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Progress Report
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Effect of microdermabrasion on skin histology in vivo: selective removal of stratum corneum for intra-epidermal vaccine delivery

Objective: The objective of this study was to test the hypothesis that microdermabrasion can be used to selectively remove the stratum corneum layer to enable delivery of vaccines primarily to the epidermal layer of the skin. The overall expectation driving this study was that targeting the Langerhans cells residing in the epidermal layer of the skin for vaccine delivery will increase the robustness of the immune response.

Methods: Microdermabrasion was performed *in vivo* on the skin of rhesus macaques and human volunteers using the mobile (back-and-forth movement on the skin) and the stationary mode of microdermabrasion. Biopsies were collected from microdermabraded skin and histologically characterized. Histological sections were stained with hematoxylin and eosin and visually examined using a microscope to assess the extent of damage of the stratum corneum and the epidermis. MVA (Modified Vaccinia Ankara) was topically applied on microdermabraded skin of rhesus macaques to test the ability of MVA to induce an immune response. In addition, sodium fluorescein was also topically applied on microdermabraded skin to assess the ability of hydrophilic and low molecular compounds to diffuse across microdermabraded skin.

Results: Selective removal of stratum corneum was observed using the mobile mode of microdermabrasion. In rhesus macaques, increase in the number of passes (10, 30, 50 80 and 100 passes) led to an increase in the degree of stratum corneum and epidermis removal (vacuum pressure = 50 kPa). At 50 passes, selective removal of stratum corneum was observed with little damage to the epidermis. Quantitative measurement demonstrated that at 50 passes, greater than or equal to 25% of the skin had stratum corneum removed, and only less than 25% of the skin had epidermal loss. Similar effects were observed for human volunteers using a vacuum pressure of 25 kPa. This suggests that with the mobile mode of microdermabrasion complete removal of stratum corneum can be achieved with minimal damage to the epidermis.

Using the stationary mode, selective stratum corneum removal was not observed. In rhesus macaques, microdermabrasion at 30 kPa and 50 kPa vacuum pressures each with a skin-contact time of 3 s and 6 s did not result in stratum corneum removal. However, blister (separation at the epidermal-dermal junction) formation was observed at the 50 kPa condition. Similar effects were observed for human subjects at a vacuum pressure of 30 kPa and 45 kPa, each with a skin-contact time of 3 s. In humans, the blisters were observed at both 30 kPa and 45 kPa conditions.

Next, delivery of sodium fluorescein and MVA virus through microdermabraded skin was demonstrated. Fluorescent micrographs of histological sections of microdermabraded skin after application of sodium fluorescein showed high degree of

fluorescence as compared to non-microdermabraded skin. Further, MVA specific antibodies were generated in monkeys following topical application of MVA on microdermabraded skin. Thus, in this study, we demonstrated for the first time that microdermabrasion can be used to selectively remove the stratum corneum layer and also demonstrated the ability to deliver model hydrophilic compounds and virus through the microdermabraded skin.

Conclusions: Microdermabrasion can be used to selectively remove the stratum corneum layer to target the Langerhans cells of the epidermis for vaccine delivery or transdermal drug delivery. Antibodies were generated against MVA following topical application of MVA on microdermabraded skin, indicating the potential of microdermabrasion as a method of intra-epidermal vaccination.