

A NEWLY DESCRIBED NATURAL POPULATION SUBGROUP OF THE MOSQUITO *ANOPHELES GAMBIAE* IS EXCEPTIONALLY SUSCEPTIBLE TO HUMAN MALARIA

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Capture of indoor-resting mosquitoes via aspirator or pyrethroid spray is a commonly used approach for *Anopheles* population sampling. However, indoor collections do not efficiently recover behaviorally distinct compartments of the population, and larval sampling followed by genotyping and genetic analysis may represent a comprehensive and less biased alternative. When this approach was used in the Sudan Savannah region of Burkina Faso, a novel group of outdoor-resting *A. gambiae* was found at high frequency in larval captured *A. gambiae*. The newly described exophilic subgroup freely segregates for both molecular form markers (>35% M/S hybrids) and the 2La chromosome inversion (>50% 2L+ chromosomes). In contrast, contemporaneous site-matched indoor collections confirmed the canonical description of the *A. gambiae* population in this region of West Africa: namely M and S molecular forms speciating and near fixation of the inverted form of the 2La inversion. Most striking is the larger population abundance and the greater susceptibility to *Plasmodium falciparum* infections of the exophilic subgroup of *A. gambiae*. The existence of a group of *A. gambiae* that is both highly susceptible to *P. falciparum* infections and not indoor resting could have significance for the efficiency of malaria control efforts, particular those targeting indoor resting mosquitoes.

CYTOGENETIC MAP FOR *ANOPHELES NILI*: APPLICATION FOR POPULATION GENETICS AND COMPARATIVE PHYSICAL MAPPING

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Anopheles nili is one of the major malaria vectors in Africa with wide geographic distribution. However, the taxonomic and population genetic studies on this species are scarce. New research tools are urgently needed to genetically characterize this important malaria vector. In this study, a high-resolution cytogenetic map was developed for *An. nili* polytene chromosomes. Chromosomes were straightened and subdivided into 46 numbered divisions according to the banding pattern. Population analysis of *An. nili* females collected in Burkina Faso revealed the presence of two highly polymorphic inversions on the 2R chromosomal arm. To determine chromosome homologies and gene order conservation between *An. nili* and other major malaria vectors, PCR probes based on the *An. gambiae* coding sequences were mapped to *An. nili* chromosomes. Comparative mapping demonstrated that *An. nili* chromosomes have an *An. stephensi*-like arm association and that whole arm translocations and paracentric inversions were the major types of rearrangement in evolution of these mosquitoes. The minimum number of fixed inversions among *An. nili*, *An. gambiae*, and *An. stephensi* was calculated using the Multiple Genome Rearrangements (MGR), Genome Rearrangements In Man and Mouse (GRIMM), and Sorting Permutation by Reversals and block-INTERchanGes (SPRING) programs. The data suggest that the *An. nili* is, at least, as

diverged from *An. gambiae* as *An. stephensi*. We provided evidence that 2La/a arrangement of *An. gambiae* is present in outgroup species *An. nili* and *An. stephensi* confirming the ancestral status of the 2La inversion in the *An. gambiae* complex. Availability of the new polytene chromosome map, polymorphic inversions, and physically mapped DNA markers for *An. nili* will further stimulate population genetic, taxonomic, and genomic studies of this neglected malaria vector.

TRANSDUCTION OF *SCHISTOSOMA MANSONI* WITH VESICULAR STOMATITIS VIRUS GLYCOPROTEIN PSEUDOTYPED LENTIVIRUS

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Retrovirus-mediated transduction offers a means to insert reporter transgenes into the schistosome genome, to elucidate schistosome gene function and expression through vector-based RNA interference, and to establish transgenic lines of schistosomes. Previously we have reported that murine leukemia virus (MLV) pseudotyped with vesicular stomatitis virus glycoprotein (VSVG) can transduce developmental stages of *Schistosoma mansoni*. In addition, we have been investigating whether human immunodeficiency virus (HIV-1) lentivirus (a complex retrovirus) might likewise be utilized for transgenesis of schistosomes. We constructed lentiviral vectors using the ViraPower Gateway (Invitrogen) system; we modified pLenti6/R4R2/V5-DEST by insertion of an endogenous schistosome gene promoter; from the spliced leader (SL) RNA gene, upstream of the reporter gene encoding jellyfish green fluorescent protein (GFP). 293 FT producer cells were transformed with this construct and viral packaging plasmids to produce replication incompetent lentivirus virions pseudotyped with VSVG. We investigated early steps of lentivirus infection of schistosomes including attachment of virions to the schistosome tegument, reverse transcription to synthesize proviral DNA, and integration of the provirus into the schistosome genome. Schistosomes were incubated with HIV virions in the presence of the cationic polymer polybrene. At several times from 0 minutes to four hours thereafter, schistosomes were washed and the surface cross-linked with formalin. Using a VSVG specific antibody as the probe, time course dependent immunolocalization was evident to both schistosomules and adult worms, with increasing fluorescence signals from 0 to 180 min after exposure. Downstream events were investigated at one day post infection. Genomic DNAs (gDNA) were extracted from infected worms and used as the template for quantitative real time PCR (qPCR). qPCR targeting linear viral cDNA and integrated viral genome were performed with single step PCR and two step anchored PCR approaches, respectively, which revealed the presence of linear viral cDNA and integrated proviruses. We are now investigating integration junctions and reporter gene activity, with the aim of establishing the potential of VSVG-HIV-1 lentivirus as a vector for genetic manipulation of schistosomes.

MOLECULAR MIMICRY BETWEEN ALLERGENS AND HELMINTH PROTEINS UNDERLIES RESPONSES AT THE HELMINTH-ALLERGY INTERFACE

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Although chronic helminth infection can diminish allergic skin test reactivity, many helminth infections are associated with allergic symptoms, possibly mediated by cross-reactivity between allergens and helminth proteins. To investigate the extent of this cross-reactivity, we performed *in silico* comparisons of 410 common (and molecularly defined) allergens