Threading the needles on immunity

By Michael J. Haas, Senior Writer

Intradermal vaccine developer **Apogee Technology Inc.** thinks it has found a polymer that kills two birds with one stone—acting as both a coating agent for the company's microneedle delivery device and serving as a vaccine adjuvant. The latter feature was a pleasant surprise, because although the polymer, poly[(dicarboxylatophenoxy)phosphazene], is a known adjuvant for intramuscular vaccines, such adjuvants have rarely been compatible with intradermal delivery.

Intradermal vaccines alone typically induce stronger immune responses than intramuscular vaccines alone because the skin is home to a larger population of dendritic cells than muscle tissue. Combining an intradermal vaccine with an adjuvant could further increase immune response, thereby reducing the dose required to provide protection and lowering the cost of vaccines.

Apogee's microneedle-based intradermal vaccine technology is a square centimeter patch of 50 microneedles that are 600 µm long.

Recognizing the dual properties of poly[(dicarboxylatophenoxy)phosphazene] (PCPP), Apogee and collaborators coated the intradermal system with a formulation of HBV antigen and the polymer. Because PCPP doubled as a coating agent during fabrication of the microneedle arrays, it obviated the need for other agents that could be toxic or adversely affect vaccine performance, according to Alexander Andrianov, VP of R&D.

Application of the arrays to the skin of healthy pigs elicited anti-HBV antibody levels that were 10-fold greater than those elicited by intramuscular injection of the same HBV antigen/PCPP formulation and up to 1,000 times greater than levels elicited by intramuscular injection of HBV antigen alone.

Results were published in the *Proceedings of the National Academy of Sciences*.¹ Andrianov was first author of the paper. The team was led by George Mutwiri, a professor of public health, a senior scientist and program manager of vaccine formulation and delivery at the Vaccine and Infectious Disease Organization at the **University of Saskatchewan**.

Another coauthor was Mark Prausnitz, a professor of chemical and biomolecular engineering at the **Georgia Institute of Technology**. His research group invented the microneedle array technology that Apogee is developing.^{2,3}

Skin in the game

The team's results demonstrated that intradermal vaccines can be more effective than injectable ones and that intradermally delivered adjuvants can increase vaccine efficacy, said Alexander von Gabain, CSO and cofounder of intradermal and intramuscular vaccine developer **Intercell AG**.

Nevertheless, von Gabain said any intradermal vaccine technology has to demonstrate clear advantages against the benchmark of intramuscular delivery.

"Intramuscular vaccines are reasonably effective in most people, so being more effective is not necessarily enough of an advantage for an intradermal vaccine," he said. "An intradermal vaccine has to prove itself acceptable in other ways too."

Intramuscular vaccines do have short-term local side effects, such as pain at the injection site or stiffness in the arm. "The multiple and increasing number of childhood vaccination schedules and the repetitive seasonal flu vaccine have made many people reluctant to accept intramuscular vaccinations," von Gabain told *SciBX*.

On the other hand, intradermal delivery has the potential for different side effects, such as skin irritation. "The art will be to sell to the customer that there are side effects from intradermal vaccines but that they are negligible or more easily tolerated compared with intramuscular vaccines," von Gabain said.

He wants to see more preclinical studies on the side effects of PCPP-adjuvanted microneedle vaccines. "If you are too hard on the skin, what is the advantage of the intradermal vaccine over the intramuscular vaccine?" he said.

Andrianov agreed that Apogee has more work to do before taking its PCPP-adjuvanted microneedle vaccines into the clinic.

At the same time, Andrianov noted that the pigs in his team's study experienced no significant adverse events. "As expected, mildly red skin marks, apparently corresponding to microneedle insertion sites, were noticed immediately after application of the patch," but these quickly disappeared, he said.

Andrianov added that Apogee's microneedles can potentially be self-administered and are "practically painless."

With a good adjuvant in hand, Apogee is focused on optimizing the fabrication process of the microneedle technology, the dosing and the product stability. Andrianov declined to disclose indications the company might pursue.

Apogee has filed patent applications on the findings described in *PNAS* and is open to partnering discussions. "Establishing partnerships is probably the fastest way to develop the technology and even to go into clinical trials, especially in the vaccine industry," Andrianov said.

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—Alexander von Gabain, Intercell AG

Haas, M.J. *SciBX* 2(44); doi:10.1038/scibx.2009.1620
Published online Nov. 12, 2009

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