Magnetically-driven cellular assembly and stimulation for soft tissue engineering

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Gentle mechanical forces applied to cells can influence their function and be used to enhance cell-cell interactions to create aggregates simply and rapidly.[1] One attractive way to achieve this is using magnetic labelling of cells placed in magnetic fields to remotely stimulate and manipulate cells via mechanotransduction pathways. In this work biodegradable magnetic microspheres of controlled sizes have been produced and functionalised with cell attachment peptides. Fibroblasts, preadipocytes and myoblasts were labelled with magnetic particles of ~5 μm diameter and magnetic fields were generated using various configurations of permanent neodymium magnets. Magnetic fields were simulated using finite element methods to estimate the forces exerted on the cells. Static magnetic fields were used to facilitate assembly of 2D and 3D structures with different spatial arrangements of cells in culture. Rates of differentiation could also be increased via stimulation *in vitro*, with stimulated myoblasts showing significant upregulation of genes associated with muscle maturation over 5 days relative to unstimulated controls.

An external magnetic field has the benefit that it can be used to create multi-cellular assemblies whilst avoiding the high shear conditions that may be experienced through methods such as 3D-printing. The magnetically labeled constructs can be manipulated to control their shape, delay tissue remodeling, and retain desired tissue structures over time in culture, as well as allowing desired forces to be imparted to stimulate the cells.

References

[1] Jafari, J., *et al.*, *ACS Biomater. Sci. Eng*., **2019**, 2532-2542.