Nanowire Templated Nanotubes for Cell Injection

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Controlled injection of foreign material into living cells (e.g cell transfection) is of great importance for cell-biological research. At present there are many methods used, including micro pipetting, electroporation, liposome mediation and mechanical disruption of the cell membrane. None of those are simultaneously reliable, precise and fast. Ideally, a parallel injection of different substances in many cells on a single chip would be desirable. Ordered arrays of nano-sized tubes connected to a micro-fluidic system might provide one way of reaching this goal. In this study we show that nanotubes can be used for injecting viable cells with substances not normally penetrating the intact cell membrane.

Free-standing nanotubes were fabricated by coating and etching of nanowire templates, grown by MOCVD (fig 1). Tubes made from such monolithic nanowires can be precisely positioned and densely packed. In this study we fabricated and utilized nanotubes with an outer diameter of 200 nm and an inner diameter of 70 nm. With such tubes, we have previously shown electrophoretic translocation of DNA-strands [1]. Substrates with free-standing nanowires have been shown to support cell growth, even under conditions were cells are penetrated by the wires [2]. Nanotube substrates support cell-growth in a similar manner and the cell-penetration allows for material transfer across the cell membrane (fig 2).

Cells (macrophages from mouse) were added to nanotube substrates and incubated for 24 h. Thereafter a fluorescent marker (propidium iodide, PI) was added to a chamber mounted at the backside of the substrate, in contact with the cell side only through the etched tubes. Confocal microscopy was used to monitor the PI uptake of cells resting on the nanotube substrates (fig 3).

[1] N. Sköld, T. Hernán, J. B. Wagner, W. Seifert, L. Samuelson, J. O. Tegenfeldt : *Nanofluidics in hollow nanowires*. Proceedings μTAS 2007.

[2] W. Hällström, T. Mårtensson, C. Prinz, P. Gustavsson, L. Montelius, L. Samuelson, M. Kanje : *Gallium phosphide nanowires as a substrate for cultured neurons*. Nano Letters 7 (10) : 2960-2965 Oct 2007.

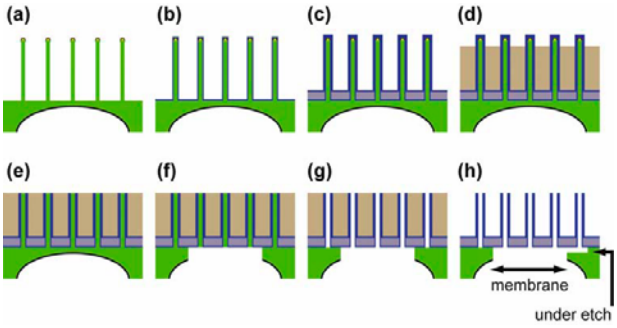

Fig 1. Schematic of nanotube fabrication. (a) Growth of nanowires on dimpled substrate. (b) Al2O3 deposition. (c) The nanowires are partially embedded in a BCB film which is capped by a second Al2O3 layer. (d) The wires are embedded in S1813. (e) Tips are cut. (f) Backside connection is etched. (g) Tubes are etched. (h) S1813 is removed.

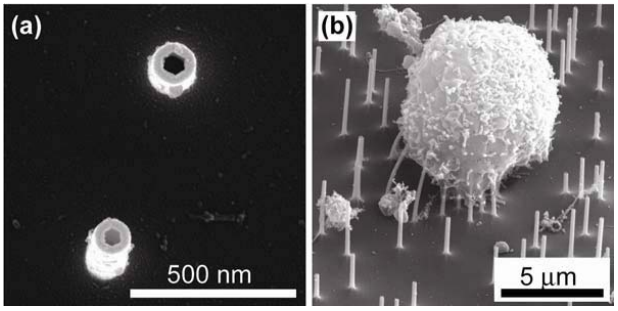

Fig 2. SEM-images of etched nanotubes. (a) Slightly tilted view of two tubes, note the hexagonal symmetry of the interior of the tubes. b) White blood cell penetrated by several nanotubes.

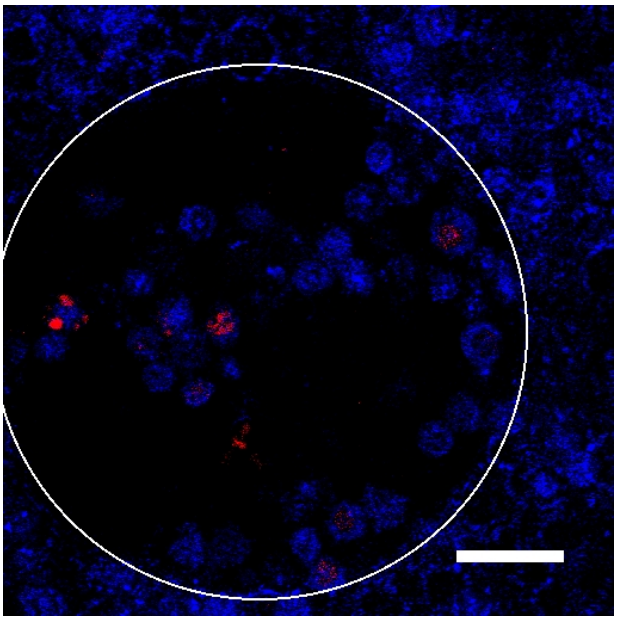

Fig 3. Macrophages injected with PI through nanotubes. The white circle indicates the position of the membrane, i.e. the active area of the device. Scale bar 25µm.