## ABSTRACT

Arboviral diseases are rapidly (re)-emerging and spreading worldwide due also to the rapid expansion of the arboviral vectors *Aedes aegypti* and *Aedes albopictus*. Since there are not specific antiviral treatments against most arboviruses and vaccines are limited, vector control operations are critical to avoid disease transmission. Limiting the abundance and spread of mosquito populations is fundamental and is best achieved using an integrated approach that merge different strategies, which should be chosen to conform to local environments and the socio-economic status of the targeted communities.

During my thesis I worked on two different projects that are related to two vector management strategies:

- Project 1: Insecticide Resistance – Challenge for the use of chemical compounds.

Insecticides, primarily pyrethroids (PY) are the main tool against vectors. Extensive use of PY posed selection pressure on mosquito populations that led to the emergence of resistance. The emergence and spread of insecticide resistance hinder the sustainable use of insecticides. Thus, detection of resistance and its surveillance are crucial. Resistance to PY and DDT can be monitored in an unbiased manner by analyzing the frequency of *kdr* mutations in vector populations. *kdr* mutations are mutations in the PY and DDT target site (i.e. the *para* sodium channel gene) that have been associated with phenotypic resistance. Two mutations (i.e. V1016G/I and F1534C) are known to be predictive of the resistant phenotype in *Ae. aegypti*. Thus, I genotyped them in 452 mosquitoes of both *Ae. aegypti* and *Ae. albopictus* geographic samples. The aim of this analyses was to verify the widespread of resistance and to investigate how the two *kdr* mutations are distributed in relation to the different ecological conditions in which the two mosquito species were sampled from. My analyses confirmed the widespread resistance to PY in samples of *Ae. aegypti*, primarily in Mexico, and identified emerging resistance in *Ae. albopictus* samples, emphasizing the importance of geographically-extending and continuing the monitoring of resistance.

- Project 2: activity of the piRNA pathway – Opportunity for the identification of effectors to be applied in genetic-based strategies of vector control.

The piRNA pathway is the most recently-identified of the three RNA interference pathways and it has been mainly studied in *Drosophila melanogaster*. In *Dr. melanogaster* the piRNA pathway is active in germline cells where it acts against transposable elements to limit their

mutagenic effect. In *Ae. aegypti* PIWI proteins are thought to have also antiviral activity because they expanded in number with respect to *Dr. melanogaster*, they are expressed in the germline and in somatic tissues, and piRNAs are produced following viral infection. On this basis, I worked towards the development of an *in vitro* assay to test the function of the different proteins of the piRNA pathways of *Ae. aegypti*. This part of the thesis was performed at Radboud University in the Medical Microbiology Institute for Molecular Life Sciences in Nijmegen, the Netherlands, under the supervision of professor Ronald van Rij and Rebecca Halbach M.Sc. During my internship, I was able to prepare all the plasmids required to establish a λN/boxB system, that is a flexible system to analyze the activity of targeted proteins through a luciferase assay. This system allows to study modifications in the protein structure to understand functional domains. Additionally, I was able to test the system once for two proteins (i.e. PIWI4 and PIWI5) with promising results.