Title: Cationic Amino Acid Transport in Mosquitoes

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Sponsor: U.S. Department of Health and Human Services
CLIA Program (Clinical Laboratory Improvement Amendment)

Summary:
The main goal of this study is the molecular characterization of the cationic amino acid (AA) translocation system in the fat body of the Yellow fever mosquito *Aedes aegypti*, the principle vector for Dengue fever. As an adaption to their unique life style, the fat body tissue of adult mosquitoes house an AA sensing and transport system which is essential for reproduction. The nutritional status of mosquitoes affects this system.

The research will be significant for human health through the identification and characterization of essential and mosquito/insect-specific transporters that present exciting high value targets for the development of insecticidal substances. We hypothesize that a group of transporter proteins, specific for cationic AAs, facilitate the uptake of L-arqinine, L-histidine, and L-lysine after the mosquito takes a blood meal and that inhibition of L-arqinine import will compromise the immune system of the mosquito.

Define the fat body transcriptome of adult female *Aedes aegypti:* We will use a state-of-the art pyrosequencing technique to produce a comprehensive picture of the differences in expression of membrane transporter proteins, including AA transporters, of two groups of mosquitoes with different nutritional status. Through the discovery of new genes and splice variants we will significantly enhance our knowledge of the mosquito fat body transportome.

Analyze the function of fat body cationic AA transporters in mosquito post-eclosion development and determination of their role in mosquito immunity: We have identified nine putative cationic AA transporters that are expressed in the fat body of adult female mosquitoes. We will prove the significance of these transporters in mosquito reproduction and immunity by RNA interference-mediated knockdown and subsequent a) analysis of the level of activation of the nutritional signaling cascade in a fat body organ culture system, b) determination of mosquito fecundity, c) quantification of mosquito lifespan, and d) testing of mosquito susceptibility to *Plasmodium* infection.

Determine the electrochemical properties of fat body cationic AA transporters via heterologous expression in *Xenopus* oocytes: This research will reveal substrate preferences and transport kinetics of the fat body cationic AA transporters. Elucidating these physiological parameters will result in a significant gain in knowledge in the field of AA transport in insects.

We will perform: a) cloning of full-length AA-transporter cDNAs into *Xenopus* expression vectors, b) synthesis and injection of AA-transporter mRNA in *Xenopus* oocytes, c) electrophysiological analysis of substrate specificity and transport kinetics via patch clamp technique.