

Development of SE36-cVLP Malaria Vaccine

Principal Investigator

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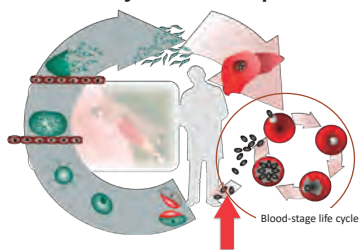
Project Outline

The BK-SE36 malaria vaccine, which combines SE36 recombinant protein with aluminum hydroxide gel (AHG), demonstrated a 72% protective efficacy in clinical trials in Uganda. Furthermore, studies indicated that increasing vaccine-induced antibody titers could potentially enhance efficacy. Thus, to boost antibody titers, the nucleic acid adjuvant CpG-ODN (K3) was added to the BK-SE36 malaria vaccine. Phase Ib clinical evaluation of NPC-SE36/CpG vaccine commenced in Burkina Faso in May 2018, with final observations completed in April 2020. However, the conventional manufacturing process proved too costly for widespread use in African countries and was limited in annual production capacity. As a result, the formulation was modified to SE36-cVLP. SE36-cVLP exhibits several-fold higher antigenicity than SE36/CpG and can be manufactured at a fraction of the cost. Currently, GMP manufacturing is underway to conduct a Phase I/IIa controlled human malaria infection (CHMI) study at the University of Tübingen.



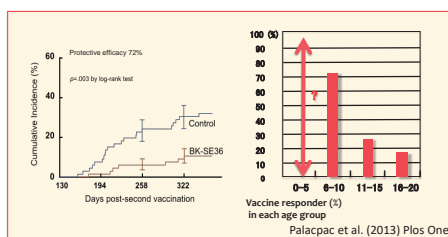
Malaria kills 0.6 million people

Life cycle of *P. falciparum*



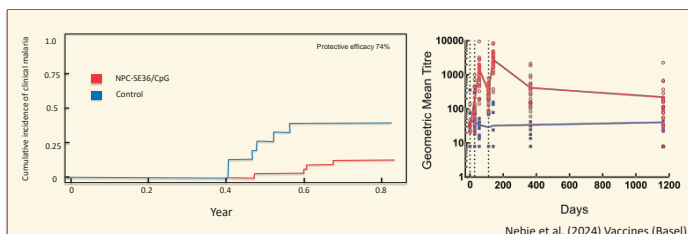
Anti SE36 antibody attacks merozoite of the parasite

The results of phase Ib clinical trial and follow-up research in Uganda



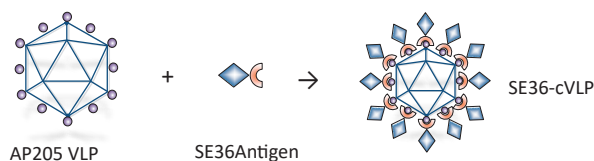
The figure on the left shows the follow-up results from the Phase Ib trial of BK-SE36/AHG vaccine in Uganda. The data suggests that vaccine responsiveness is more prevalent in younger age groups, while repeated infections with age may lead to development of immune tolerance. Consequently, a higher proportion of vaccine responders is anticipated among children aged 0-5 years, who are identified by the WHO as the primary target population for malaria vaccination.

Protective efficacy of BK-SE36/CpG in Phase Ib clinical trial and changes in vaccine-induced antibody titers over time



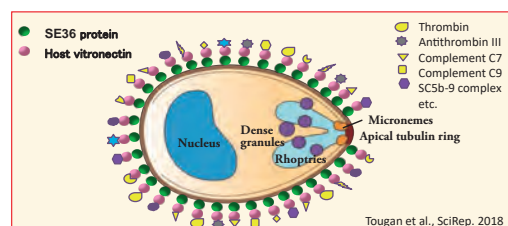
A Phase Ib safety study of BK-SE36/CpG was conducted in Burkina Faso with no serious vaccine-related adverse events reported. Malaria incidence was also measured for one year following vaccination, with a protective efficacy of 74% ($p=0.035$). Furthermore, a three-year follow-up assessment of vaccine-induced antibody titers revealed that high antibody titers were maintained even three years after vaccination.

Development of a malaria vaccine using a new formulation combining phage capsid and SE36



The clinical trials conducted in Africa demonstrated that SE36 is an excellent candidate for a malaria vaccine. However, the conventional manufacturing method is prohibitively expensive for widespread use in Africa, and is limited in annual production capacity. To address these challenges, the formulation was redesigned as SE36-cVLP, which combines the SE36 protein and the capsid of the *E. coli* RNA phage. SE36 protein is efficiently produced in another bacterial expression system. SE36-cVLP exhibits several-fold higher antigenicity than SE36/CpG and can be manufactured at a fraction of the cost. GMP manufacturing is currently underway to be able to conduct a CHMI study at the University of Tübingen.

Biological function of SE36 protein



SE36 hijacks host proteins and molecularly camouflages the surface of merozoites to avoid attack by the immune system. It also induces immune tolerance to SE36 by tightly binding to host vitronectin. In endemic areas, antibody responses against SE36 are low due to immune tolerance. The lack of selective pressure from host immunity is thought to be the reason for the low level of SE36 genetic polymorphism.

Target disease: Malaria

Patent information: Patent pending.

Technology features: A novel malaria vaccine, SE36-cVLP, combining the malaria *Plasmodium* antigen polypeptide SE36 with cVLP.

Marketability: Falciparum malaria is an infectious disease that infects 200-300 million people annually and kills more than 600,000 people, mainly infants under the age of 5 (WHO Report 2024). The development of a highly effective vaccine is expected as a drastic measure.

Development challenges: Obtaining funding to conduct large-scale clinical trials in endemic areas.