Nanoneedle Arrays for Intracellular Sensing and Delivery

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Nanoneedles are rapidly emerging as a tool to interact with the intracellular environment of a large number of cells simultaneously, with limited perturbation of their physiological processes. This interaction provides characteristic advantages for minimally invasive cell and molecular biology investigations, as well as progression of biomedical translation of regenerative and precision medicine approaches.
A quick string of several successful proofs of principles have established nanoneedles' potential to efficiently deliver impermeant molecules and nanoparticles directly to the cell cytosol, and to sense the intracellular milieu across biological systems ranging from cells in culture to living organisms.
This talk presents an overview of our recent research advances in leveraging the nanoneedle biointerface to enable intracellular sensing and delivery in the context of diagnostics and tissue engineering.
High aspect ratio nanostructures provide a unique biointerface [1] that stimulates multiple mechanosensory elements within the cell, inducing non-canonical regulation of the YAP and Lamin A mechanosensors.[2] This interfacing also enhances payload delivery across the cell membrane and the harvesting of biomolecules from the intracellular space through a combination of enhanced endocytosis and increased membrane permeability [3].
Using nanoneedle arrays as a delivery vector for nucleic acids enables highly efficient transfection *in vitro* and localised delivery with minimal invasiveness in living organisms [4]. In particular the nanoneedle-mediated delivery of a plasmid coding for the vascular endothelial growth factor (VEGF) to the muscle of a mouse stimulates neovasculature formation driven by exogenous VEGF expression, in the first example of nanoneedle mediated gene therapy. This method of delivery does not impact on the structure of the tissue, induce cell death or elicit an immune response.
Nanoneedles can also sense the intracellular environment [5]. Nanoneedle sensors can map the activity of cancer biomarkers across cell cultures and tissues, with the potential to identify tumour margins and detect cancerous dissemination beyond the margin [6].

References

[1] C. Chiappini, E. DeRosa, J.O. Martinez, E. Tasciotti, M. Stevens. Biodegradable nanoneedles for localized delivery of nanoparticles in vivo: exploring the biointerface, ACS Nano 9, 5500-5509 (2015).
[2] C. Hansel, S.W. Crowder, S. Cooper, S. Gopal, M.J. Pardelha da Cruz, L. de Oliveira Martins, D. Keller, S. Rothery, M. Becce, A.E.G. Cass, C. Bakal*, C. Chiappini*, M.M. Stevens*. Nanoneedle-Mediated Stimulation of Cell Mechanotransduction Machinery, ACS Nano 13, 2913–2926 (2019).
[3] S. Gopal, C. Chiappini*, J. Penders, V. Leonardo, H. Seong, S. Rothery, Y. Korchev, A. Shevchuk*, M. Stevens*, Porous Silicon Nanoneedles Modulate Endocytosis to Deliver Biological Payloads, Adv. Mater. 31 1806788 (2019). *Corresponding Authors.
[4] C. Chiappini, E. DeRosa, J.O. Martinez, X. Liu, J. Steele, M. Stevens, E. Tasciotti, Biodegradable silicon nanoneedles delivering nucleic acids intracellularly induce localized in vivo neovascularization, Nature Materials 14, 532-539 (2015).
[5] C. Chiappini. Nanoneedle-Based Sensing in Biological Systems. ACS Sensors 2:1086–1102 (2017)
[6] C. Chiappini*, P. Campagnolo, C. Almeida, N. Abassi-Ghadi, L. Chow, G. Hanna, M. Stevens*, Mapping Local Cytosolic Enzymatic Activity in Human Esophageal Mucosa with Porous Silicon Nanoneedles, Advanced Materials 27, 5147- 5152 (2015). *Corresponding Authors.

Figures

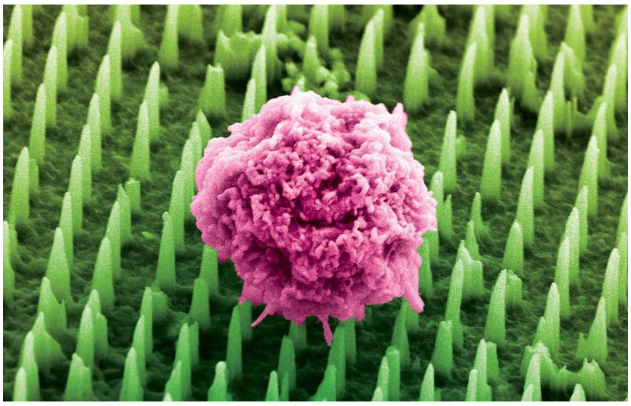

Figure 1. False-colored SEM micrograph of a human cell in the early stages of adhering to a nanoneedle array.