Novel immunoisolative microcontainer with nanoslots defined by nano imprint lithography

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Cell therapy is a promising alternative to treatment with exogenous drugs. The transplantation of cells that secrete biotherapeutic molecules eliminates the need for access to drugs and adherence to regimen. Cell allografts and xenografts are often encapsulated in polymer microbeads to immobilize and immunoisolate them from the host. However, these microbeads do not have reproducible porosity and are therefore minimally effective. In order to overcome this issue, we have developed a micro-container (Fig. 1) with nanoporous lid that permits the free transport of ions, nutrients and waste products to support cell survival, but that immunoprotects the encapsulated cells by preventing the passage of large molecules of the immune system. Here we detail a novel technique to achieve stricter pore size by creating a membrane barrier with nanoslots using nano imprint lithography (NIL).

The microcontainer has two components, a hollowed cubic base (Fig. 1a) and a nanoporous lid (Fig. 1b) that closes the microcontainer after it is filled with its cellular payload. A conventional SU-8 photolithographic process was used to fabricate the hollowed cubic base with a 200 x 200 x 200 µm encapsulation space using 50 µm thick SU-8. Nanoslots on the lid were fabricated by NIL using a mold with ~20 nm line gratings. To make the mold, PMMA, on an oxidized Si wafer, was imprinted with another mold containing a large area of 100 nm line and space gratings (Nanonex). The imprinted PMMA lines were selectively coated with metal (Cr) by oblique angle metal deposition, followed by inductively coupled plasma (ICP) etching in oxygen to remove exposed PMMA and ICP etching in a mixture of C_4F_8, CHF_3 and Ar to transfer patterns to oxide. Then, PMMA and Cr were removed and the profile was transferred into Si by ICP etch in chlorine. The resulting Si gratings were repeatedly oxidized and etched to gradually reduce the grating dimension. To make nanoslots on the lid, 600 nm of SU-8 was imprinted with the new mold containing ~20 nm gratings. Then, metal was again selectively coated on the imprinted SU-8 gratings at an angle of 10˚, followed by ICP etching in oxygen to etch exposed SU-8, resulting in formation of deep nano-trenches. This method provides a controlled process to make uniform nanoslots of narrow dimensions over large areas and enables fast and low-cost fabrication of microcontainers with nanoporous lids.

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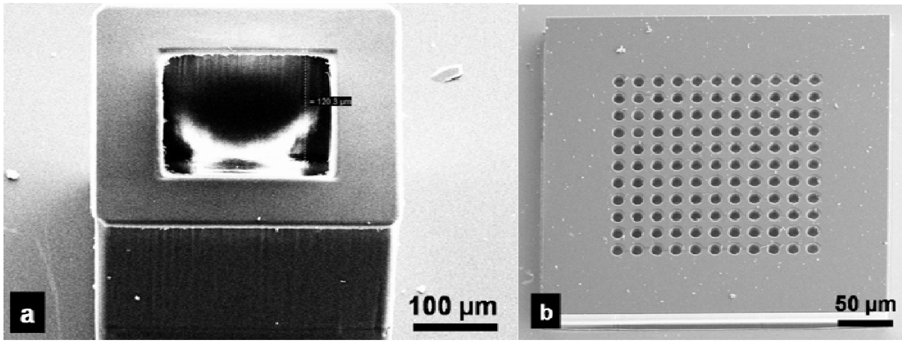

Fig 1: SEM images showing (a) the SU-8 hollowed cubic base and (b) the microcontainer lid.

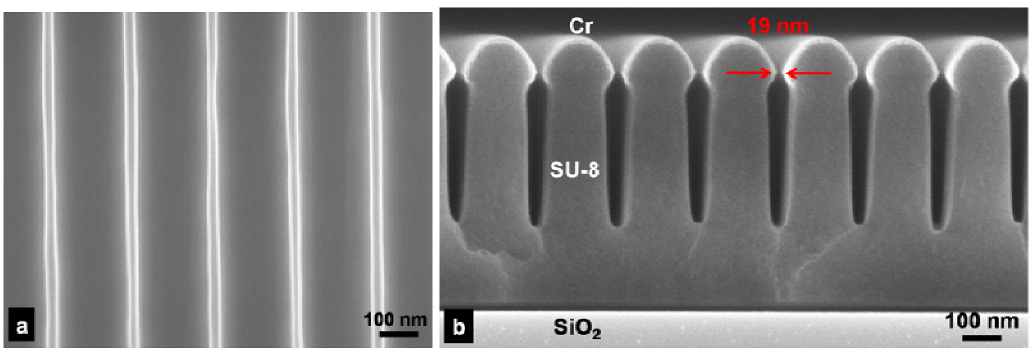

Fig 2: SEM image showing (a) the ~20 nm grating mold fabricated by repeated oxidation and etch and (b) the nano-trenches in SU-8 for the microcontainer lid.

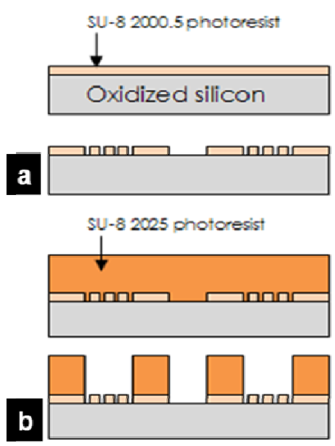

Fig 3: Fabrication of the microcontainer lid, showing the nanoslots in SU-8 (a) around which the walls for the lid are constructed (b).