Prize Winner's lecture

JSTM (Japanese Society of Tropical Medicine)
Young Investigator Award

**A SINGLE-CHAIN ANTIBODY FRAGMENT SPECIFIC FOR THE *PLASMODIUM BERGHEI*
OOKINETE PROTEIN PBS21 CONFERS TRANSMISSION-BLOKADE
IN THE MOSQUITO MIDGUT**

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Pbs21 is a protein expressed on the surface of macro-gamete, zygote, ookinete and oocyst stages of the rodent malaria parasite, *Plasmodium berghei*, as they develop in/on the mosquito midgut. It has been reported that anti-Pbs 21 mAbs effectively block the development of *P. berghei* ookinetes *in vitro* and oocysts in *Anopheles stephensi* mosquitoes. The antigen has thus been identified as an important target in transmission-blocking immunity and is a model for development of transmission-blocking vaccines. Ideally, transmission-blocking vaccines should induce high titre, long-lasting transmission-blocking antibodies after single immunization. However, since the vaccine candidate antigens of Pfs25/28 family are expressed by parasites in the mosquito stage but not in vertebrate host, boosting of the immune response following a natural infection has never been expected. Nonetheless the induction of transmission-blocking antibodies in patients in combination with anti-malarial drugs could be of considerable importance to prevent the spread of the drug-resistant parasites.

To examine the properties and potential uses of a single-chain antibody fragment (scFv) for blocking transmission of malaria parasites to the mosquitoes, we have cloned and sequenced the genes encoding variable regions of the immunoglobulin heavy and light chains (V_H and V_L) of mAb 13.1. The V_H and V_L genes were assembled as an scFv gene, and expressed in a baculovirus expression system. Following purification of 13.1 scFv, Western blotting and inhibition ELISA assays confirmed that 13.1 scFv retained the binding specificity of the parent mAb 13.1 for Pbs21. Furthermore, 13.1 scFv bound to the surface of *P. berghei* ookinete, and blocked oocyst development in mosquito midgut by at least 93%, as assessed by oocyst counts in mosquitoes. We suggest that the 13.1 scFv gene could be useful not only in studying for the mechanism of transmission-blockade but also in generating, by mosquito germline transformation, a model system to evaluate the production of mosquitoes refractory to malaria.