

The Emerging Pathogens Institute

Presents

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**Developing novel transgenic ribozyme strategies for
suppression of Dengue Fever and other virus
pathogens in mosquito cells and tissues**

**Wednesday, February 20, 2008
4:00pm - Room G-112, HPNP Building**

Dengue Fever Virus is the most prevalent vector borne virus in the world with an estimated 50 million cases per year and 2500 million persons at risk worldwide. During epidemics of dengue, attack rates among susceptible individuals are often as high as 50%, putting entire populations at risk for the disease and causing severe overburdening of the health care systems in affected countries. At present there is no effective vaccine for this disease agent, and the most effective control measures involve insecticidal spraying during epidemic outbreaks. Alternative, possibly long-lasting control measures that operate at the level of the vector, *Aedes aegypti*, are currently being sought, including the possible introduction of transgenic mosquitoes refractory to Dengue Virus transmission. Toward that goal we are exploring transgenic ribozyme approaches for effecting immunity towards Dengue Fever Virus, or potentially other vector-borne viruses, in mosquito tissues. Specifically we are designing and testing hammerhead ribozymes and group I trans-splicing introns as a means of preventing virus establishment in mosquito cell cultures or tissues. In the case of hammerhead ribozymes, we have identified several that reduce virus replication in cell cultures transformed to express these ribozymes by as much as 2 logs. In the case of the group I introns approach, we have designed and tested trans-splicing introns that effectively target the Dengue virus genome in a region of high sequence conservation, allowing us to generate new RNAs in infected tissues that could be used to generate death upon infection, effectively eliminating infected cells from the mosquito and rendering it immune to the virus. We also believe this latter approach may have utility for a number of important human diseases for which *ex-vivo* transgenic approaches are practical.

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