A therapeutic nanoparticle vaccine against *Trypanosoma cruzi* in a mouse model of Chagas disease

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**INTRODUCTION**

Chagas disease is a neglected tropical disease of great importance in the Americas, with 7.8 million people infected. The causative agent is *Trypanosoma cruzi* (T. cruzi), and results in acute febrile illness that progresses to chronic chagasic cardiomyopathy in 30% of patients. Current pharmacological treatments are plagued by significant side effects, poor efficacy, and are contraindicated in pregnancy. There is an urgent need for new treatment modalities. A therapeutic vaccine for Chagas disease has potential advantages that include cost savings, reduced adverse effects, and the potential to be used as a replacement for current therapies or when paired with chemotherapy. Prior work in mice has identified an efficacious T. cruzi antigen (Tc24).

We hypothesized that the recombinant Tc24, when delivered in a poly(lactic-co-glycolic acid) (PLGA) nanoparticle delivery system with CpG motifs-containing oligodeoxynucleotides (ODN) as an immunomodulatory adjuvant, will induce a T\(_4\)-mediated CD8+ T cell immune response, ultimately resulting in decreased parasite burden, increased survival, and reduced cardiac pathology in our murine model.

**VACCINE FORMULATION**

**Antigen:** Tc24

**Adjuvant:** CpG ODN

**Characterization of Nanoparticles**

- Morphology & size
- Size distribution
- Loading efficacy

**Delivery System:** PLGA nanoparticles

**Findings:** The PLGA nanoparticle serves as a depot, similar to alum, allowing a prolonged release of protein over time.

**IMMUNOGENICITY**

**Kinetics of Antigen Dispersion**

**THERAPEUTIC EFFICACY**

**Findings:** The vaccine results in improved survival and significant reduction in parasites in the cardiac tissue.

**CONCLUSIONS**

Our nanoparticle vaccine, comprised of Tc24 and CpG ODN encapsulated in PLGA nanoparticles, produced a robust TH1-based immune response. When tested for therapeutic efficacy in T. cruzi infected BALB/c mice, improved survival was seen. Additionally, there was a significant reduction in the number of parasites in the cardiac tissue, suggesting protection from parasite-driven cardiac damage. These data demonstrate the immunogenicity and efficacy of a Tc24/CpG ODN nanoparticle vaccine and are convincing evidence for a potential new therapeutic vaccine against Chagas disease.

**ACKNOWLEDGEMENTS**

We thank Coreen M. Beaumier and Brian P. Keegan for their invaluable help.

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