Recent Advances of Dip-Pen Nanolithography in Lifesciences, Biosensing and Cell Biology

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Abstract

Dip Pen Nanolithography® (DPN®) is an established method of nanofabrication in which materials are deposited onto a surface, often in nm dimensions, via a sharp tip. We will contrast DPN used as a top-down fabrication method with structures created in a bottom-up manner from DPN generated templates. Recent developments in the use of the technique for diagnostics and screening will be presented including miniaturized ELISA-type arrays and the direct functionalisation of biosensor chips and microfluidic devices.

The deposition of biomaterials at sub-cellular scales (micro and nanometer) of complex multiplexed patterns holds huge promise for studies in medical and life sciences. The flexibility of the methods presented here enables the construction of complex micro-environments for cell culture studies and the ability to address cells at an individual level. For example, co-culture studies have been useful for mimicking the in vivo environment and studying effects on stem or progenitor cell function. However, there are many experimental variables that cannot be properly controlled and may lead to confounding results. Herein we demonstrate a technique that allows spatial control of multiple cell types at single cell levels on a substrate. This single cell co-culture concept is demonstrated by utilizing the binding dynamics with fibronectin and laminin of 3T3 fibroblasts and C2C12 myoblasts. We further demonstrate the delivery of biology-effecting agents, including toxins, to a fraction of cells on a surface and determine the effects.

References

[1] R. D. Piner, J. Zhu, F. Xu, S. Hong, C.A. Mirkin, *Science*, 283, (1999), 661.

[2] J. M. Collins,* R. T. S. Lam, Z. Yang, B. Semsarieh, A. B. Smetana and S. Nettikadan, Lab on a Chip, 12, (2012), 2587.

Figures

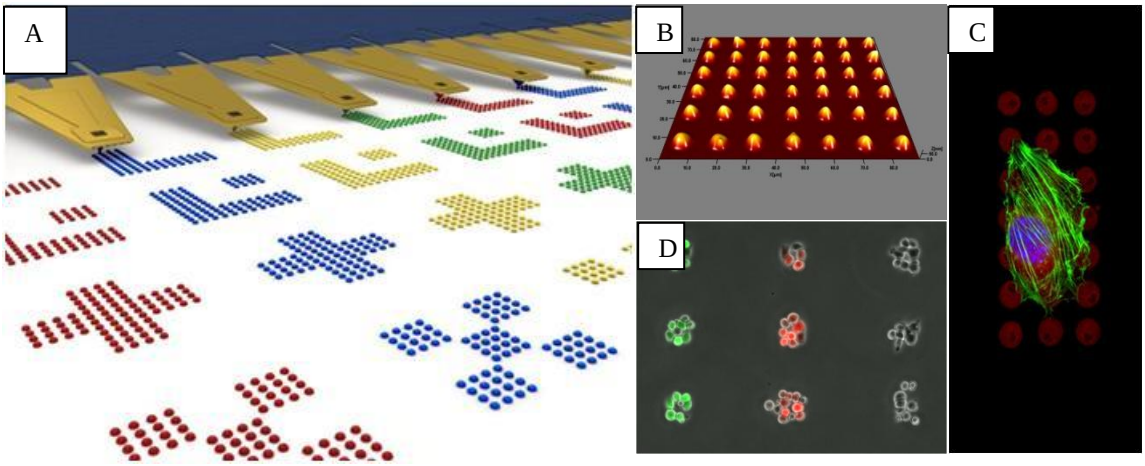

Figure: Examples of the application of DPN to biomaterials A: Illustration of the patterning of biomaterials materials over a large area using multiple pens. B: AFM image of a PEG hydrogel pattern, C: Cell interaction with DPN patterned fibronectin features, D: Targeted delivery of materials to populations of 3T3 cells.