Shear-Stress Evaluation on Dendritic Cells Viability Pre- and Post-Ejection Using VAX-ID® For Intradermal Immunotherapy Delivery

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INTRODUCTION

Based on research from the past 3 decades, immunotherapy with Dendritic Cells (DCs) has been shown to be safe and able to induce antitumor immunity in cancer patients even at advanced stage disease. The rich immune network in the skin makes it a desirable target for immunotherapy administration; hence, intradermal delivery of DCs is an often-preferred delivery method for immunotherapy.

For the treatment to be effective, it is important that a large number of viable, functional cells reach the site of action. Shear stress during intradermal injection is considered the main cause of potential cell damage, a decrease in cell viability, and a change in cell phenotype. The aim of this study was therefore to evaluate the shear stress effect on tolerogenic DCs (tolDCs) viability following ejection using VAX-ID®, a newly developed drug delivery device, pre-configured with various needle gauges.

Figure 1: VAX-ID® intradermal drug delivery device.

MATERIALS & METHODS

The effect of shear stress on the viability and functionality of tolDCs was measured during needle flow.

TolDCs harvested from blood were injected through five different needles:
- **23G** x**25mm** length
- **26G** x**13mm** length
- **27G** x**13mm** length
- **32G** x**13mm** length

at a constant flow rate of 13.5µL/s using a syringe pump to assess the viability and phenotype of the tolDCs.

For every needle included, a total of 400 µl tolDC-based vaccine was used. 100 µL was used as the control sample and not ejected through the needle. The other 300 µL were ejected per 100 µL, resulting in three studied samples per needle.

After the test, propidium iodide was used to evaluate viability and phenotype of the tolDCs. Four phenotypic markers (CD86, CD80, HLADR, CD40) were studied. The Wilcoxon test with non-parametric comparisons for each pair was used to examine for a significant difference in phenotype between the studied samples and their comparable control sample on a significance level of 5%.

Additionally, a calculation model was set up to design, compare and predict future needle ratios and configurations.

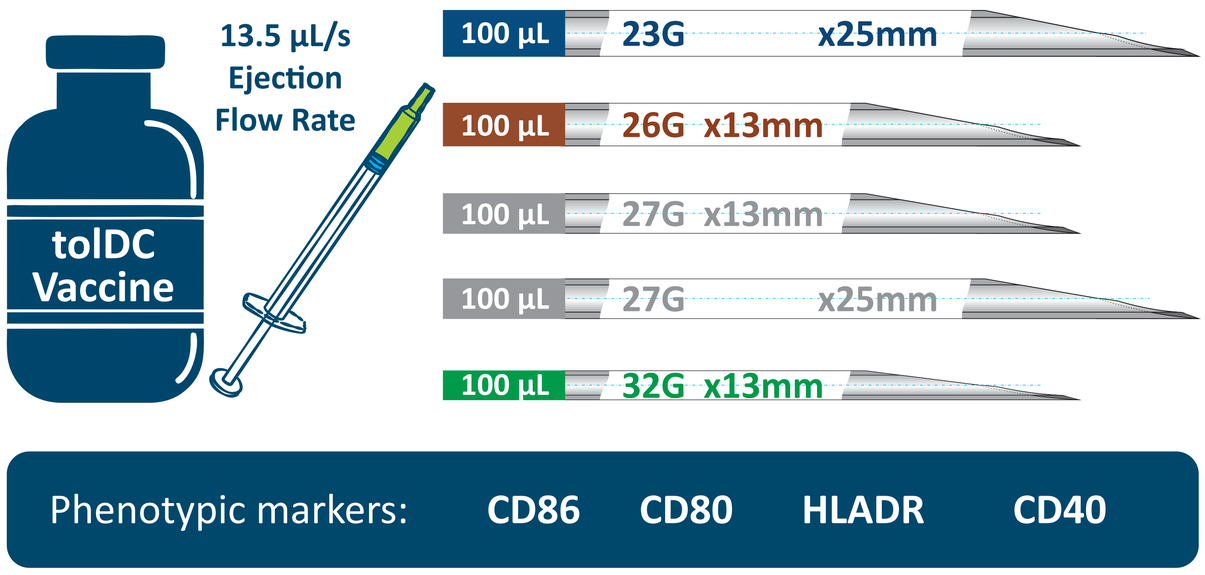

Figure 2: Study design.

