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# Novel Engineered Trypanosomes as Vaccine Delivery Vectors
RU 962

## Technology Summary

The use of protective vaccines to prime the immune system to elicit specific antibodies that recognize, and neutralize infectious agents has been an extremely successful approach that has resulted in the near-eradication of many childhood diseases. In addition to preventing disease, there is an increase in the efforts to treat disease via therapeutic vaccination. In these cases, a vaccine is developed to generate specific antibodies against a variety of non-infectious, yet pathogenic targets, such as tumor antigens, misfolded proteins, and potentially toxic molecules. The key question is how to activate the immune system to recognize specific peptides derived from self-tissue, or against small molecules. Traditional methods rely on the conjugation of these on carrier molecules, but such immunization approaches are generally quite inefficient in generating high affinity responses, and usually fail in establishing B cell memory for reasons that we are just beginning to appreciate.

To circumvent these issues, our scientists are exploring the use of organisms that have evolved to induce (and then evade) precisely the type of immune responses that we seek to elicit: antibody-based, specific, and long lasting. Their studies take advantage of the natural characteristics of the blood-borne parasite *Trypanosoma brucei*, that interfaces with the immune system through its dense and repetitive surface coat (an array of 11 million identical glycoproteins). This surface coat is used by the parasite as a decoy: it generates a strong and long lasting antibody response which the parasite then evades by switching its coat eliciting a new antibody response etc. Our scientists have co-opted this system and have generated engineered *T.brucei* coats, decorated with a range of antigens, to which then the immune system responds by generating specific and long lasting antibody immunity. Their initial studies show that this approach is successful and potentially a powerful way to develop specific vaccines as well as a potential approach to producing therapeutic antibodies especially to small molecules and antigens toward which there is immune tolerance. This novel approach relies on using the patterned and repetitive nature of the *T.brucei* surface coat as a display platform and is therefore distinct from using trypanosome coats as PAMPs or using trypanosomes to only produce recombinant proteins of interest.

## Main Points and Advantages

- Trypanosomes are obligate extracellular parasites; they live free in the bloodstream and interface with the immune system through their surface coat, an ordered array of 11 milion repeats of a single protein
- Trypanosomes can be genetically engineered to display surface coats decorated with exogenous antigens thus presenting these antigens to the immune system within the ordered array the coat (up to 11 million epitopes, which exceeds by several orders of magnitude any other antigen presenting platform)
- This antibody response does not require live trypanosomes; formalin-fixed (dead) parasites can recapitulate a robust response
- The antibody response to the trypanosome coat (and the exogenous epitopes that decorate it) is rapid, robust, and long lasting, and can also break immune tolerance allowing for the generation of antibodies against otherwise tolerizing antigens

## Area of Application

- The engineered trypanosomes can be used as a vaccine delivery vector capable of eliciting strong antibody responses in situations where a typical peptide immunogen is not effective. They can also be used to generate antibodies to small molecules or epitopes that require a bypass of tolerance, which can then be used therapeutically. It is likely that the trypanosomes can be used in both therapeutic and prophylactic vaccine applications for humans and animals.

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## Stage of Development

- Early stage – engineered trypanosomes have been made and used to successfully generate antibody responses in mice against particular immunogens for which other approaches had failed.

## Lead Inventor

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## Patent Information

- PCT patent application WO 2012/057934 A1 pending.

## References


- Stavropoulos, P. & F. Nina Papavasiliou, 2010. *J. Immunol. Meth*., 362(1-2):190-4.



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