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Thinking on a global scale, Emergex Vaccines using lessons from Ebola outbreak

By Nuala Moran, Staff Writer

LONDON – The lessons of the Ebola epidemic have come together with a series of scientific advances, and expertise acquired over a lifetime in biotech, to inspire a novel vaccine technology that is designed to provide genus-wide protection against viral infections.

In addition to broad-spectrum protection, the fully synthetic technology will provide long-term immunity, be low-cost to manufacture, provide vaccines that are stable at ambient temperatures, are suitable for stockpiling and are administered by microneedle patches.

"I had decided to grow roses," said Tom Rademacher, who rather than retiring as planned in 2014, was caught up in a chain of events that led him to set up Emergex Vaccines Ltd., in a bid to ensure a vaccine is available for future Ebola outbreaks.

At the start of the Ebola epidemic in West Africa in December 2013, the two lead vaccines in development against the filovirus were preliminary constructs, with no human safety data and no approved manufacturing facilities.

Despite a huge international effort marshalling resources from across governments, pharma and regulators, it took a year to get the two products, Glaxosmithkline plc's ChAd3-Ebov and Merck & Co. Inc.'s V-920 (VSV-Zebov) through phase I and to ship supplies of the vaccines to Africa for field testing. (See *BioWorld Today*, Jan. 29, 2015.)

By that time the strict infection control measures meant, thankfully, the incidence of Ebola was falling markedly. However, that made it difficult to stage meaningful challenge trials.

V-920 did deliver positive data in a phase III ring vaccination trial, in which contacts of Ebola patients were vaccinated. But the study did not test subjects in advance of vaccination to assess if they had already developed immunity and was not placebo controlled.

"You can't do challenge tests in Ebola. In future, we need the vaccine ready to go at the start of an epidemic," Rademacher said.

It was as a result of co-founding and spending 14 years at gold nanoparticle (GNP) specialist Midatech Pharma plc that Rademacher found himself drawn into high-level discussions on future preparedness.

Midatech had worked on using its GNPs for the delivery of antigens, and a former company board member, David King, who also was the U.K. government chief scientist from 2000 – 2007, drew attention to their potential use in an Ebola vaccine.

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> CEO and CSO, Emergex Vaccines

"I was asked to write a position paper." Rademacher said. "It went a bit viral."

The upshot was the formation of Emergex in January 2016, and the licensing of rights to use Midatech's GNPs in vaccines for influenza, meningitis, pneumonia, Ebola, Marburg, Zika and dengue.

To date, the company has raised £2.5 million (US$3.4 million) from private investors and VC funds.

Lead candidates have been identified for a universal flavivirus vaccine, designed to protect against dengue, Zika and yellow fever, and a universal filovirus to protect against Ebola and Marburg. Both are due to enter phase I trials at the start of 2019.

Armed with initial safety and immunogenicity data, Emergex aims to set up an international vaccine repository of post-phase I vaccines, for subscription by governments, non-governmental organizations and charities, to act as a first line of defense against epidemic outbreaks. The company aims to provide vaccines at less than $1 per dose.

The cost of storing vaccines and the need to continuously refresh stocks when products reach the end of their short shelf life means that currently only five countries have emergency vaccines stockpiles.

"We are thinking on a global scale; we can expand the repository market. I was surprised to find that only five countries have a repository," Rademacher said. "But you need to make cheaply, store cheaply, it has to be cost effective – and you also need to know how it should be dosed."

Finding a virus' signature

GNPs are ideal delivery vehicles because they mimic exactly what happens in a live infection, when bits of viral infected cells slough off into the blood and reach the lymph nodes.

"When you put GNPs into the bloodstream, they enter the lymph nodes and circulate to dendritic cells and antigen presenting cells, just as in a live infection," said Rademacher. "No processing is required – it is direct information transfer to the lymph nodes."

While the properties of GNPs make them ideal carriers, it is advances in the field of immunoproteomics that enables Emergex to identify which antigens to deliver.

Previously, identifying the amino acid signature of a virus on the surface of an infected human cell that alerts T cells to mark them for destruction was "beyond needle in a haystack stuff," Rademacher said.

Immunoproteomics now makes it possible to find those signatures. Emergex then undertakes some reverse engineering, mixing the signature with blood from people who contracted a particular infection and recovered.

"The aim is to immunize people in the same way as someone who caught [an infection] naturally, mounted an immune response and recovered. By mixing the signature of dengue with post-infection blood we can identify what part of the signature generated the immune response and can make a vaccine that does what happened naturally," Rademacher said.

The approach also provides the basis for a potent in vitro assay, in which vaccine constructs can be tested against post-infection blood to check that they work. "You can't do that with antibodies or attenuated live vaccines," Rademacher noted. "This uniquely opens up an aspect of vaccine validation that you can't do any other way."

That is particularly important in the context of vaccines against such serious infections as Ebola. "You will have a repository with phase I data for a vaccine designed to generate the same immune response as someone who was infected naturally and recovered. You can go to a pivotal trial very quickly," Rademacher said.

Further extending the hoped-for utility, Emergex has taken individual signatures of different flaviviruses and filoviruses and cross-referenced them to come up with a genus-specific signature.

Applying that, the lead program is a cross reactive dengue vaccine incorporating peptides that target Zika and yellow fever. The construct has been synthesized and has entered toxicology testing, with a phase I expected to start in early 2019.

Close behind is a universal filovirus vaccine to target Ebola, and a pandemic flu vaccine.

Rademacher claims another advantage of Emergex's approach will be to restrain viral mutations. "It will be nonselective; it won't force mutations, because it does not attack the virus per se, but looks at its signature," he said. "This is what the world needs." ♦