Human Antibody Response Against Aedes aegypti D7 Salivary Proteins

Danielle Morton[1,2] Paula Rozo and Berlin Londono-Renteria[1]

[1]Department of Entomology, College of Agriculture, Kansas State University

Introduction

Dengue is one of the most geographically significant mosquito-transmitted diseases caused by dengue virus (DENV). In endemic areas of tropics and subtropics, this disease has become the leading cause of morbidity and mortality. In the Americas, DENV is primarily transmitted to humans by *Aedes aegypti and Ae. albopictus* mosquitoes. During blood feeding, the female mosquito injects saliva into the human skin to facilitate meal intake. The salivary proteins (mSP) stimulate immune responses that may lead to antibody production and modulation of cellular and cytokine function with a strong effect on viral infectivity. Previous studies have showed that the salivary allergen D7 exhibits anti-viral properties for DENV in the human skin. It is hypothesized that in endemic settings, after repeated exposure to mosquito bites, human hosts develop an immune response against mSP that can enhance or block viral infectivity.

Purpose

We attempt to establish whether people residing in non-endemic areas for DENV develop antibodies against D7 salivary proteins. These findings will help to understanding host–mosquito interaction in the absence of the disease.

Questions, Hypotheses, and Predictions

Question: What are the levels of antibody response against a D7 salivary proteins in healthy individuals from Kansas?

Hypothesis: The antibody response against *Ae. aegypti* saliva is directly correlated with the level of exposure to mosquito bites.

Prediction: People engaged in outdoor activities with no use of protective strategies such as repellent will present higher antibody levels against *Ae. aegypti* D7 proteins than people using repellent or staying indoors during vacations.

Study System

We designed two peptides from the D7 long salivary protein from *Ae. aegypti* mosquitoes. These peptides contain 18 (D7L1) and 21 (D7L2) aminoacids. The peptides where used as antigen in an ELISA test to measure IgG, IgM and IgE antibodies from **human blood**.
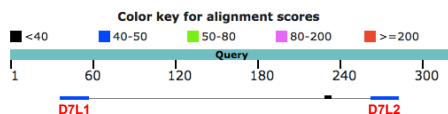


Methods and Experimental Design
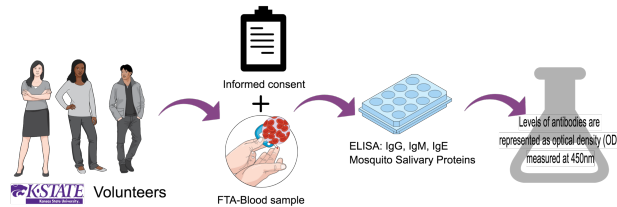
Results

We enrolled 13 healthy volunteers (7 females and 8 men) living in Manhattan, KS, with ages between 19 and 42 years old (mean age = 24.08). The average time residing in the city was 3.3 semesters (calculated based on the number of semesters attending KSU). All participants were engaged in any type of outdoor activity (i,e. gardening, hiking, camping); however, only 7 out of 13 (54.9%) reported the use of repellent.
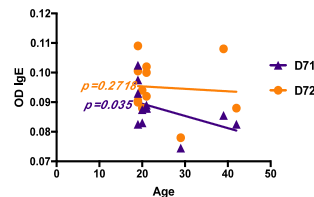

Figure 1: Correlation between participants age and levels of IgE.

We found a significant negative correlation between age and D7L2; which means that the older the person the lower the level of IgE antibodies against D7.
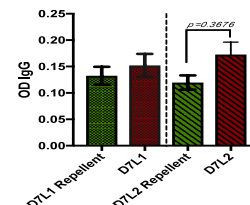
Figure 2: IgG levels of antibodies in in relation with the use of repellent among the participants.

When we compared the levels of antibodies against each protein, we found that higher IgG antibodies are associate with the no-use of use repellent.
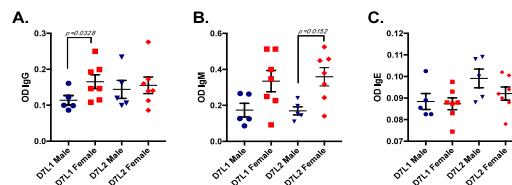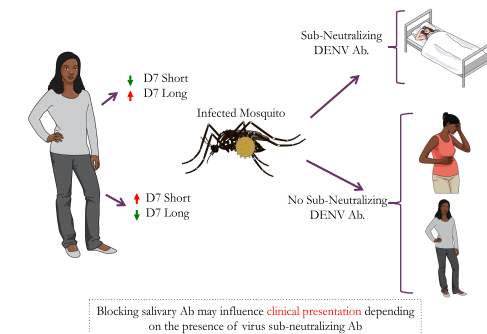

Figure 3: Antibody levels of IgG (A), IgM (B), IgE (C) in males and females.

We compared level of exposure and response in males versus females and found that IgG antibodies against D7L1 were significantly higher in females (A) as well as IgM antibody levels for both D7L1 and D7L2 (B). We did not find significant differences between males and females for IgE antibodies.

Conclusions

Mosquito saliva plays an important role in vector-borne disease transmission and pathology. Here we show that IgG antibody levels against D7 salivary proteins are higher in people that does not use repellent, which suggest that D7 proteins might be useful markers to measure human–mosquitoes contact. We also found that males and females respond differently to mosquito salivary antigens. Our results may have implications for pathogen transmission and presentation of clinical disease. Since mSP have a profound impact on pathogen transmission, additional studies characterizing factors that may influence immune response against salivary proteins are needed.

Future Directions

Blocking salivary Ab may influence clinical presentation depending on the presence of virus sub-neutralizing Ab

Acknowledgements

References

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