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Effective DNA Vaccine Delivery Using Coated Microneedles and Electroporation

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A new DNA vaccine delivery system has been developed called Easy Vax™. The delivery system uses coated, electrically conductive microneedles to deliver DNA into cells in the epidermis. It provides efficient and easily tolerated delivery. It induces a good immune response in mice, the dried DNA is stable at room temperature, and the device's small size minimizes medical waste.

In spite of their recognized promise, DNA vaccines using other delivery methods have not performed as well as expected. This is partially due to inefficient delivery of the DNA into cells *in vivo* (when using naked DNA for instance). The Easy Vax™ vaccine delivery system was developed to improve vaccine plasmid delivery so that DNA vaccines can induce an adequate immune response.

The Easy Vax™ vaccine delivery system has several components. One is a DNA-coated microneedle array. Other components are a case with handle, an inserter, a pulse generator, control circuitry, and a shield to steady the skin during insertion.

Proprietary methods were developed to coat DNA onto needles in a manner that allows the DNA to readily come off of the needles immediately after insertion. These methods were evaluated *in vitro* and *in vivo*.

For *in vivo* evaluation of the device and array coating methods, a reporter gene luciferase was delivered to mouse skin. Expression in mouse skin was high in comparison to injection of an equivalent amount of DNA without electroporation. During these experiments, pulse current was measured. Expression in skin was directly related to pulse current. Since the depth of insertion was the predominant factor governing pulse current, the results show that expression is directly related to array insertion depth as expected.

Varying pulse patterns were evaluated with the Easy Vax™ vaccine delivery system. One experiment compared a range of electric fields. One optimal pulsed electric field protocol was 6 pulses of 1500 V/cm (mid needle) and a pulse width of 100 μs. Luciferase expression was, however, robust to changes in electric field with good expression noted in a range of electric fields.

Since luciferase expression in skin was good using the Easy Vax™ vaccine delivery system, immunizations were done to evaluate the delivery system. Immunizations were done using several infectious disease models (dengue, smallpox and hepatitis B). In all of these, a good immune response was noted. In one experiment, a hepatitis B DNA vaccine was evaluated. The Easy Vax™ vaccine delivery system was compared to gene gun delivery and to intradermal inoculation followed by skin electroporation. Antibody response was higher in both electroporation groups compared to gene gun delivery. The Easy Vax™ vaccine delivery system and the traditional vaccine delivery induced equivalent responses.

These results, and others to be presented, show that DNA vaccines, delivered using the Easy Vax™ vaccine delivery system, are effective.