RESULTS & DISCUSSION

Using the Hagen-Poiseuille equation, the wall shear stress on the tolDCs was calculated. Results showed that needles ranging from 23G up to 32G showed no increase in shear stress upon ejection of tolDCs.

For all the studied needles, there were no significant differences in the phenotype for tolDCs before and after ejection. Additionally, there was no significant difference in cell viability of the studied samples and their control sample on a significance level of 5%.

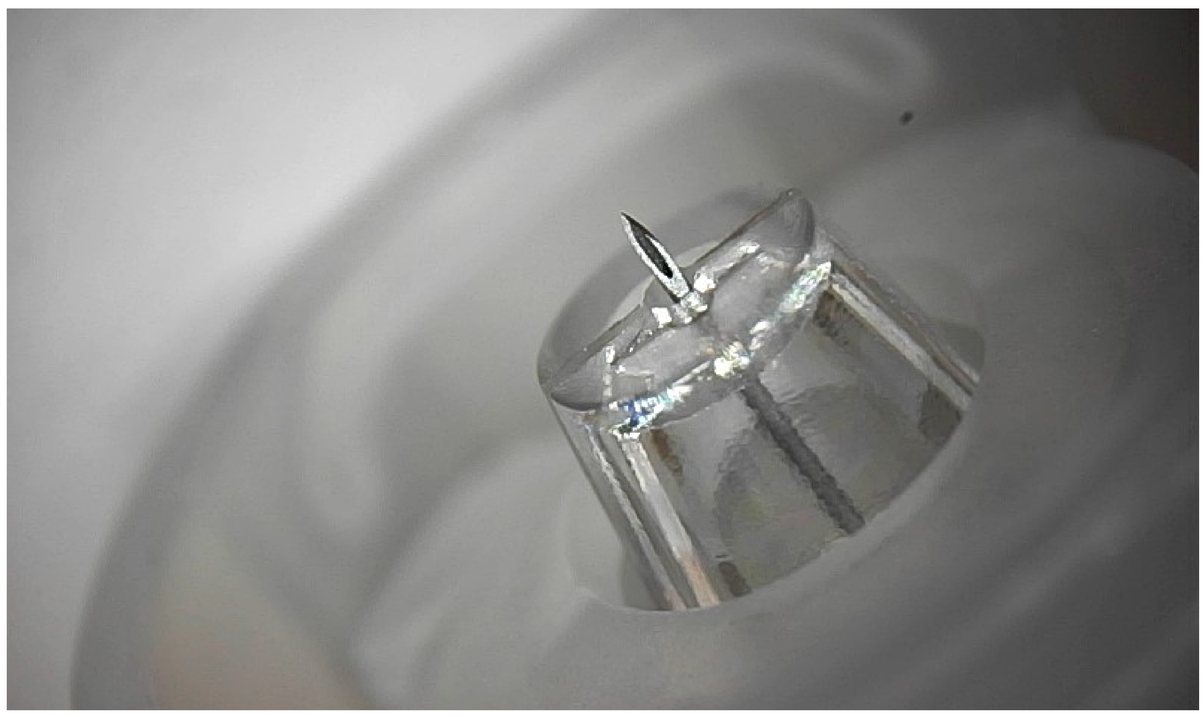

Figure 3: a short 27G needle protruding from the VAX-ID® intradermal drug delivery device.

CONCLUSION

This specific range of needles has shown to not cause shear stress on tolDCs, thereby maintaining their viability and functionality. VAX-ID® pre-configured with 32G, 27G or 26G needles can be considered a promising solution for reliable delivery of cell-based immunotherapy compared to regular injection methods.

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