Exploring the Cell with Nanoneedles

Ciro Chiappini
Centre for Craniofacial and Regenerative Biology, King's College London, London UK.
London Centre for Nanotechnology, King's College London, London UK.
ciro.chiappini@kcl.ac.uk

Nanoneedle arrays, consisting of high-aspect-ratio nanostructures on nanotextured surfaces, have emerged as powerful tools to explore cells by probing and manipulating the intracellular environment. Their unique design allows them to interact with cells with minimal perturbation, making them highly effective in delivering a variety of therapeutic agents—including small molecules, nucleic acids, proteins, and nanoparticles—into cells without inducing toxicity. Notably, nanoneedles have shown high efficiency in targeting cells that are traditionally difficult to transfect, such as primary human cells, stem cells, immune cells, and neurons. This capability is unlocking new possibilities for the *ex vivo* genetic engineering of primary cells with unprecedented efficiency. Moreover, the application of nanoneedles *in vivo*, particularly on the skin and eye, is paving the way for novel topical therapies involving nucleic acids and biologics. These advances underscore the potential of nanoneedles in developing advanced therapy medicinal products, including cell and gene therapies, as well as CRISPR-based gene editing.

In addition to their delivery capabilities, nanoneedles enable minimally invasive, repeatable access to the intracellular environment. This feature supports longitudinal sampling of cellular contents, allowing real-time monitoring of cell and tissue states. Building on this, nanoneedle platforms are being developed as biosensors capable of detecting specific biomarkers within living cells and tissues. Through selective analyte capture, they also facilitate the extraction of representative molecular material for spatially and temporally resolved -omics analyses. This versatile biosampling and biosensing functionality positions nanoneedles as powerful tools to study dynamic, non-cell-autonomous gene regulatory networks that drive development, disease progression, therapeutic response, and the emergence of treatment resistance. By integrating these capabilities, nanoneedles advance both our fundamental understanding of biological systems and the development of more personalised and adaptive therapeutic strategies.

This talk outlines our progress in developing nanoneedles for delivery and biosensing and their applications in topical gene therapy, cell therapies and spatial omics. It will highlight fabrication methods for incorporating nanoneedles within a broad range of medical devices, including bandages, contact lenses, catheters and hydrogel. It will demonstrate the application of nanoneedles to skin wounds in epidermolysis bullosa for Collagen Type VII gene editing and gene therapy, and nucleic acid therapy for the topical treatment of corneal endothelial dysfunction. Nanoneedles also mediate the base editing of primary skin fibroblasts and the introduction of chimeric antigen receptor genes in regulatory T cells for cell-based therapies in epidermolysis bullosa and graft-vs-host disease. It will highlight the development of a strategy for noninvasive sampling of brain tissue for glioma stratification and longitudinal monitoring of chemotherapy response.

References

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