An invariant *Trypanosoma vivax* vaccine antigen eliciting protective immunity

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Animal African Trypanosomiasis (AAT) has a significant impact on animal agriculture in Sub-Saharan Africa by threatening the livelihood of farmers and food security in endemic countries, and is mainly caused by two species of African trypanosomes, *Trypanosoma congolense* and *T. vivax*. While vaccination would be an ideal solution to manage AAT, effective vaccines against African trypanosomes were considered unachievable due to the sophisticated system of antigenic variation employed by these pathogens to elude the host immune response. By using a systematic genome-led vaccinology approach and a murine model of *Trypanosoma vivax* infection, we have shown that protective invariant subunit vaccine antigens can be identified. Vaccination with a single recombinant protein comprising the extracellular region of a conserved cell surface protein localised to the flagellum membrane termed “invariant flagellum antigen from *T. vivax*” (IFX) induced long-lasting protection. Immunity was passively transferred with immune serum, and recombinant monoclonal antibodies to IFX could induce sterile protection and revealed multiple mechanisms of antibody-mediated immunity, including a major role for complement. Our discovery identifies a vaccine candidate for an important parasitic disease that has constrained the socioeconomic development of sub-Saharan African countries and provides evidence that highly protective vaccines against trypanosome infections can be achieved.