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Insect microbiomes and insect- specific viruses a new key for understanding the arboviruses diseases?

¿Los microbiomas de insectos y los virus específicos de insectos son una nueva clave para entender las enfermedades de los arbovirus?

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INSECT MICROBIOMES AND INSECT- SPECIFIC VIRUSES A NEW KEY FOR UNDERSTANDING THE ARBOVIRUSES DISEASES?

The ISF can be used as biological control but the unpredictable power of virus mutation is a high risk, are we ready to take this risk to solve biomedical problems? or it is better the use of *Wolbachia* in insects to stop the neglected diseases, despite the problems of mutations that bacteria carries itself?

The last past two decades, there has been a tremendous expansion in the discovery and description of novel insect-specific viruses (ISVs). This has corresponded with progresses in metagenomics analyses for virus revealing and the increasing attention in insect microbiomes. Plentiful of the new ISVs seem to be members of the family *Flaviviridae*, genus *Flavivirus*, and are usual in insect populations in wildlife, with a global geographic circulation.

The gut microbiota of insects exhibits critical functions in the growth, expansion and environmental adaptation to the host insects (1). Currently the insect microbiota and their microbiome, discovered from insects were recognized as major genetic resources for bio-processing industry. Accordingly, the development of insect gut microbiome by means of metagenomics advances will facilitate to discovery innovative biocatalysts and to improve novel strategies for recognizing smart molecules for biotechnological and medical purposes such as vaccines (1).

On the other hand, the expressions “insect-specific” or “insect-restricted” viruses in up-to-date practice usually indicate to viruses that naturally infect hematophagous Diptera and that reproduce in mosquito cells in vitro, but do not replicate in vertebrate cells or infect humans or other mammals. This is differing to the conventional arthropod-borne viruses (arboviruses) that are sustained mainly, or to a significant size, through biological transmission between prone vertebrate hosts by hematophagous arthropods. The arboviruses are dual host (vertebrate and arthropod) viruses, whereas the ISVs seem to comprise merely hematophagous insects (2).

Recent studies corroborate that the ISFs can be separated into two different groups. The first and greatest abundant cluster is the classical ISVs, they similarly show slight or no antigenic correlation with the flavivirus vertebrate pathogens in the phylogenetic trees. The second ISF cluster consists of the arbovirus related insect specific flavivirus, this branch are genetically more related to the mosquito-borne flavivirus pathogens, such as WNV, Ilheus, dengue, Zika, and Japanese encephalitis viruses (2)

In 2016 Hoyos et al (3) detected in Cordoba, Colombia a *Culex flavivirus*, our group recently detected for the first time a novel ISV *Culex flavivirus* from *Culex coronator* (Diptera: Culicidae) from the Caribbean

area in Cordoba, Colombia; the geographical distribution is not exclusive to Colombia, the virus has been found in Brazil, Argentina, Guatemala, Mexico and elsewhere like Japan, China and Asiatic southeast.

On the other hand, where did the ISF originate? It is likely to be originated in the Paleozoic 541-252 million years when the insects appeared before the placental mammals in the Mesozoic (dinosaurs) and Cenozoic when the primates and *Homo sapiens* appeared. Then the viruses and insects evolved each other in parallel to reach a success adaptation and wait million years until vertebrates and mammals including *Homo sapiens* appeared as part of the chain of evolution.

ISFs are not pathogenic for human beings, thus what is the interest of the ISF in Medicine? ISFs are also closely associated antigenically to several of the flavivirus pathogens, like West Nile, Zika, YF and dengue viruses. These relationships increase the opportunity that some of the ISFs could modify arbovirus infection and transmission in a dually infected mosquito host or that they could be useful in initial likely flavivirus vaccines or reagents.

However, there are some problems with ISF; could an ISF mosquito virus emerge sometimes in the future as a human or animal pathogen? This is not a fiction movie. Recent metagenomics reports have revealed that flavivirus-like and other negative-sense RNA viruses are much more frequent and dissimilar in invertebrates than in vertebrates, suggesting that the flavivirus pathogens may have developed from earlier arthropod viruses. Thus it seems possible that an ISF could emerge as a vertebrate pathogen, although at present it is incredible to realize how or when this might occur. However, this is another motive to determine, distinguish, and observe novel ISFs (2).

The ISF can be used as biological control but the unpredictable power of virus mutation is a high risk, are we ready to take this risk to solve biomedical problems? Or it is better the use of the bacteria *Wolbachia* in insects to stop the neglected diseases, despite the problems of mutations that bacteria carries itself?

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