Using magnetic force to colonize fibrillar scaffolds with stem/progenitor cells

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Background. Tissue engineering increasingly utilizes fibrillar scaffolds, made of natural or artificial polymers, colonized with cells. These scaffolds can be used either as carriers of cells to the place of deployment (if the polymer is biodegradable), or as permanent supports for the cells. Importantly, given their ability to provide more natural growth support than flat, two-dimensional surfaces, scaffolds can also be used to drive the differentiation of stem/progenitor cells, or to support their growth in vitro [1].

Progress in this field has been hindered by the difficulty of seeding three-dimensional fibrillar scaffolds with cells of a given phenotype in a predictable and controlled manner. Methods currently being used include gravitational settling of a cell suspension on top the scaffold, vacuum-assisted seeding, and the co-deposition of cells and scaffolds (by combined electrospinning-electrospraying) [1]. A major drawback to the electrospinning-electrospraying approach is that it is technically demanding and involves large numbers of scarce cells.

A promising alternative is magnetically-assisted scaffold colonization. Here, cells in suspension are pulled down through the virtual pores of the fibrillar scaffold via magnetic beads attached to the cell surface. A refinement of this method is the selective attraction of cells of a particular phenotype (e.g. rare stem/progenitor cells) from a heterogeneous cell suspension (Fig. 1), followed by removal of those remaining in suspension. Suitable growth factors are added to the retained cells to stimulate their further proliferation.

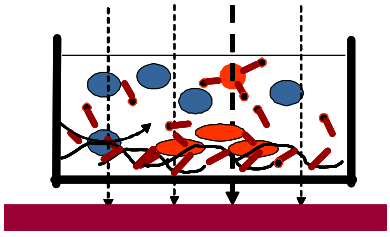

Figure 1. Schematic representation of the magnetic pull down experiment.

The problem. The study group is asked to develop a mathematical model of magnetically-driven cell colonization of the scaffold. Common endpoints of the scaffold colonization experiments are the density of cells in the unit volume of scaffold, and their spatial distribution. Also of interest are the efficiency of labeled cells collection from suspension during a given time period, or the amount of scaffold contamination with non-labeled cells. These endpoints depend on several parameters, too many and too difficult to be empirically optimized [2]. The control parameters are: the size and density of magnetic particles on the cells' surfaces; the size and density of the cells in suspension; the concentration of target cells; the strength of the magnetic force; fluid viscosity; the height of fluid column on top of the scaffold; diameters, geometry, volume distribution of the fibers; cell deformability; cell-fiber interaction (friction and adherence) [3]. For longer-term incubations cell migration and proliferation are also important.

Participants will be provided with data (fiber morphology and distribution and nuclear density) from analysis of digitized, three-dimensional confocal image stacks obtained at the end of a pull down experiment. From the modeling standpoint, a similar problem involving the extravasation of macrophages loaded with magnetic nanoparticles [4,5]. Here it is suggested that the virtual pores created by the randomly distributed microfibers of the scaffolds represent a porous environment similar to that represented by the microvascular network.

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