The role of actin in cell deformation - A microfluidic study

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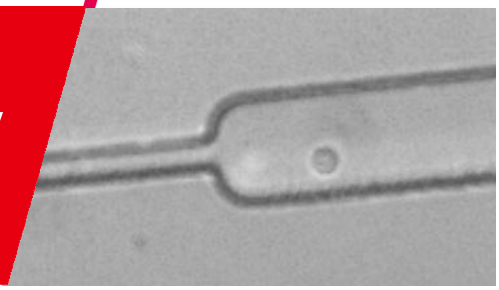

Introduction

Atherosclerosis is an inflammatory condition occuring in large and medium-sized arteries. The complex interplay of circulating monocytes with the blood flow and the endothelium triggers a number of cytoskeletal changes. During the process of activation, the monocytes undergo polymerization of cortical actin [1]. This process is required for cell migration but greatly stiffens the cell body. Therefore, it is hypothesized that activated monocytes get more resistant to deformation and they might be trapped in the vasculature.

Objective

The objective is to develop a microfluidic test set-up in order to distinguish healthy monocytes from diseased cells. To test our hypothesis, we investigated the role of actin structure on cell mechanical properties by analyzing cell deformation through a narrow channel.

Methods

The leukocytic HL-60 (human acute promyelotic leukaemia) cell line can be used as a model system for monocytes [2]. Cells were treated with cytochalasin D (CytoD), known to be an actin disrupting agent, to examine the role of actin structure on cell mechanical properties. The microfluidic device consists of a 50 µm inlet channel, followed by a 6 µm constriction channel and a 150 µm serpentine relaxation channel (Fig. 1A).

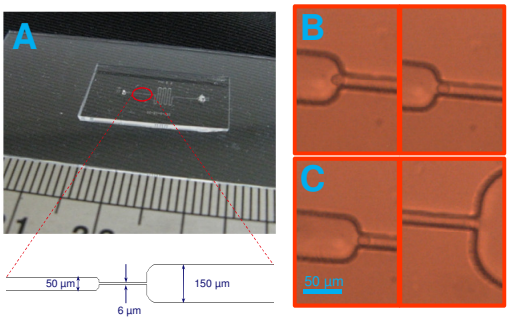

Fig. 1 – (**A**) Image of the device with magnification of the narrow channel. (**B**) Entry time: time interval between the leading edge of the cell crossing the entry of the narrowed channel and the trailing edge clearing the entry. (**C**) Cell transit time: time interval between the trailing edge clearing the entry of the narrowing channel and the leading edge crossing the exit of the constriction.

Cells were video-recorded with a high-speed camera during the different stages of single cell crossing the 6-µm-wide constriction. Videos were then analyzed frame by frame to acquire the entry time (Fig. 1B) and the transit time (Fig. 1C) in the constriction.

Results

Cells appeared to be smaller after treatment with Cyto-D. For untreated-HL60 cells, the entry time was strongly dependent on cell diameter. CytoD-treated cells exhibited shorter entry time compared to untreated cells and entry time seemed independent of cell diameter (Fig. 2).

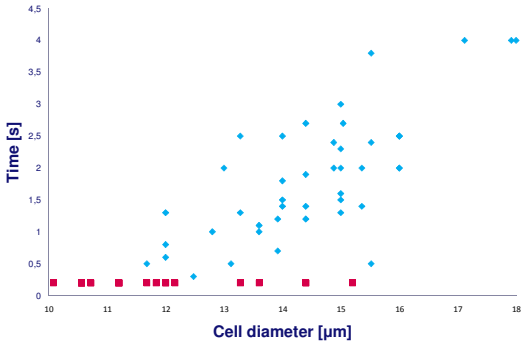

Fig. 2 – Cell entry time. ◆ HL60 cells, ■ cyto-D treated HL60 cells.

Cell velocity in the narrowed channel decreased with cell diameter both for Cyto-D treated cells and for control HL60 cells. CytoD-treated cells were characterized by higher trafficking velocity compared to control cells (Fig. 3).

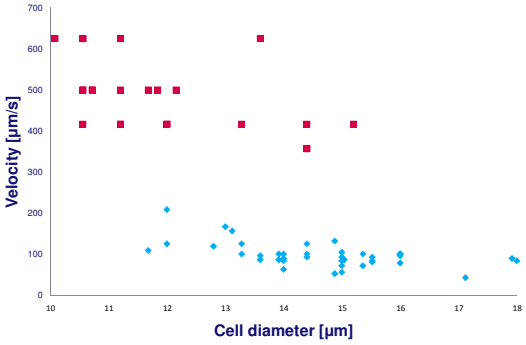

Fig. 3 – Cell speed in the 6 µm constriction. ◆ HL60 cells, ■ cyto-D treated HL60 cells.

Conclusion

Actin polymerization and organization strongly influences cell deformation in a narrow channel.
Future work aims at increasing the sensitivity of the setup and at testing the feasibility of distinguishing cells affected by atherosclerosis from healthy cells.

[1] M. Vicente-Manzanares and F. Sánchez-Madrid, *Nature Reviews*, 2004
[2] R.A. Fleck *et. al.*, *Clinical and Diagnostic Laboratory Immunology*, 2005