Plan Overview

A Data Management Plan created using DMPTool-Stage

Title: Mosquito evolution in response to a dengue envelope protein-guided insecticidal peptide

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Grant: https://grants.nih.gov/grants/guide/pa-files/PAR-21-155.html

Template: NIH-GDS: Genomic Data Sharing

Project abstract:

The long-term objective of this project is to provide a solution to the alarming increase in insecticide resistance in mosquito vectors of human pathogens. Insecticides target specific proteins in the mosquito and resistance mutations in these proteins prevent the binding and toxicity of the insecticide. In the proposed research, an orally toxic peptide insecticide which specifically targets the mosquito gut receptor of dengue virus-2 will be fed to *Aedes aegypti*, the mosquito vector of dengue virus, to force the evolution of resistance in the mosquito. It is hypothesized that mosquitoes that have lost the ability to bind the insecticide will have also lost the ability to bind and vector dengue virus itself. Thus, mosquito populations would evolve away from vectoring dengue if resistance were to develop. This peptide insecticide is modular, fusing the commercially successful insecticidal peptide, Hv1a, to a guide peptide comprising 15 amino acids from the envelope protein of dengue virus-2 which specifically bind mosquito cells but not human cells. Guide peptides for future mosquitocidal peptides could be sourced from other vector-borne pathogens to control other mosquito genera or other vectors attracted to sugar baits. Specific Aim 1 is to evolve populations of mosquitoes which are resistant to the guided Hv1a peptide insecticide. Three populations will be passaged, being fed the dose in 10% sucrose which kills 80% of the population (LD80). Survivors will be mated and the resulting eggs provide the next passage, with dosage increased with increased survivorship, until the entire population can survive the original LD100. Control populations fed unguided Hv1a and plain 10% sucrose will be in parallel passages. Another set of populations will be fed deltamethrin insecticide at the LD80 to evolve resistance, providing an in-house comparison to standard insecticides. In Specific Aim 2, eggs from guided Hv1a-evolved and control populations will be sent to our collaborator, Berlin Londono of Kansas State University, to assay for the ability of dengue virus-2, provided in an oral blood meal, to infect the adult mosquitoes. RNA-Seq and specific sequencing of the dengue virus receptor protein gene (prohibitin) will track the evolution of gene expression and prohibitin through the passaging. If vectorial capacity is lost, the project hypothesis is proven and an inexpensive means of modulating

vectorial capacity will have been discovered. If vectorial capacity is maintained over the entire 3-year term of the passaging, then an insecticide uniquely impervious to resistance will have been discovered instead.

Start date: 03-31-2022

End date: 03-30-2025

Last modified: 06-18-2021

Mosquito evolution in response to a dengue envelope protein-guided insecticidal peptide

Gene expression data from RNA-Seq analysis will be collected in this project from mosquito populations at various time points throughout the passaging to track changes in gene expression as the mosquito populations evolve in response to increasing dosages of guided Hv1a peptide insecticide offered in 10% sucrose. Other populations monitored in similar fashion will be populations evolving in response to increasing dosages of deltamethrin insecticide and also two types of control populations, namely populations given the nontoxic Hv1a peptide and populations supplied only with plain 10% sucrose.

All of this RNA-Seq data will be posted on Gene Expression Omnibus at http://www.ncbi.nlm.nih.gov/geo/

PacBio sequencing will be performed, at various time points in the mosquito passaging, on the prohibitin receptor in the mosquito gut, which naturally binds dengue virus but is also targeted by the guided Hv1a protein insecticide. These sequences will trace the evolution of the prohibitin gene in response to guided Hv1a during passaging. Sequencing will also be done on the two control populations offered Hv1a or plain 10% sucrose.

All of these full-gene-length reads of prohibitin gene evolution will be posted on the Sequence Read Archive at http://www.ncbi.nlm.nih.gov/Traces/sra/sra.cgi

The RNA-Seq and prohibitin gene sequencing data mentioned above will be loaded onto these public servers within a few months of analyzing the data and all data will be completely loaded before publication of the research in a journal.

All of this RNA-Seq data will be posted on Gene Expression Omnibus at http://www.ncbi.nlm.nih.gov/geo/

All of these full-gene-length reads of prohibitin gene evolution will be posted on the Sequence Read Archive at http://www.ncbi.nlm.nih.gov/Traces/sra/sra.cgi

All data submitted will be available with unrestricted access to the public.

In addition to the sequencing data, submissions to these servers will include metadata on the sequencing devices used and the sequencing conditions, the extraction of the RNA and DNA, library preparation, and details on the passaging experiments (including explanations of treatment labels) to allow for full interpretation of the sequencing data by those that download the data.

The RNA-Seq and prohibitin gene sequencing data mentioned above will be loaded onto these public servers within a few months of analyzing the data and all data will be completely loaded before publication of the research in a journal.

Human subject data will not be collected in these experiments.

All data will be made publicly available with no exceptions.

No intellectual property will be pursued with this data. This data will remain freely available, without any licensing requirements.

Planned Research Outputs

Dataset - "RNA-Seq data for gene expression changes in Aedes aegypti in response to treatment with guided Hv1a peptide insecticide "

Intended Repository: Gene Expression Omnibus at http://www.ncbi.nlm.nih.gov/geo/

This dataset is RNA-Seq data from Aedes aegypti mosquito populations in serial passaging with increasing dosages of guided Hv1a, which is the peptide insecticide omega-hexatoxin Hv1a from the spider Hadronyche versuta, fused to a guide peptide derived from the binding site in the envelope protein of dengue virus-2 for the mosquito gut receptor prohibitin.

Dataset - "Prohibitin full-gene-length sequences for evolution in Aedes aegypti in response to guided Hv1a treatment"

Intended Repository: Sequence Read Archive at http://www.ncbi.nlm.nih.gov/Traces/sra/sra.cgi

Prohibitin full-gene-length PacBio sequences from Aedes aegypti mosquito populations in serial passaging with increasing dosages of guided Hv1a, which is the peptide insecticide omega-hexatoxin Hv1a from the spider Hadronyche versuta, fused to a guide peptide derived from the binding site in the envelope protein of dengue virus-2 for the mosquito gut receptor prohibitin.

Planned research output details

Title	Type	Anticipated release date	Initial access level	Intended repository(ies)	Anticipated file size	License	Metadata standard(s)	May contain sensitive data?	May contain PII?
RNA-Seq data for gene expression changes in Aedes ...	Dataset	2025-04-17	Open	None specified	1 GB	None specified	None specified	No	No
Prohibitin full-gene-length sequences for evolutio ...	Dataset	2025-04-17	Open	None specified	1 GB	None specified	None specified	No	No