New frontiers of magnetic materials for regenerative medicine

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Over the past years, the fundamentals of magnetism and magnetic materials have been widely employed in medicine (such as, in drug and gene delivery and hyperthermia treatment of tumors). The possibility to apply these principles to tissue engineering has opened an interesting wide research area of interest. Tissue engineering aims to develop multi-disciplinary approaches for the repair/regeneration of damaged tissues. The main goal is to reconstruct tissues using three-dimensional biodegradable and biomimetic "scaffolds" as a template for cell growth and extracellular matrix deposition. In the design of scaffolds with magnetic properties, the main driving idea was to obtain structures able to be manipulated through magnetic force gradients attracting bio-aggregates, linked to magnetic carriers (i.e. vascular endothelial growth factors) and stimulating angiogenesis and bone regeneration. Furthermore, they can also be used as hyperthermia agents for delivering thermal energy to targeted bodies. Great attention has been focused on the manufacturing process, the material and scaffold features including morphological, chemical-physical, mechanical and mass transport performances through a suitable topological optimization. In particular, fully biodegradable and magnetic nanocomposite scaffolds were produced through additive manufacturing. The properties of the scaffolds were assessed through experimental/theoretical *in vitro* investigations and *in vivo* tests. Morphological studies were performed with Micro-Tomography and Scanning Electron Microscopy. Micro-, Macro- and Nano-mechanical analyses were also carried out. A magnetic analysis was performed in order to assess the behavior of these materials, highlighting their ability to be magnetized at 37°C with an external magnetic field. Human mesenchymal stem cell adhesion and viability were assessed by means of Confocal Laser Scanning microscopy and Alamar Blue assay, whilst cell differentiation was evaluated by the measurement of ALP activity. Furthermore, the influence of a time-dependent magnetic field on cell-laden constructs was also studied. In conclusion, this work suggested these materials as suitable candidates for bone regeneration.

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