**Orchestrating human neural stem cell differentiation and cellular processes using engineered vertically aligned silicon nanowire arrays**

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Vertically aligned silicon nanowire (VA-SiNW) arrays are biocompatible, semi-conductive, and readily tuneable to enable unprecedented manipulation of cell functions and processes in vivo, in situ and in vitro. VA-SiNW arrays have been instrumental in spurring advances in four main fields of cellular nanotechnology: nanoelectrode-based electrophysiology, biosensing, mechanotransduction, and intracellular delivery and sampling. Recent use of the arrays – for in vivo transfection and to gain fundamental insights into transmembrane cell trafficking in response to extracellular topographic cues – demonstrates the powerful potential of the interface as a highly efficient, universal, and scalable intracellular delivery platform, with significant prospects for clinical translation.

Here, we show the genuine utility of this platform for complex and protracted biological applications by culturing, for the first time, human neural stem cells of both embryonic and induced pluripotent lineages on VA-SiNW arrays in excess of 30 days. We demonstrate that our neural progenitor cells can become functional forebrain neurons when differentiated on VA-SiNW arrays of diverse topographies.

Despite extensive use of VA-NWs in bionanotechnological applications, little research has focused on the intracellular response to the intimate interfacing with these diverse but defined, engineered nanoscale topographies. Cells translate mechanical cues from their environment into biochemical signalling responses in a process called mechanotransduction. Defined nanostructured extracellular environments influence cell signalling and cellular processes such as morphology, migration, proliferation and gene and receptor expression. This paper will also present findings of how defined VA-SiNW topographies affect human neural precursor cell behaviour and biochemical signalling, and any downstream effects on neural stem cell differentiation. Our aim is to promote further, more complex interdisciplinary research that can capitalise on the mechanical, physiochemical and semi-conductive characteristics of engineered VA-SiNW arrays.

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