

Poster presentation

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Developing a vaccine for African trypanosomiasis: only wishful thinking or a definite possibility?

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African trypanosomiasis is an emergent disease with significant social and economical impact in 36 African countries. Available drug regimens are very limited and highly toxic so the development of a vaccine would be extremely advantageous. Since the parasite has the ability of misleading the immune response through antigenic variation of its surface coat the development of vaccine was thought to be highly unlikely. However research focused on the identification of invariant components to be used as therapeutic targets and the evolution of DNA vaccine technology bring this objective into the realms of possibility.

Ten DNA vaccine prototypes were constructed encoding ISG (invariant surface glycoprotein) and TSA (trans-sialidase) genes from *Trypanosoma brucei*. These were linked to different targeting sequences to direct the protein to the major antigen processing pathways: (1) LAMP-1 signal targets the protein to the lysosomes (pISGlamp, pTSAIamp); (2) E1A directs the protein to the ER (pe1aISG, pe1aTSA) (3) secretion signal promotes protein secretion (pscISG, pscTSA) (4) E1A and LAMP combined (pe1aISGlamp, pe1aTSAIamp).

The candidate vaccines were tested alongside two controls (PBS and pVAX1GFP). Groups of six CD1 female mice were immunised 50 µg DNA (or control) by intramuscular injection. Animals were killed 28 days post-immuniza-

tion and the right popliteal and axillary lymph-nodes removed for mRNA extraction and histological analysis. In a second experiment the delayed hypersensitivity response (DTH) to trypanosome lysate was assessed. At 14 days post immunization mice were injected with 25 µg of trypanosome lysate into the right footpad. The contralateral footpad was injected with 25 µl saline. Footpad thickness was measured at 0, 24 and 48 hours after injection.

The expression of IFN-γ, TNF-α, IL-1β, IL-2, IL-4, IL-10 and IL-6 in lymphoid tissue was assessed using reverse transcriptase-PCR analyses. Expression levels were applied to rank the candidate vaccines on a scale of 1–12, 1 being the lowest and 12 the highest expression; pe1aISG, pISGlamp, pTSAIamp and pe1aISGlamp groups obtained the best scores. DTH analysis revealed an increase in footpad thickness in mice immunised with all ISG plasmids, pTSA, pscTSA and pe1aTSA compared to PBS.

Histological analysis was used to determine the degree of activation present within the lymph-nodes. pISGlamp and pe1aISGlamp were found to induce the highest levels of stimulation.

On the basis of these experiments pISGlamp, pe1aISGlamp, pe1aISG and pTSAIamp were selected as

the most promising vaccines. Challenge assays will determine their effect on progression of the disease.

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