Nanoscale control of mesenchymal stem cells

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Bone and the bone marrow niche are regenerative tissues comprising multiple cell types. This presentation will focus on using nanoscale approaches to drive bone regeneration and to bioengineer niche environments to allow enhanced self-renewal and retention of immune suppressive mesenchymal stem cell (MSC) phenotype.
For bone formation, we have used nanoscale topographies to show that physical cues alone can drive osteogenesis[1]. This data highlighted that integrin/growth factor receptor co-localisation is critical for efficient MSC osteogenesis[2]. Thus, we have developed a simply-engineered polymer (polyethylacrylate, PEA) system that facilitates integrin/BMP-2 co-localisation for the cells with the aim to further enhance osteogenesis[3]. With this bioengineered system, it is easy to upscale and move to 3D as the polymer can be applied via spin coating or plasma polymerisation. Recently, we successfully trialled bone graft coated with the PEA - BMP-2 in a compassionate veterinary case, a giant Münsterländer, Eva, who had suffered a major non-union fracture and was facing amputation; she now enjoys a normal quality of life with enhanced bone regeneration allowing her to retain her foreleg. Finally, from understanding that as cells adhere, they vibrate their focal adhesions, we have developed a nanovibrational bioreactor that uses 1000 Hz, 40 nm vibrations to drive osteogenesis in 3D hydrogels; the Nanokick[4]. This non-invasive and non-chemical differentiation protocol is allowing us to prepare lab-grown graft in readiness for a human trial in 2021.
For MSC self-renewal, we, again, used a nanotopography to show that MSCs could be grown with a retained MSC phenotype in the lab for prolonged periods[5]. This is important as out of their marrow niche, MSCs tend to quickly differentiate into e.g. fibroblasts. This makes it hard to grow large numbers of high quality stem cells in vitro. It is notable that MSCs are finding use in transplant treatments – not for their regenerative capacity per se, but for their immune-suppressive capacity. This capacity is also lost with time in vitro, but can be maintained using nanotopography. Using a metabolomics pipeline that we developed to understand MSC differentiation[6], we identify key glycolytic pathways that can be modulated with drugs in order to achieve prolonged immune suppressive effects and thus generate better MSCs for use with transplant protocols. Going forwards, we are using this information to develop bioengineered MSC niche environments.

References.

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