

## Microbial Based Vector-Borne Disease Management - A Future Prospect

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Vector-borne diseases are major causes of morbidity and mortality worldwide mainly in tropical and subtropical regions. World Health Organization (WHO) has reported more than one billion infections and over one million deaths annually caused due to vector-borne diseases, contributing more than 17% among all infectious diseases. Mosquitoes are one of the most dangerous vectors responsible for transfer of several deadly diseases like malaria, dengue, chikungunya, Japanese encephalitis, filariasis, yellow fever, zika, etc. Mosquitoes require blood for the egg development and during blood meal they ingest pathogens and parasites from infected person/animal and transfer to new host during their subsequent blood meal. Mosquito borne diseases are affecting half of the world population mostly in tropical and subtropical regions by inflicting illness and death, and physical, psychological and monetary losses to mankind.

Vector control is the main strategy in the control of vector borne diseases. Since several decades, various chemical insecticides are being used to control mosquito populations however it have several disadvantages like heavy and prolong use lead to resistance development in vectors, provide short period relief and also affect the human as well as other organisms of environment. Hence, it is essential to focus on eco-friendly alternative control methods to vector borne disease management. Interests in the microbial based control strategies have increased drastically in last several years.

Several bacterial species or their by-products may be used either for control of mosquito population or control the growth and development of pathogens and parasites inside mosquito body. Certain midgut microbiota may increase the immune response against invading pathogens, including dengue, chikungunya, malaria parasites, etc. It may also help in the development of the vector incompetence and also directly involved in various important functions of mosquitoes like food digestion, growth development, hindering of pathogens etc. One of the best example *Wolbachia* mediated cytoplasmic incompatibility (CI) prevent the generation of viable progeny. *Wolbachia* strain also cut the lifespan of *Aedes aegypti* mosquito to an extent that they cannot pass on the dengue virus to the host. *Wolbachia* infected *Aedes* populations are also found resistant to the viruses. The bacterial species *Enterobacter* generate the reactive oxygen species (ROS) which shows anti-Plasmodium activity and block the development of *P. falciparum* in *Anopheles species*. *Serratia marcescens* frequently isolated from mosquito's midgut and secretes some effector molecules which inhibit the sexual and asexual stages of *Plasmodium*. The midgut bacteria potentially influence the fertility and fecundity and pre-oviposition in mosquitoes. Bacterial species of *Bacillus* and *Staphylococcus* affects the fertility of *Culex pipiens*. It has been proved that gut bacteria are essential for normal development of the embryo.

Paratransgenesis is another emerging technique by which mosquito can be changed into a non-transmitting one by reintroducing GM bacterium of mosquito origin in their gut after genetic modification. So that these modified bacteria will secrete anti-disease molecules in the vector gut and do not allow parasite development, thus disease transmission cycle is interrupted. Work is going on such bacterium *Asaia*, a naturally occurring in the mosquito gut of *Anopheles stephensi*. A symbiotic bacteria *Rhodococcus rhodnii* was genetically modified for expression of effectors molecules in the gut of *Rhodnius prolixus* against the parasite *Trypanosoma cruzi*. Apart from *Rhodococcus rhodnii*, several other midgut bacteria such as *Escherichia coli*, *Pantoea agglomerans*, *Asaia sp.*, *Enterobacter cloacae* have been used for the development of Paratransgenesis technique. Recently genus *Enterobacter cloacae* has been considered as a potential candidate for

the paratransgenic to control termites, cotton bollworm and corn borer larvae; *Enterobacter agglomerans*, to control grasshoppers; and *Enterobacter gergoviae*, targeting pink bollworm. Transformed *Enterobacter cloacae* may be also used to control the Leishmania transmission due to secretion of antileishmanial peptides within gut of *Phlebotomus papatasi* sand fly.

Some bacteria have larvicidal properties due to which they may be used as biolarvicides for prevention of larval development. *Lysinibacillus sphaericus* from *Aedes* mosquitoes; contain two potent toxins namely, Mtx and Bin that have larvicidal properties. The bacterial species *Bacillus sphaericus* (*Bs*) and *Bacillus thuringiensis israelensis* (*Bti*) showing potent biolarvicides properties and may be used to control of mosquito larvae.

It has been described that mosquito's microbiota plays important roles in various aspects including immunity of mosquitoes, vector incompetency, fertility and fecundity, food digestion etc. due to which interest in midgut-associated bacteria have increased manifolds in the last few years. Many studies have been done on midgut-associated bacteria however; the diversity, functions, and genetic potential of bacteria associated with mosquitoes are still poorly understood. Prior to development of microbial based defense mechanism, it is essential to find out sound knowledge about bacterial community of mosquitoes. Further understanding of bacterial communities of mosquitoes is essential for better understanding the adaptation and vectorial capacity, as well as development of an ecofriendly, effective, and cheap techniques like paratransgenesis without fear of resistance development in mosquito populations.

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