Interaction Between Zika Virus and a Mosquito Axl-like Protein

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Although many of the mosquito-borne Flaviviruses are not a major concern in the temperate regions of the world, they should be with the rise of global warming. These viruses could spread into new parts of the world as their mosquito vectors migrate. Similar events may occur with other vector-borne or climate specific viruses and pathogens. Regarding Zika, migration to temperate climates could result in an exponential increase in microcephaly due to the significant proportion of the world population living within the temperate regions (the other major region being the subtropics, where Zika can currently be found). Studying these, and all other viruses will be evermore important given both the changing environment and the recent global pandemic.

This study will look at the use of Axl-homologs (particularly Down Cell Adhesion Molecule, or DSCAM) for binding by Zika virus, on both human and mosquito cells. Axl is already a suspected protein used for binding to human cells, however, this protein does not exist within the mosquito genome. Thus, a DSCAM is selected for the study.

Currently, we are working on a process known as RLM-RACE (RNA Ligase Mediated- Rapid Amplification of cDNA Ends). This process is helping us to isolate and amplify the very end of the gene we are looking to replicate. The purpose of doing this is to get an exact sequence and determine where the gene starts (there are multiple possible starting points along the predicted sequence). Once this is completed and a sequence has been obtained, custom primers will be designed to replicate the desired gene via PCR (polymerase chain reaction) and will also attach restriction sites on either end of the amplified gene.

The purpose of the restriction site is so we can splice the gene into a plasmid. This plasmid will then be transferred to a bacterial culture who's purpose is to clone the plasmid and gene. Once enough genetic material is available, the plasmid will be transferred from the bacterial culture to a mammalian tissue culture (likely a human 293 T Cell) which is void of the Axl protein and the homolog we are studying (DSCAM). The cells will the read the genetic material and express the intended protein. After expression is confirmed, we can then infect the sample with inactive Zika virus and test for binding interactions.

The overall outcome of this project is identify how Zika binds to its mosquito host. However, future research could involve the use of the receptor in mosquitoes as a potential source to develop preventions or treatments of Zika Virus and similar Flaviviruses. Alternatively, we already know that Axl plays many roles in cancer pathologies, thus Axl-homologs could be studied in oncogenic viral infections, or the potential for Flaviviruses to be used as vectors for cancer treatments.