The influence of shear stress on stem cell differentiation – a microfluidic approach

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Background

- One challenge faced by bone tissue engineering is obtaining a reliable cell source for individual patients.
- Bone marrow stromal cells (BMSCs) are a popular candidate because they are able to differentiate into the osteogenic linear *in vitro*.
- However, current biochemical methods of BMSCs differentiation are not optimal due to the added chemicals and growth factors.
- Studies have shown that mechanical forces alone (such as stretching) is able to induce the osteogenic differentiation of BMSCs [1, 2].

Why study fluid flow induced shear stress?

1. Fluid flow in bone has been found to be induced by mechanical loading [2].
2. Shear stress strongly influences the differentiation of the progenitors of endothelial cells which are naturally subjected to fluid flow-induced shear stress *in vivo* [1, 3].
3. When subjected to short durations of fluid flow, BMSCs expressed an increased level of osteogenic markers and alkaline phosphatase (ALP) [4].

Thus, further investigation will be carried out to determine whether fluid-induced shear stress can result in the osteogenic differentiation of BMSCs.

Objectives

Long term goal: to develop microfabricated scaffolds for the application of bone tissue engineering.

In this poster:

1) Validate the multipotency of BMSCs.
2) Present a microfluidic approach for studying the effect of shear stress on BMSCs differentiation.

1. Current work with human bone marrow stromal cells (hBMSCs)

Primary adult hBMSCs were cultured in α-MEM medium with 16 % FBS (at 37°C and 5 % CO_2). Cells between passages 3-7 were incubated in osteogenic and adipogenic medium for 21 days and stained histologically (Figure 1); all experiments were performed according to the protocols provided by Texas A&M Health Science Center.

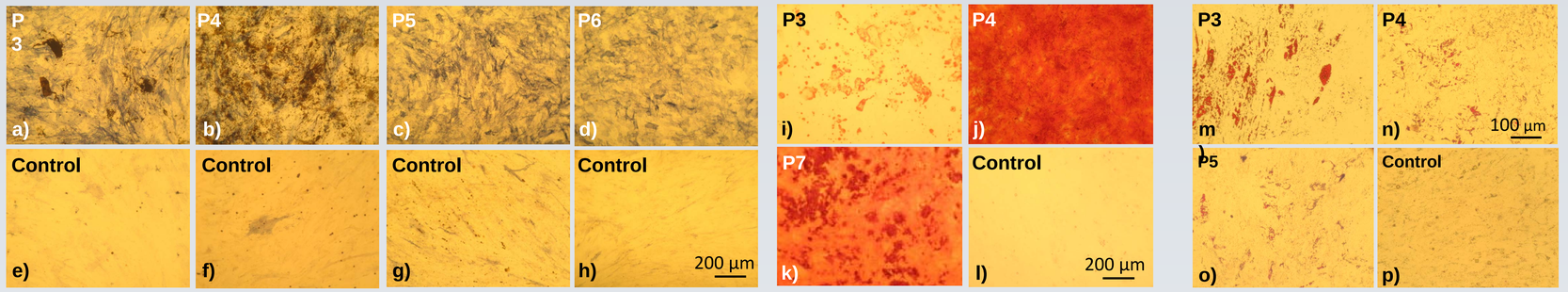

Figure 1 Representative images of hBMSCs incubated in the osteogenic (a-l) and adipogenic (m-p) differentiation medium. Histological stains: ALP & von Kossa (a-h); Alizarin red (i-l); Oil Red O (m-p). P: passage number.

2. Experimental design and proposed experiments

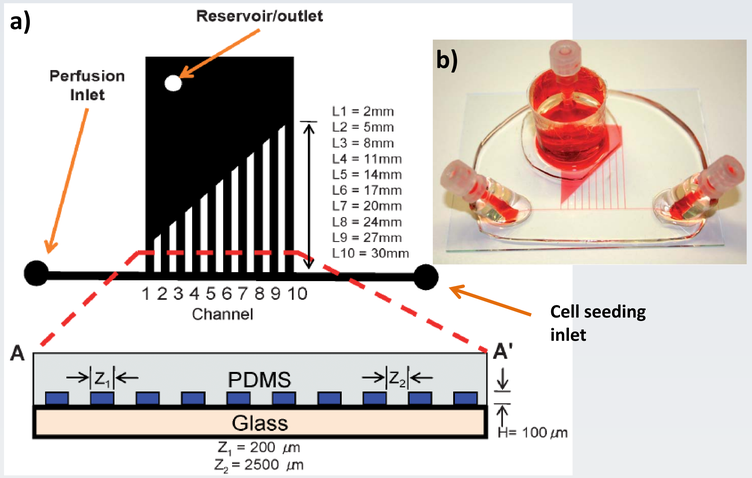

Figure 2 a) Schematic of the multishear device containing 10 channels with varying length; b) the fabricated microfluidic device shown with inlets and outlet [5].

Experimental design: Recently, a multichannel microfluidics device was developed for studying the effect of fluid shear stress on endothelial cells (Figure 2) [5]. This device allowed the simultaneous evaluation of 10 different shear stress levels, between 0.07–13 Pa.

Proposed experiments: Utilize this device to study the effect of shear stress on the osteogenic differentiation of hBMSCs. I will also study and compare the effect of different flow patterns: oscillatory, pulsatile, and steady. hBMSCs differentiation and mineralization will be evaluated with ALP & von Kossa staining and gene expression analysis.

Potential applications: This study will provide insight into the conditions (i.e. flow pattern and magnitude) which will result in the optimal osteogenic differentiation of hBMSCs. This knowledge will aid in the design of bioscaffolds for bone tissue engineering.

References

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