Clinical Development of NPC-BKSE36/CpG Malaria Vaccine

Principal Investigator

Department of Malaria Vaccine Development,
Research Institute for Microbial Diseases, The University of Osaka

Endowed Chair Professor Toshihiro HORII

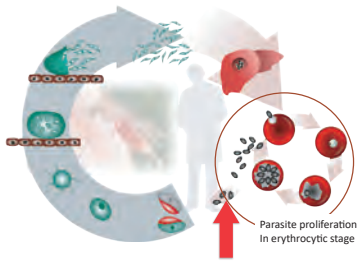
Project Outline

BK-SE36 malaria vaccine is a combination of recombinant SE36 protein and aluminum hydroxide gel (AHG). From a clinical study in Uganda, a 72% protective efficacy could be obtained, with children from 6-10 years old responding more to the vaccine. A study in children 1-5 years old was also successfully carried out in Burkina Faso. In further clinical trials with Japanese adults, adding CpG-ODN(K3), a nucleic acid adjuvant, to BK-SE36 malaria vaccine resulted in 3-4 times increase in the antibody titer. We have completed a BK-SE36/CpG clinical trial in Burkina Faso from adults to 1 year-old child without vaccine related severe side effects and we are now under analysis of obtained data. We also plan to carry out a Phase I/IIa trial utilizing controlled human malaria infection to have supporting efficacy data. BK-SE36 was renamed as NPC-SE36, reflecting the development of the vaccine with Nobelpharma Co., Ltd. as sponsor.

Patients in Apac, Uganda.

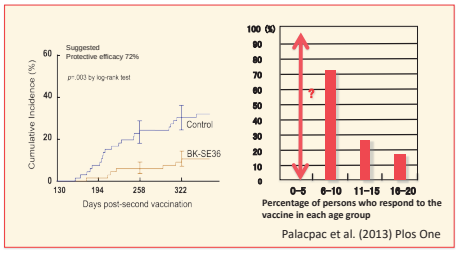
In 2018, there were roughly 400,000 deaths due to malaria.

Life cycle of the falciparum malaria parasite



anti SE36 antibody targets the late stages of the blood-stage life cycle.

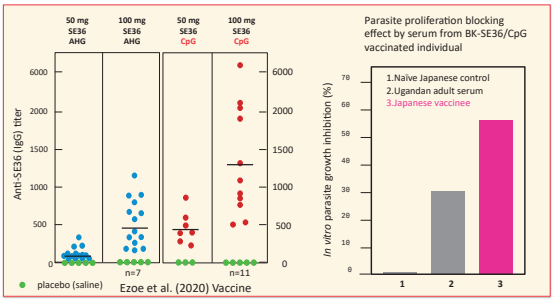
Results of BK-SE36/AHG Phase Ib trial in Uganda



Palacpac et al. (2013) Plos One

In Uganda a promising 72% protective efficacy against high parasitemia and fever was obtained. A larger number of vaccine responders were observed in the younger age group, suggesting immune tolerance occurs with repeated malaria infection. Children, 0-5 years old, the target age group under WHO, are expected to respond favorably to the vaccine.

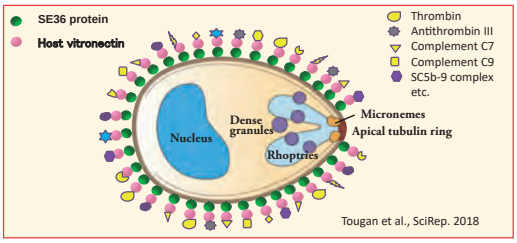
Results of BK-SE36/CpG Phase Ia clinical trial



Ezoe et al. (2020) Vaccine

A comparison of vaccine induced antibody titers from Japanese male adults vaccinated with BK - SE 36 and BK-SE 36/CpG (left panel), highlights the increase in antibody titer 3 weeks after the second vaccine dose. Combination of CpG enhanced antibody titer resulted in more than 3 times higher antibody titer compared to BK-SE36 alone. Furthermore, using serum obtained from 1 volunteer vaccinated with BK-SE36/CpG, *in vitro* growth inhibition assay (GIA) showed inhibition of parasite proliferation.

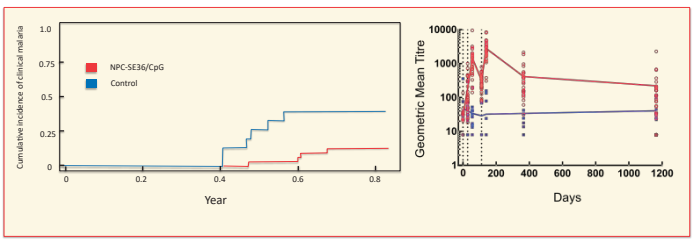
Biological function of SE36 protein



Tougan et al., SciRep. 2018

SE36 protein tightly binds to host vitronectin that binds to other host proteins, components of compliment. These complex camouflage the surface of merozoite to evade host immune attack. The complex of SE36 with host vitronectin causes immune tolerance against SE36. Thus resulted immune tolerance causes low antibody response in the endemic area, then the observed low genetic polymorphism of SE36 gene is thought to be by this low host immune pressure.

NPC-SE36/CpG in Burkina Faso Phase Ib clinical trial; Protective efficacy and duration of vaccine-induced antibody titer over 3 years



In Phase Ib of NPC-SE36/CpG in Burkina Faso, no serious side effects due to vaccination were reported. Malaria onset was measured for one year after vaccination. As a result, a prevention effect of 74% (p=0.035) was obtained. Furthermore, a three-year follow-up study of the antibody titers induced by vaccination revealed that high antibody titers were maintained even three years after vaccination.

Target disease: Malaria; Patent information: (1) Patent No. 4145145 (June 27, 2008), (2) No. 4145348 (June 27, 2008), (3) Patent No. 5748658 (May 22, 2015); Technical features: New malaria vaccine of plasmodium antigen polypeptide SE36 and its variants combined with adjuvant CpGODN (K3); Marketability: Falciparum malaria is an infectious disease that infects 200-300 million people annually and kills more than 400,000 people, mainly infants under the age of 5 (WHO Report 2018). 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. Information to clarify the division of roles between companies and academia: Joint research agreement with Nobelpharma Co.,Ltd. (concluded on March 18, 2019).