Evaluation of a Transdermal Murine Breast Cancer Vaccine administered via Micro-needles

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ABSTRACT SUMMARY

This study aims to evaluate a particulate breast cancer vaccine delivered via micro-needles. This whole cell lysate-particulate breast cancer vaccine was evaluated in vivo and was capable of generating protective immune response in vaccinated animals.

INTRODUCTION

Breast cancer is one of the most fatal forms of cancer for the female population of the country. Currently surgery, chemotherapy and radiation therapy remain to be the main forms of therapies available to combat breast cancer. All these therapies are invasive and painful with several adverse effects. Recently the focus of cancer researchers has shifted towards immunotherapy in an attempt to find a better line of treatment, which can be well tolerated by cancer patients. Use of vaccines to boost immune response against cancer antigens seems to be a promising approach in this direction. Here we attempt to formulate and evaluate the efficacy of a particulate breast cancer vaccine delivered via skin using micro-needles.

EXPERIMENTATION METHODS

To visualize the micro-channels created by a 1200µm metal micro-needle array, they were stained with either methylene blue or with calcein dye (FluoSpheres® 0.2µm) and observed by light and confocal microscope respectively. For the whole cell lysate, murine breast cancer cell line 4T07 was used as the source of antigens. The protein content of the whole cell lysate was determined by Bio-Rad DC protein assay. Further, vaccine particles were formulated by spray drying an aqueous suspension of the whole cell lysate, β-cyclodextrin, ethyl cellulose, trehalose and hydroxyl-propyl methylcellulose acetate succinate (HPMCAS). Vaccine particles were characterized for shape, size and charge. For in vivo evaluation, 4-6 week old Balb/c
mice were divided in three groups of animals: (a) animals receiving vaccine particles via micro-needle array (n=6). (b) Animals receiving vaccine particles subcutaneously (n=6) and (c) control animals receiving no treatment (n=6). Six booster doses were given at an interval of two weeks from the prior dose and blood samples were collected a week after each dose to detect serum IgG levels by ELISA. After the final booster, animals were challenged with $1 \times 10^6$ live 4T07 cells subcutaneously to determine the efficacy of 4T07 micro-particulate vaccine.

RESULTS AND DISCUSSION

The average size of the particulate vaccine was 1.5\(\mu\)m, which ensured its uptake and further activation of immune response in a murine model. The particulate vaccine was delivered via skin using micro-needles and subcutaneous injection. Formation of micro-channels was visualized by methylene blue staining and confocal microscopy (Figure 1). The results showed that micro-needles created aqueous conduits of $50\pm10\mu m$ to deliver the micro-particulate vaccine to epidermis allowing uptake and activation of immune response.

CONCLUSION

Micro-needle based vaccine delivery bears the potential to be used for cancer vaccination.