Advances in skin science enable the development of a COVID-19 vaccine

Louis D. Falo, Jr, MD, PhD
Pittsburgh, Pennsylvania

Jenner's skin inoculation preventing smallpox exemplifies the capacity of a skin-targeted vaccine to successfully combat a pandemic. Skin biologists have elucidated the intricate cutaneous immunoregulatory networks that are highly responsive to environmental conditions and capable of inducing potent immune responses that can be local and systemic.[1,2] Skin is rich in antigen-presenting cells and in accessory cells with innate immune function such as resident T cells, innate lymphoid cells, mast cells, neutrophils, neurons, and keratinocytes.

Our group and others have focused efforts on developing skin-targeted immunization strategies including skin-targeted delivery of protein, plasmid DNA, and viral vectored vaccines. These efforts are enabled by advances in bioengineering that are resulting in more effective and controlled delivery of vaccine components to skin microenvironments such as microneedle arrays.

Microneedle arrays span a broad range of technologies, including several being explored for the development of vaccines against influenza, malaria, diphtheria, and other infectious diseases.[3] Our efforts have focused on microneedle arrays made of a dissolvable matrix. Deliverables, including antigens and immunomodulators, can be integrated into the matrix so that the needles are actually the vaccine. When applied to the skin, the dry sharp needles penetrate the stratum corneum and then absorb moisture and dissolve, releasing vaccine components into the epidermis and upper dermis. Therefore, the delivery of very small amounts of cargo results in high local concentrations within the skin microenvironment that improves effectiveness while minimizing systemic exposure to improve safety. An important benefit is that vaccine components embedded in these microneedle arrays are stable at room temperature, obviating the "cold chain" that has been a major barrier to global immunization campaigns. We used this technology platform to construct and test a skin-targeted coronavirus disease 2019 vaccine consisting of a recombinant S1 subunit protein from severe acute respiratory syndrome coronavirus 2 embedded in a microneedle array. The efficiencies of this process enabled us to rapidly design and fabricate a prototype vaccine, and to begin animal testing within a few weeks of the release of the viral sequence. This resulted in the first peer-reviewed description of a coronavirus disease 2019 vaccine generating potent severe acute respiratory syndrome coronavirus 2 antibody responses.[4] This "PittCoVacc" vaccine is now being developed for a phase 1 clinical trial and would join our ongoing clinical trial evaluating microneedle array delivery of an immunogenic cell death–inducing chemotherapeutic for the treatment of skin cancer. Most recently, we showed that adenoviral vectors could also be embedded in microneedle arrays and maintain their infectivity.[5] The multicomponent microneedle array fabrication strategy enabled the delivery of both antigen-expressing adenovectors and adjuvant in the same microneedle arrays, resulting in a vaccine that induced both antibody responses and enhanced cytotoxic cellular immunity that is likely important for "universal" vaccines and cancer immunotherapies.

Taken together, these and studies by others demonstrate the potential for the development of cutaneous immune engineering strategies to control systemic immune responses, including the potential for developing novel vaccine strategies and immunotherapies, and even negative immunization strategies to treat systemic allergy and autoimmune diseases. Advances in skin biology are making important contributions to the fight against the coronavirus disease 2019 pandemic, demonstrating

From the Department of Dermatology, Departments of Dermatology and Bioengineering, and the University of Pittsburgh Clinical and Translational Science Institute, Hillman Cancer Institute, and McGowan Institute for Regenerative Medicine.
Funding sources: None.
Conflicts of interest: Dr Falo is an inventor of related intellectual property and founder and scientific advisor of SkinJect.
Reprints not available from the author.

Correspondence to: Louis D. Falo, Jr, MD, PhD, University of Pittsburgh, Dermatology, Medical Arts Bldg, Ste 500, Pittsburgh, PA 15213. E-mail: lof2@pitt.edu.
J Am Acad Dermatol 2020;83:1226-7.
0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2020.05.126

once again that dermatology is more than skin deep.

REFERENCES

1. Kabashima K, Honda T, Ginhoux F, Egawa G. The immunological anatomy of the skin. *Nat Rev Immunol*. 2019;19(1):19-30.
2. Kashem SW, Haniffa M, Kaplan DH. Antigen-presenting cells in the skin. *Annu Rev Immunol*. 2017;35:469-499.
3. Kim YC, Park J-H, Prausnitz MR. Microneedles for drug and vaccine delivery. *Adv Drug Deliv Rev*. 2012;64(14):1547-1568.
4. Kim E, Erdos G, Huang S, et al. Microneedle array delivered recombinant coronavirus vaccines: immunogenicity and rapid translational development. *EBioMedicine*. 2020;55:102743.
5. Erdos G, Balmert SC, Carey CD, et al. Improved cutaneous genetic immunization by microneedle array delivery of an adjuvanted adenovirus vaccine. *J Invest Dermatol*. 2020. https://doi.org/10.1016/j.jid.2020.03.966. Published online April 21, 2020.