BEHAVIOUR AND BREEDING OF GRA*MMOM*YS SURDASTER (AFRICAN TREE RAT) IN CAPTIVITY; HOST-PARASITE INTERACTIONS IN THIS NATURAL HOST OF THE RODENT MALARIAL SPECIES PLAS*M*OD*I*U*M* BERG*HEI*

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There is increasing evidence now that the interactions between parasite and host are strongly dependent on the host species or strain. Inbred laboratory mice, though receptive to P. b*er*gh*ei* are artificial hosts of this parasite species. For this fundamental reason we developed a colony of the natural host of the rodent malaria parasite P. b*er*gh*ei* belonging to the genus G*ramm*o*mys*. The tree rat G. *s*ur*daster* is the natural mammalian host and reservoir of P. b*er*gh*ei*. G. *s*ur*daster* was first found naturally infected with P. b*er*gh*ei* in Katanga (Congo) near the town of Lubumbashi in 1948. A set of these rodents were recaptured from Zambia in 1996, and a colony established in the animalarium of the Institute of Tropical Medicine, Antwerp. Behavioral and breeding characteristics were studied. For vaccine studies we chose the attenuated parasite vaccine established by Ruth Nussenzweig and based on the irradiated sporozoite. Information regarding the functional and protective capacities of the irradiated sporozoite vaccine was assayed in the G*ramm*o*mys* in terms of inhibition of sporozoite invasion, inhibition of liver stage development and host protection.

The P. b*er*gh*ei* ANKA strain used in our studies was originally isolated from G. *s*ur*daster*, thus classifying these wild rodents as the natural host of P. b*er*gh*ei*. In 1996, 60 animals belonging to the genus G*ramm*o*mys* were trapped in an area within 5km of Kaindu, 20km north west of Mumbwa (Zambia), near the Kafua national park (location 14°41'S 26°35'E; altitude 1130m a.s.l.; mean temperature 19.1°C). The animals were brought to Antwerp, where they were housed in small groups, in straw filled cages, in the dark quarters of the animalarium of the Institute of Tropical Medicine, with low noise and light infiltration. The adult tree rat bore the appearance of a small rat, with brown fur and a pale cream white colour on the belly. Animals were nervous by nature, and capable of jumping high in the air upon being disturbed. Animals grew large with age, the males growing larger and bore a characteristic long tail that they often lost upon being alarmed. Food constituted mainly of sunflower seeds, apples and fresh green leaves. After initial secluded behaviour, the animals mated successfully, the earliest age of mating being about 6 weeks after birth. Litter consisted of up to 5 young ones and mating behaviour was observed monthly. In 2 years about 300 animals were present in our animalarium. These wild rodents were confirmed to be G*ramm*o*mys s*ur*daster* on the basis of their mitochondrial DNA. Upon infection with P. b*er*gh*ei* sporozoites by intravenous inoculation via the tail vein, high susceptibility was noted to infection, with as few as 12 sporozoites inducing full-blown blood stage parasitemia in the G*ramm*o*mys*. Two peaks of blood stage parasites were generally observed, and the animals succumbed by day 20 post infection. A study of liver

sections after parasite inoculation depicted the presence of at least 3 times more parasites in G*rammomys* liver sections, as compared to susceptible inbred mice strains. Upon irradiated P. b*erghei* sporozoite immunizations, partial protection (50%) was observed in the natural host as compared to total host protection in artificial mice hosts. Associated with host protection IgG, T cell and cytokine responses were detected to liver stages in the G*rammomys*.

Our results indicated that the G*rammomys* were much more difficult to protect by irradiated sporozoite immunizations than inbred mice strains, yet were more susceptible to parasite infections as compared to artificial hosts. A reduced protective effect with irradiated sporozoite reflects similar observations in man and supports our belief that the natural host is more difficult to protect by vaccination relative to artificial hosts. We believe that the G*rammomys* model represents an improved intermediate step in the transfer of results from inbred mice data to humans. Moreover primate models are getting too expensive and there is a tendency to test candidate vaccines directly in people of developing countries, which we think is ethically unacceptable.

The WHO estimates that there are 300 million clinical cases of malaria every year, occurring mostly in Africa, but also across Asia and in South and Central America. Over the years the increased spread of drug resistance of the parasite and insecticide resistance in the vector has highlighted the need for the development of effective antimalarial vaccines. We propose the use of the G*rammomys*-P*lasm*od*ium* (natural host-parasite) model to study candidate vaccine molecules to get a better understanding of their functional and immunological activity.