Anopheles gambiae, an African Malaria Vector: Genome to Gene Functions

Young Seok Hong, Jim Hogan, Lucas Ton and Frank Collins
Center for Tropical Diseases Research and Training University of Notre Dame
Notre Dame, IN, USA

Anopheles gambiae is the most important African malaria vector that transmits *Plasmodium falciparum*, the most deadly malaria parasite, to humans in Africa. It is estimated that annually there are about 300 to 500 million clinical cases of malaria infection worldwide, claiming 1 2 million lives. Most of the victims are children under the age of 5. Malaria transmission in Africa is expanding because of mosquito resistance to insecticides and malaria parasite resistance to anti-malarial drugs. To overcome these obstacles, new research efforts to control malaria infection are desperately needed. Although there is active research into developing vaccines against malaria parasites, many countries suffering from malaria are under-developed, lacking suitable socioeconomic abilities to procure vaccines and other alternative anti-malarial drugs. In contrast, methods to control mosquito vector populations still remain more practical in many malaria endemic regions. This is because once implemented adequately, vector control programs are expected to be relatively cost-effective and self-supportive for many malaria-ridden African nations.

As a part of our laboratorys integrated efforts toward ultimately developing a more effective and durable mosquito control measure, several research projects are underway. First, we are one of a group of laboratories that has recently initiated an *An. gambiae* genome

project. As a result, an international consortium is now carrying out a genomic sequencing project, aiming for completion in the fall of this year. Secondly, we and other labs are currently carrying out EST projects, which will produce EST databases of different resources such as strain-specific (i.e., susceptible and refractory to malaria infection) and tissue-specific ESTs. Thirdly, we have isolated an *A. gambiae* strain (L35) that is refractory to malaria parasites, showing encapsulation of the parasite. As a result, this mosquito strain prevents the malaria parasite from developing into normal oocysts in the mosquito midgut. This interesting phenotype named as *Pen* (Plasmodium encapsulation), is now actively being investigated. *Pen* genes were characterized as QTL involving at least three loci (*Pen 1* to *3*). Among the three *Pen* genes, *Pen1* appears to play a major role. Currently, we are trying to identify the *Pen1* locus using map-based cloning (i.e., BAC contig), computational methods, and expression profile analysis by RT-PCR.

A BAC contig of about 700 kb for *Pen1* is about to be made, which will facilitate cloning of the *Pen1* locus. Lastly, we are investigating germ-line transformation of *An. gambiae* using *pPiggyBac* element and eGFP as a selection marker. This technique will provide us with a much-needed tool for transgenesis in *An. gambiae*. In addition to the above-mentioned, other research interests in our laboratory will be also discussed.