Chagas disease vaccine demonstrating enhanced immunogenicity

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Technology description

Technology Summary

Pathogen-associated molecular patterns, or PAMPs, are molecules associated with groups of pathogens that are recognized by cells of the innate immune system. These molecules can be referred to as small molecular motifs conserved within a class of microbes. They are recognized by toll-like receptors (TLRs) and other pattern recognition receptors and activate innate immune responses which protect the host from infection by identifying conserved non-self molecules.

Though PAMPs are known to be fundamental in instigating pathogen-specific immune responses, their role in directing these responses beyond their initiation is less well understood. The persistent pathogenTrypanosoma cruzi,innately deficient in strong PAMPs, presents an ideal template to investigate the impact of temporary or continuous exogenous expression of PAMPs on pathogen control.

UGA researchers have developed a method of using of Toll-like receptor (TLR) ligands—and potentially other PAMPs— as tools to enhance immunogenicity of vaccines, particularly those that might persist for an extended period of time in hosts.

More specifically, they have demonstrated that expression of PAMPs by transgenicT. cruzienhances both innate immune responses andT. cruzi-specific CD8+ T-cell responses. It is thought that the continuous expression of PAMPs by the transgenic parasite is required to sustain the enhanced response and thus promote better control of the infection. Preliminary results of an attenuated Chagas disease vaccine candidate that makes use of PAMPs to enhance immunogenicity are promising.

Research in the Tarleton laboratory focuses on the immunology and pathogenesis ofT. cruziinfection and Chagas disease. Three broad questions are being addressed: 1) How is immune control initiated and maintained during the infection; 2) How doesT. cruzimanage to avoid immune clearance and maintain an infection for decades in hosts; and 3) What is the relationship between immunity, parasite persistence, and disease development? The ultimate goals of these investigations are to provide insights into the immunologic basis of parasite control and pathogenesis inT. cruziinfection and to use this information to design methods for prevention of infection or intervention in chronic disease.

Application area

Vaccine for Chagas disease
Enhanced immunogenicity, especially against organisms that do not have strong PAMP expression, thereby increasing the efficacy of the vaccine
Therapeutic for infection through enhanced host immune response
Especially relevant for long-persisting infections

Advantages

Increased immunogenicity of vaccine, compared to co-delivery of PAMP or temporary presentation of the beginning of a vaccination regimen, leading to a more protective immune response to the pathogen Demonstrated proof-of-concept using flagellin fromSalmonellaand porin fromNeisseriaPilot study is for Chagas disease, but this methodology is a platform that could be used to develop vaccines against a variety of pathogens—viral, protozoal, or bacterial

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