charge of the DNA-coated nanoparticles influenced their *in vitro* skin permeation and *in vivo* ability to induce immune response. TCI with plasmid-DNA-coated cationic nanoparticles elicited a stronger immune response than the same performed with anionic nanoparticles as well as than the intramuscular injection of the same dose of plasmid DNA alone. Furthermore, TCI by plasmid-DNA-coated cationic nanoparticles applied upon the MN pretreatment or by intramuscular injection induced comparable immune responses (i.e. comparable levels of total IgG) and proliferative reponses, but only TCI induced specific mucosal response, indicating the advantage of TCI. According to the authors (Kumar et al. 2012), the high efficiency of cationic nanoparticles is proposed to be due to their ability to increase the expression of the antigen gene encoded by the plasmid and more effectively stimulate the maturation of APCs.

Zaric et al. (2013) investigated the potential of dissolving MNs loaded with antigen encapsulated in PGLA nanoparticles to increase vaccine immunogenicity by targeting antigen specifically to DC network within the skin. Authors reported that this approach provided complete protection *in vivo* against the development of both tumors and virus. It was found that nanoencapsulation facilitates antigen retention in the skin layers and provides antigen stability in MNs. According to the authors, the use of biodegradable polymeric nanoparticles for selective targeting of antigen to skin DCs through dissolvable MNs is a promising technology for improved vaccination efficacy, compliance and coverage.

Siddhapura et al. (2016) investigated the potential of tetanus toxoid loaded chitosan nanoparticles (TT-Ch) for immunization with and without the use of MNs. The *in vitro* analysis demonstrated higher skin penetration of TT when used in combination with MNs. *In vivo* immunization studies showed that TT-Ch nanoparticles combined with MN treatment induced comparable IgG and IgG1 titer, and higher IgG2a titer than the commercial TT vaccine. The authors showed that MNs, especially hollow MNs applied with TT-Ch nanoparticles could be considered as the best solution for immunization due to induction of more balanced Th1/Th2 biased immune response.

Yang et al. (2017) incorporated ebola DNA vaccine into PLGA-PLL/γPGA nanoparticles and administered them onto the skin using MN patch. The incorporation of ebola DNA vaccine into the nanoparticles increased the vaccine thermostability and immunogenicity compared to the free vaccine. Furthermore, the vaccination by the MN patch produced a stronger immune response than the intramuscular administration of the vaccine.

Seok et al. (2017) developed an intradermal pH1N1 DNA vaccine delivery platform using MNs coated with a polyplex containing poly lactic-co-glycolic acid/polyethyleneimine (PLGA/PEI) nanoparticles. Stainless steel MNs were used, with enhanced hydrophilicity, manufactured by silanization. MNs were further coated with the polyplex encapsulating pDNA vaccine, without severe aggregation of the polyplex in the dry form. After MNs insertion into the porcine skin, the coated polyplex rapidly dissolved (within 5 minutes) and induced a greater humoral immune response compared to the intramuscular polyplex delivery or naked pH1N1 DNA vaccine delivery by a dry-coated MN. The authors showed that intradermal delivery of pDNA vaccines within a cationic polyplex coated on MNs is promising method for TCI (Seok et al., 2017).

Du et al. (2017) developed and compared four types of nanocarriers for vaccine delivery, i.e. PLGA nanoparticles, liposomes, mesoporous silica nanoparticles (MSNs) and gelatin nanoparticles (GNPs), which they loaded with OVA with and without an adjuvant (poly(I:C)). The nanocarrier dispersions were injected precisely into murine skin at a depth of about 120 μm. OVA/poly(I:C)-loaded nanoparticles and OVA/poly(I:C) solution elicited similarly strong total IgG and IgG1 responses, while the co-encapsulation of OVA and poly(I:C) in nanoparticles significantly increased the IgG2a response compared to OVA/poly(I:C) solution. PLGA nanoparticles and liposomes induced stronger IgG2a responses than MSNs and GNPs, correlating with sustained release of the antigen and adjuvant and a smaller nanoparticle size (Du et al., 2017). Regarding cellular responses, OVA/poly(I:C)-loaded liposomes induced the highest $CD8^+$ and $CD4^+$ T cell responses.

Mönkäre et al. (2018) developed hyaluronan (HA)-based dissolving MNs loaded with PLGA nanoparticles (NPs) co-encapsulating OVA and poly(I:C) for intradermal immunization. The authors found that the delivered antigen dose in mice from MNs was 1 μg OVA, in nanoparticles or as free antigen.