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Researchers publish review article on developing vaccines for human parasites

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Helminthic parasites, like hookworm and liver flukes (schistosomiasis), affect an estimated 1 billion people worldwide. Infection from hookworm and schistosomiasis result in a combined loss of as much as 92 million disability-adjusted life years annually. Little progress has been made to relieve this global burden and eradicate these parasites until now.

A partnership between the George Washington University (GW) School of Medicine and Health Sciences and the Texas Children's Hospital Center for Vaccine Development has led to development of several hookworm and schistosomiasis vaccine candidates. A paper published in *Trends in Parasitology* outlines lessons learned along this critical path.

"It is more critical now, than ever, to address questions around helminth vaccine development," said Jeffrey M. Bethony, Ph.D., professor of microbiology, immunology, and tropical medicine at the GW School of Medicine and Health Sciences. "Due to our unique partnership and leadership in this area, we are in a position to offer guidance to those researchers looking to help make progress in eradicating these diseases of poverty."

For almost two decades, this partnership has worked to identify, produce, and test recombinant protein-based vaccines against human hookworm and schistosomiasis. The lengthy critical path includes five stages: pre-clinical development; process development; production according to current good manufacturing practice; pre-clinical safety and

toxicity testing; and clinical trials conducted in compliance with current good clinical practice. Each stage meets criteria included within the investigational new drug application that is submitted to the regulatory bodies of the United States, Europe, and Brazil.

The paper outlines the following five lessons learned:

1. Avoid the immunoglobulin E (IgE) trap. One of the first recombinant larval helminth vaccines tested in humans was the 21.3 kDa *N. americanus Ancylostoma* Secreted Protein-2 (Na-ASP-2). Allergic reactions in a small group of study participants led to the conclusion that Na-ASP-2 may interact with IgE antibodies induced by previous hookworm infection in individuals living in endemic areas, triggering this response. This halted development, leading to different vaccine targets and a revised critical path.

2. Allow for ample time and resources during process development and manufacturing of helminth vaccines, with a focus on ability to scale-up to industrial-level manufacturing.

3. Develop vaccine potency assays that do not rely on the traditional immunization-challenge potency model (as used for vaccines against pertussis, diphtheria, and rabies) as neither helminth pathogen induce reliable mortality in an animal model nor do these vaccines induce sterilizing protection.

4. Overcome the 'deficient acquired immunity' that occurs during chronic helminth infection, in order to attain sufficient vaccine immunogenicity in these individuals.

5. Accelerate vaccine efficacy testing in humans through use of controlled human infection models as currently established at GW for controlled human hookworm infection.

"Creating a helminth vaccine is arduous. There are challenges at all stages, and at many points, we were responsible for creating novel testing, formulation, and manufacturing processes, in order to advance to the next step in our clinical trials," said David Diemert, MD, associate professor of medicine at the GW School of Medicine and Health Sciences. "We hope this paper will help accelerate activities for other researchers as they progress along this critical path."

The paper "Lessons along the Critical Path: Developing Vaccines against Human Helminths," was published in *Trends in Parasitology*.

More information: David J. Diemert et al. Lessons along the Critical Path: Developing Vaccines against Human Helminths, *Trends in Parasitology* (2018). DOI: 10.1016/j.pt.2018.07.005

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