INTRADERMAL ADMINISTRATION OF SYNTHETIC DNA VACCINES INDUCE ROBUST CELLULAR AND HUMORAL IMMUNE RESPONSES

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There has long been an interest by health agencies such as Program for Appropriate Technology in Health (PATH) and the World Health Organization (WHO) to deliver vaccines by the intradermal route (ID). The skin is full of immunological cells, most notably antigen presenting cells. Therefore, ID injection may be an efficient means of inducing an immune response to vaccines. Inovio has developed ID injection followed by a shallow *in vivo* electroporation (ID-EP) for synthetic DNA vaccine delivery. We have tested a number of our vaccines in clinical trials using the ID-EP delivery system including vaccines targeted against HIV, ZIKA virus and EBOLA virus. The success of the ID method takes on particular importance for a vaccine that will be used in an emergency setting such as during a possible Ebola virus outbreak. Such a vaccine will need to quickly induce robust, protective immune responses. INO-4201, our DNA based *Zaire Ebolavirus* (EBOV) vaccine, was analyzed following ID delivery. Immune responses generated by INO-4201 after the 2mg intradermal administration using the Cellectra in vivo electroporation device in volunteers revealed the induction of robust Ebola virus GP-specific antibodies, CD4+ as well as CD8+ T cell responses. Specifically, 100% seroconversion, as gauged by binding ELISA, was detected after two doses of INO-4201. The reciprocal geometric mean endpoint titer at that time was 39,664.20 and was boosted by administration of the third dose to 46,968.00. Examination of the EBOLA virus GP specific T cell response as assessed by Interferon gamma (IFNγ) ELISpot revealed a mean peak response magnitude of 295.3 SFU per 10^6 PBMCs. Importantly, the induction of robust immune response by ID-EP was mirrored in the ZIKA virus and HIV DNA vaccine clinical trials. These results indicate that ID methods to deliver DNA-based vaccines are important for further clinical development.