

# A Microfluidic Device for Observation of Adipose Derived Stem Cell (ASC) Response to Growth Factor Gradients

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Human adipose tissue provides a uniquely abundant and accessible source of adult stem cells for applications in tissue engineering and regenerative medicine. In response to chemical, hormonal or structural stimuli, the human adipose derived stem cells (ASCs) can differentiate along multiple lineage pathways, including adipocytes, chondrocytes, myocytes, neurons and osteoblasts. As new stem cell based therapies (gene, stem cell transplant, or immunotherapy) become the standard of care for a wide variety of diseases, several concerns with ASC cultures currently limit their therapeutic promise. One major problem is the inability to precisely control ASCs behavior in culture, such as their proliferation, cell-cell communication and differentiation into different cell types. Conventional cell culture technology is not suited to handle this complex problem. For example, precise and thorough micromanipulation studies with multiple growth factors are technically infeasible using traditional culture techniques and traditional cultures require relatively large volumes of media and correspondingly large amounts of costly growth factors and other reagents. Recent research suggests that, microfluidic cell cultures have the potential to overcome some of the problems imposed by traditional culture tools<sup>1</sup>.

We propose a simple, reproducible and cost effective microfluidic device based on the modular microfluidic platform<sup>2</sup> to conduct such studies. The device consists of two primary modules – a fluidic gradient generation module and a culture module. Multiple levels of solutions dividers are featured inside the gradient generator to confine diffusive mixing between two adjacent streams so that arbitrary concentration gradient profiles can be generated at the output from the two input solutions. The cell culture module is used to grow ASCs and study their migratory characteristics in response to controlled chemotactic factor gradients that are generated in the gradient generation module. ASCs will initially be cultured under normal cell culture conditions. When a sufficient population has been reached, the chip will be sealed and the microfluidic system will be activated. The precise and restricted diffusive mixing in gradient generation module results in a distributed concentration gradient that flows down channels of the cell culture module. Resultant behavior of the ASCs on exposure to nonlinear concentration gradients of the two input bimolecular solutions will be observed.

The initial proof-of-concept device is fabricated by polymer hot embossing using a micromilled brass mold insert. Subsequent generations of the devices will be fabricated using molding tools fabricated by X-ray Lithography to yield smaller, high aspect ratio structures that will provide more continuous gradient generation and better uniformity. The option to integrate gas exchange membranes and filter structures into the device will also be explored.

1. Meyvantsson, I and Beebe, D.J. Cell Culture Models in Microfluidic Systems. *Annual Review of Analytical Chemistry* 1, 2008, 423-449
2. Datta, P., et al. *Microfluidic Platform for Education & Research*. in *COMS2008, Commercialization of Micro and Nano Systems*. 2008. Puerto Vallarta, Mexico.