Anti-Pfs25 monoclonal antibody 32F81 blocks transmission from Plasmodium falciparum gametocyte carriers in Cameroon

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Keywords: malaria, Plasmodium falciparum, transmission-blocking antibody

Pfs25 is a target protein for the induction of antibodies that block transmission of Plasmodium falciparum. Anti-Pfs25 monoclonal antibody (mAb) 32F81 has been generated against gametes of strain NF54 and shown to block the oocyst development in mosquitoes fed on red blood cell suspensions containing NF54 gametocytes (Vermeulen et al., 1985). Comparison of the genes encoding Pfs25 in 8 isolates of different geographical origin showed almost complete sequence homology (Kaslow et al., 1989). Since transmission blocking activity of 32F81 has been reported for NF54 only, we wanted to test the capacity of this mAb to block transmission of field isolates by experimentally feeding local Anopheles gambiae on blood from naturally infected carriers of P. falciparum gametocytes. mAb 32F81 was added to the blood meal at a concentration of 50 µg/mL. A blood meal from the same gametocyte carrier without the mAb was used as a control. Gametocyte density was estimated from the parasite/leucocyte ratio by counting gametocytes against 1000 white blood cells and assuming an average leucocyte count of 8000/µL. In 5 mosquitoes, fed on persons with >200 gametocytes per µL, round forms (activated macrogametocytes and zygotes) were searched for 4 h after the blood meal, using mAb 32F81 labelled with fluorescein isothiocyanate. Ookinetes were also looked for in 5 mosquitoes 24 h after the blood meal. After 7 d, surviving mosquitoes were examined for the presence and number of oocysts. Thirty-three infection experiments were performed and 2292 mosquitoes were dissected. The mean age of the gametocyte carriers was 20-3 years (range 4-44 years) and the mean gametocyte density was 232/mm³. Mean numbers (per mm³) of round forms (10-4±9.6) and ookinetes (0-6±1.3) were lower in the 32F81 group, but not significantly so, than in the control group (18-7±26.7 and 9-0±20-1, respectively). Blood meals from 13 gametocyte carriers gave rise to oocysts (Table). Their mean age was 18-5 years and their mean gametocyte density was 400/mm³. In the experimental group 430 mosquitoes were dissected, and in the control group 498. The mean percentage of oocyst-infected mosquitoes in the control group was 35%, while in those fed on blood containing mAb 32F81 it was 77% (P<0-002, Mann-Whitney U test). While the mean oocyst number in the control group was over 7, the 32F81 experimental group yielded a mean of less than one oocyst per mosquito (P<0-003, Mann-Whitney U test). The 3 subjects with the highest gametocyte numbers showed significantly higher infection percentages even in the 32F81 group (P<0-05 Mann-Whitney U test).

We conclude that mAb 32F81 can block transmission from naturally infected P. falciparum gametocyte carriers to a local strain of A. gambiae, as has been shown by VERMEULEN et al. (1985) and MULDER et al. (1994) for a laboratory-adapted strain of P. falciparum. These findings are in agreement with the almost complete genetic homology of Pfs25 in different isolates, which has been considered to support the development of a transmission-blocking vaccine based on this protein. Transmission blocking is more effective at low gametocyte densities, which are prevalent under natural conditions, and this confirms previous findings in experimental infections (Ponndururai et al., 1987). In addition to naturally occurring transmission-blocking activity of P. falciparum in endemic countries (MULDER et al., 1994), immunization using a Pfs25 vaccine might further reduce malaria transmission (KASLOW et al., 1991; KASLOW, 1993).

Acknowledgements
We thank the staff and patients of the Masa dispensary, Yaoundé, for their co-operation, Julienne Essong and Marienne Sieben for technical assistance, and Isabella Quakyi for critically reading the manuscript. Written permission for blood taking was given to OCEAC by the Cameroonien Ministry of Public Health.

References

Received 12 June 1995; revised 25 September 1995; accepted for publication 27 September 1995