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Potential Chagas vaccine candidate shows unprecedented efficacy

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Scientists are getting closer to a Chagas disease vaccine, something many believed impossible only 10 years ago. Research from the Sealy Center for Vaccine Development at the University of Texas Medical Branch at Galveston has resulted in a safe vaccine candidate that is simple to produce and shows a greater than 90 percent protection rate against chronic infection in mice.

In a paper published online in *PLOS ONE*, the researchers describe how they identified and tested potential *Trypanosoma cruzi* (also known as *T. cruzi* or Chagas disease) antigen candidates and delivery models to establish the safety and efficacy of a vaccine formulation known asTcVac3. This potential vaccine could halt the irreversible heart and organ damage that afflicts approximately 30 percent of those infected with Chagas.

"This signals a scientific breakthrough – unprecedented vaccine efficacy for a common parasitic disease with no cure for chronic sufferers," said lead author Nisha Garg, PhD, professor of microbiology, immunology and pathology at UTMB. "If this vaccine proves practical, it could be approved in as few as five years for use in canines, which are reservoir hosts of the disease. As many as 20 percent of dogs may be infected in Texas alone, developing the same heart conditions as humans but mistaken by vets for heartworm."

The study also provides further evidence that a human Chagas vaccine is possible, a topic of debate among some who still believe that Chagas

heart disease is the result of an autoimmune disorder, she added.

T. cruzi, transmitted by the triatomine insect, or "kissing bug," is prevalent in almost all Latin American countries and is becoming more common in the U.S. The World Health Organization estimates that approximately 10 million people – mostly children – are infected worldwide. Approximately 13,000 die each year from the complications of Chagas-induced heart disease – a result of the chronic infection Garg and her team aim to vaccinate against. It is estimated that the global economic burden of Chagas is about $7 billion a year.

TcVac3: The Path of Discovery

TcVac3 is the result of rigorous computational/bioinformatics analysis and screening of the *T. cruzi* genome for potential candidate antigens over several years by Garg and her team. These analyses led the researchers to three potential antigens (TcG1, TcG2 and TcG4) for further investigation.

Next, they began testing these antigens and potential vaccine delivery models – how the components are arranged in the actual vaccine – to determine the best approaches.

Early experiments proved that delivery of the candidate antigens by a DNA-prime/protein boost approach, along with co-delivery of IL-12 and GM-CSF cytokine adjuvants meant to enhance the immune response, was effective in generating antibody and T cell responses capable of providing more than 90 percent control of acute infection and parasite burden in infected mice.

Recognizing, however, that this vaccine delivery model was quite complex, the scientists sought to simplify the vaccine using a DNA-prime/Modified Vaccinia Ankara (MVA)-boost approach – a delivery

model that offers many advantages: it can accommodate multiple foreign genes in its genome; may be administered by a variety of routes; has an excellent safety record; and has been shown to generate immune responses to a variety of foreign antigens. MVA itself can act as an adjuvant since it provides a signal to the innate immune system and can boost T cells.

Based on preliminarystudies by the researchers that showed this delivery model to be potent, the scientists next tested the protective efficacy of TcVac3, constituted of just the TcG2 and TcG4 candidates and lacking the adjuvants, delivered by the DNA/MVA approach.

With two doses of the vaccine, the mice with TcVac3-induced antibodies exhibited 92 to 96 percent protection against chronic infection. They found that the DNA/MVA approach increased the vaccine efficacy enough to omit one of the antigens and the adjuvants, making it a much simpler but still highly effective vaccine.

"Because Chagas is most prevalent in developing countries, it is essential that a potential vaccine be inexpensive to develop and easy to deliver," said Garg. "TcVac3 accomplishes this goal, making it not just an effective candidate, but an ideal one."

Future research will determine if the vaccine composition can be simplified even further. In addition, the scientists are already conducting related trials in canines. Garg and her team are also working on pre-clinical trials of human patient samples, testing for immune response in patients that are already infected but not showing signs of chronic disease. Results of both studies are anticipated later this year.

Provided by University of Texas Medical Branch at Galveston