

Rui Wang
Dr. sc.hum.

Microsatellite genotyping and sequencing in the study of population biology and phylogenetic relationship of the *Anopheles gambiae* complex

Geboren am 25.10.1963 in Liaoning, V.R.China
Reifeprüfung am 20.07.1981 in Benxi, Liaoning, V.R.China
Studiengang der fachrichtung „Mechanical Engineering“ vom WS 1981 bis SS 1985 an der „Northwestern Polytechnic University“, Xi’an, V.R.China
Studiengang der fachrichtung Physik vom SS 1992 bis WS 1995
Diplom am 13.11.1995 an der Universität Heidelberg

Promotionsfach: Genetik
Doktorvater: Prof. Dr. med. C.R. Bartram

Microsatellite genotyping analysis is a powerful method for population and phylogenetic studies. In this study, an accurate, reproducible and high-throughput microsatellite genotyping method was developed and a reference set of microsatellite markers of *Anopheles gambiae* was selected. This method and the reference markers are well-suited for population genetic studies of field mosquito populations, and for the clarification of phylogenetic relationships in the *A. gambiae* complex. Experimental microsatellite genotyping data of three *A. gambiae* populations and four species of the *A. gambiae* complex were analyzed using different statistical methods; the congruence of different statistical methods were then examined using these data. The statistical parameters F_{ST} and R_{ST} for genetic difference measurement, though often used in previous studies, were found to have some limitations for evolutionary studies. We propose instead the genetic distance W , as the most appropriate indicator for microsatellite data evaluation.

Extensive gene flow between the three *A. gambiae* populations was inferred by their similarity over most of the genome, except for cytogenetic divisions 5 and 6 (outside the *Xag* inversion region), where one population (Sel.) clearly showed statistically significant differences relative to the other two populations. Comparing with other species, the genotyping results revealed that in the Sel. population (but not in the other two populations) this part of the *A. gambiae* genome was similar to that of *A. arabiensis*. Furthermore, within the *Xag* inversion region, *A. gambiae* and *A. arabiensis* were the most distantly related species, while for the autosomes the two species were indistinguishable. Sequencing data at locus *HI58* (located on the 3rd chromosome) showed that complex mutations were shared in these two species, reinforcing the possibility of sequence exchanges through introgression.

The phylogenetic relationship of the four species of the *A. gambiae* complex emerged, especially for the two very important human malaria vectors, *A. gambiae* and *A. arabiensis*. In the autosomal region as well as in some *A. gambiae* populations at the base of the *X* chromosome outside the *Xag* inversion, they share similarities: these may reflect introgression between the species. In contrast, within the *Xag* inversion, the genome of the two species was highly divergent, suggesting that the inversion may act as a barrier to introgression.

In light of these observations, the genotyping and sequencing approaches are complementary. The genotyping data indicated the phylogenetic and population relationships and confirmed the mosaic nature of the genome. On the other hand, the sequence data revealed mutations, which appeared to antedate particular speciation events in the *A. gambiae* complex, and illuminated the nature of the null alleles.