatment can be used, whereas for larger defects and severe osteoarthritis a partial or whole joint arthroplasty is performed. Methods to repair osteochondral defects have been improving over the years as the inter-disciplinary understanding of joints and what is required to repair them has increased. However, there are still issues to solve in order to achieve consistently good results in both joint replacement and repair of cartilage. Main issue faced with the current techniques used for joint replacement is poor integration of the artificial joint, leading to loosening at the bone interface over time, while cartilage repair techniques face the problem of generating mechanically inferior fibrocartilage. It is known that surface chemistry and structures at micro- and nanoscale influence cell behaviour, which can be utilised to guide their attachment, proliferation and phenotype. Scaffold-free approaches and mechanical stimulation have previously given promising results in generating articular neocartilage.

This thesis aims at exploring tools and solutions to the problems involved in implant integration, chondrocyte expansion and neocartilage tissue engineering. We hypothesised that 1) ultra-short pulsed laser deposition can be used to create biocompatible coatings; 2) micropillars with nanoscale features can improve the maintenance of the chondrocyte phenotype and 3) hypergravity can aid in the production of more native-like neocartilage constructs.

Our studies showed that ultra-short pulsed laser ablation can be used to create various surfaces for studying cell behaviour. Cell viability was slightly higher on a rough titanium oxide, whereas the cell area was significantly smaller on rough titanium oxide, indicating a lower amount of focal adhesions. Nanopatterned microstructures were not capable of maintaining the chondrocyte phenotype, but they were not disadvantageous either. Hypergravity might help in creating a native-like distribution of collagen and proteoglycans. The constructs were more uniform in shape, but biomechanically the constructs were not different from non-centrifuged controls.

Keywords
Cell biology, chondrocyte, osteoarthritis, surface materials, topography, tissue engineering, mechanical stimulation