Uncovering the Hidden Defense Mechanisms of Flaviviruses

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Flaviviruses, such as the Zika and Dengue virus, are positive-sense, single-stranded RNA viruses that have caused widespread epidemics and morbidity throughout the world. Little is known about the proliferation mechanisms for these viruses, which in turn has led to the slow development of drugs and vaccines against Flaviviruses. A part of Flaviviruses that has been theorized to have important pathogenic purposes is the 3' untranslated region (UTR), which forms various 3D structures that could potentially protect and aid the virus. This study aims to determine the structure of the dumbbell region of the 3'UTR of multiple Flaviviruses to thereby aid in vaccine and therapeutic development. Two Flaviviruses were studied in this project: the Zika virus and the Dengue virus. Both viruses were expressed as subgenomic RNA via in vitro transcription and then purified. While the Zika viral RNA required native purification, the Dengue virus was more apt for denatured purification. Following purification steps, both viral RNA segments were structurally studied via Small Angle X-ray Scattering (SAXS) analysis. Results from SAXS produced molecular envelopes for these viral genomic segments which showed the presence of a pseudoknot in both viruses. The conservation of a pseudoknot in these Flaviviruses means that the Flavivirus dumbbell most likely serves a role in pathogenesis, translation, and perpetuating the viral lifecycle. Furthermore, the presence of multiple pseudoknots in the viral 3'UTR and their structural characterizations suggest that these types of structures can be targeted for vaccine and therapeutic development in order to effectively counteract these deadly viruses.

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Third Award of $1,000