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## Enabling topical immunization via microporation: a novel method for pain-free and needle-free delivery of adenovirus-based vaccines.

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### **Abstract**

The skin represents an excellent site for vaccine inoculation due to its natural role as a first line of contact with foreign pathogens and the high local frequency of antigen presenting cells. To facilitate skin-directed immunization, a new technique has been developed (termed microporation) whereby a vaporization process is used to remove tiny areas of the stratum corneum creating microscopic pores that allow access to the underlying viable epidermis. Reporter gene expression was 100-fold increased following application of an adenovirus vector to microporated skin when compared to intact skin. Furthermore, 10-100-fold greater cellular and humoral immune responses were observed following topical administration of an adenovirus vaccine to microporated skin versus intact skin. Hairless mice responded to the microporated adenovirus vaccine equivalently to mice with normal hair follicle distribution demonstrating the activity of the microporated vaccine was not related to follicle count. In a tumor challenge model using a surrogate antigen, microporation increased vaccine efficacy by approximately 100-fold compared to intact skin. Finally, microporation enabled delivery of an adenovirus vaccine carrying a relevant melanoma antigen resulting in the development of auto-immune vitiligo and tumor protection. Thus, the microporation technology has proven to be a reliable and easy method to enable skin-directed vaccination.

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