Dynamic Extracellular Control of Mesenchymal Stem Cell Angiogenic Potential

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Statement of purpose

Pro-angiogenic cell based therapies in regenerative medicine have a still unrealized potential. Mesenchymal stem cell (MSC) secretory profile is affected by their external environment[1]. We had shown before that factors such the composition and compliance of the extracellular matrix (ECM) can modulate the pro-angiogenic properties of MSCs[2]. In this work, we study the effects of in-vitro modulation of hydrogel compliance on MSC fate and pro-angiogenic potential using a magnetically-tunable hydrogel system.

Materials and Methods

Magnetically tunable hydrogels were made by embedding magnetic iron oxide particles in a polyacrylamide matrix. Acrylated ECM protein was tethered chemically to the hydrogel during gelation. The hydrogels can be switched between 'soft' and 'stiff' states by subjecting them to a magnetic field[3].

MSCs are cultured on the surface of these gels and conditioned media, collected after 1 day, is used in a functional angiogenesis assay using human microvascular endothelial cells (hMVECs) on matrigel.

Fluorescence microscopy was used to study MSC morphology and marker expression. HMVEC angiogenesis was analyzed by quantitating tube area[2,4]. MSC conditioned media was analyzed for cytokine expression using RT-PCR and western blotting.

Results

Using a magnetic field, stiffening of hydrogels can be achieved in vitro. There is a corresponding increase in MSC area. The change is reversed upon removal of the magnetic field. Long term culture showed further effects on MSC differentiation and marker expression.

Conditioned media from MSCs cultured under a magnetic field show higher tube formation in the angiogenesis assay then those cultured without. The secretory profile of the MSCs is shown to differ depending on the presence of a magnetic field.

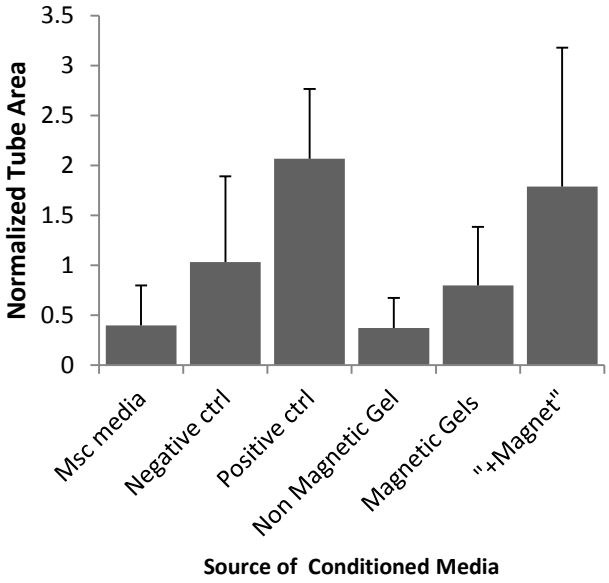

Figure 1 Quantitation of tube formation in HMVECs cultured with conditioned media from MSCs on magnetic gels with/without a magnetic field.

Conclusions

To attain the full therapeutic potential of MSCs, their external culture conditions must be optimized. Pericytes, often act to promote angiogenesis in response to external stimuli[5]. Tunable hydrogels give us an opportunity to study how dynamically modulating the external environment of the gels can impact MSC fate and therapeutic properties. Such a system may find use as a way to 'prime' MSCs in vitro for optimum angiogenic potential before use for therapy.

References

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