be of a major interest for future development. Given the biological response yielded through this approach, we propose that non-covalent, peptide-based delivery technologies hold a strong promise for therapeutic administration of siRNA.

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A86
High-efficient transfection using cationic lipids with programmed biodegradability

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Delivery of nucleic acids into cells has an ever-increasing number of applications with outstanding advances in both gene therapy and biotechnology, highlighting the induction of pluripotency in somatic cells. While the use of viral vectors is currently the most efficient transfection method, their antigenicity along with the risk of potential mutagenesis, among other inconvenients, are important limitations that hinder its application in medicine. Non-viral delivery systems (cationic lipids and polymers) represent an attractive alternative, particularly because of their low-cost, tuneable design and procedural simplicity. However, the *in vivo* efficacy of these carriers needs to be increased for both research purposes and clinical application. As repetitive dosing would be required in any gene therapy treatment, the cytotoxicity due to the use of these chemicals needs to be reduced, ideally by regulating their metabolic fate. To address these issues, a tripodal cationic lipid [1] was specifically designed to undergo complete intracellular metabolisation into naturally occuring compounds aiming to minimise the toxicity associated with its cytoplasmatic residence. Besides the toxicity issue, the incorporation of hydrolysis-prone linkages was addressed to enhance the cationic lipid-DNA dissociation once the lipoplexes have entered the cell by endocytosis. The novel compounds showed remarkable transfection efficiency along with reduced toxicity in a variety of immortalized cells and stem cells. Moreover, preliminary *in vivo* studies underlined the potential applicability of these non-toxic reagents for the delivery of DNA into mouse lung. These reagents, contrary to the most of chemical carriers commercially available, might offer a viable chemical alternative to viral transfection.

Reference

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A87
Immune stimulation following microneedle delivery of influenza virus-like particle (VLP) vaccines to human skin

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Virus-like particles (VLPs) possess a number of features that make them attractive vaccine candidates for immunization against infectious disease. Efficient intra-epidermal delivery of VLP vaccines would exploit the abundance of Langerhans cells (LCs) that reside within the skin epidermis to generate an efficient host immune response. Microneedles (MNs) are currently being developed for the convenient and pain-free delivery of drugs and vaccines across the skin barrier layer. Whilst MN-based vaccines have demonstrated proof-of-concept in mice, it would be extremely valuable to understand how MN targeting of influenza VLP vaccines to the skin epidermis affects activation and migration of LCs in the real human skin environment. MNs with lengths of 700 μm were laser-etched from stainless steel sheets and surface-coated with either influenza H1 (A/PR/8/34) or H5 (A/Viet Nam/1203/04) VLPs. The coated MNs easily and reproducibly penetrated freshly excised human skin, depositing approximately 80% of the vaccine load within 60 s. Experiments conducted in cultured human skin showed that H1 and H5 VLPs, delivered via MNs, stimulated LCs causing morphological changes and a significant decline in total LCs number in epidermal sheets at 24–48 hours compared to untreated skin at the same time points. Histological sections showed that LCs in VLP treated samples were more dispersed throughout the epidermis with substantial numbers in the vicinity of the basement membrane. The response made by LCs was more manifest in human skin treated with H1 VLPs, compared with H5 VLPs. These findings corroborate observations in mouse studies, where H1 VLPs were shown to be significantly more immunogenic than H5 VLPs. Our data provide strong evidence that MN-facilitated delivery of influenza VLP vaccines initiates a stimulatory response in LCs in human skin epidermis. The results complement and support data gained from animal models, suggesting dendritic cells (DCs), including LCs, targeted through intra-epidermal or intra-dermal deposition of the vaccine generates immune response. This study also emphasizes the value of cultured human skin alongside animal studies for informative preclinical testing of intra-dermal vaccines.

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Electrically based transdermal techniques for delivery of therapeutic macromolecules

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Advances in molecular biology have given us a wide range of protein and peptide based drugs that are unsuitable for oral delivery because of their high degree of first-pass metabolism. Though parenteral delivery is successful for developed and commercially available protein and peptide based drugs, chronic and self administration formulations are not the ideal choice through this route. Transdermal delivery is emerging as the biggest application target for these agents, however, the skin is extremely efficient at keeping out such large molecular weight compounds and therapeutic levels are never going to be realistically achieved by passive absorption. Therefore novel transdermal drug delivery systems have been developed with the aim to achieve the objective of systemic medication through topical application to the intact skin surface with benefits of deliver therapeutic macromolecules in desire therapeutic doses to overcome the difficulties associated with the oral route, namely poor bioavailability of drug and the tendency to produce rapid blood