FIRST WORKSHOP
"DYNAMICAL SYSTEMS APPLIED TO BIOLOGY AND NATURAL SCIENCES "

1-3 FEBRUARY 2010
CMAF, LISBON UNIVERSITY

ABSTRACT | Cláudio Struchiner

Title

On the Distribution of Mosquito Susceptibility to Malaria

FIOCRUZ, Brazil
stru@fiocruz.br

Abstract

The malaria model developed in association with the Garki Project in Nigeria by Dietz, Molineaux and Thomas (DMT) explicitly addressed the implications of the human immune response on the transmission dynamics of this mosquito-borne disease. Although this contribution was originally conceived for discussing intervention strategies based on the use, alone or in combination, of house-spraying with propoxur (a residual insecticide) and universal distribution of anti-malarial drugs (sulfalene and pyrimethamine), the presence of this human immune response component also made the model suitable as a starting point for discussing the development of the various malaria vaccines made possible by the new molecular biology paradigm that became widespread in the 80's. Expansions to the Garki's DMT model have shown to be useful to uncover the complex implications of intervention programs against mosquito-borne diseases by focusing on the changes in immune profile of the target human population and the evolution of pathogen virulence and resistance as a result of selection pressures imposed by a vaccine or drug.

The original paradigm described above addresses within-vertebrate host stages of the parasite's life history and was motivated by the possibility of developing vaccines that elicit stage-specific immune responses in humans. Recent advances in molecular genetics and mosquito ecology motivates the expansion of the original paradigm to also encompass those stages of the pathogen that take place in the vector. These genetic methods for controlling vector transmissions are designed to reduce or eliminate vector populations, to selectively kill only those vectors infected by the pathogen, or to modify (replace) natural vector populations by introgressing genes that eliminate vector competence. However, as became evident from the Garki data since the 70's, the genetic diversity of traits that modulate vector competence posed an important challenge to control programs based on domiciliary spraying of residual insecticides as evidenced by the degree of exophily among the population of individual vectors members of the gambiae complex. More recently, the diversity of the immune response exhibited by vectors, i.e., the means whereby they are able to kill invading pathogens, has been well established by the availability of the genome sequences of vectors, hosts and parasites that enabled genome wide comparative studies. Those advances provide new tools to monitor diversity among the three players, pathogens, vertebrate and invertebrate hosts. In

particular, important issues, such as parasite virulence and resistance, are not fixed properties of infection but are affected by the genetic diversity of the players involved, and the environmental conditions under which those players interact.

An expanded paradigm that accounts for the vector-pathogen systems explicitly can contribute to avoid a large underestimation of the pathogen polymorphism as well as polymorphisms of traits that modulate the invertebrate host competence. These two processes together contribute to genetic drift and selection since the higher the pathogen diversity within a host, the greater is the expected genetic change between the original host and the load delivered to the next host. Within-vector competition adds one more level of selective differences affecting the local pathogen diversity since resistance genotypes in vectors could select against some pathogen genotypes more than others.

By using population-genetic models, we explore the evolutionary epidemiologic dimension of genetic strategies currently being proposed to control mosquito-borne diseases. In our three-players system, reciprocal selection pressures determine the distribution of each player's polymorphism. In our work, we focus on the forces that determine the current distribution of traits associated with dimensions of epidemiologic importance such as vertebrate and invertebrate immune response, and pathogen virulence and resistance to drugs. By explicitly describing the forces that determine the current distribution of traits, we hope to add to the discussion of gene drive mechanisms and their relative chances of success in changing the current distribution of traits by the introgression of new genes into the vector population. Finally, we validate our models against the empirical information collected so far from the genome wide studies comparing vectors of medical importance as well as other insects.