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Host species drive mosquito virome composition

Metatranscriptomic data from more than 2000 mosquitoes of 81 species show that the composition of mosquito viral communities is determined more by host phylogeny than by climate and land use factors, helping to inform arbovirus surveillance.

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Viruses that are transmitted to animals by blood-feeding arthropods like ticks and mosquitoes are a major and increasing threat to humans worldwide. In the past decades we have seen the emergence of Chikungunya and Zika viruses¹ as two new arboviruses. In response to the risk posed by unknown arboviruses, research into the diversity of mosquito viruses in their insect reservoir -- without using *a priori* virus detection approaches -- has led to the discovery of hundreds of viruses in mosquitoes^{2,3,4,5}. Yet our knowledge of the epidemiology and ecology of mosquito-associated viruses remains comparatively very limited, as most of those studies focussed on inventorying viruses. The lack of information on the factors governing the distribution of viruses in mosquitoes hampers the development of surveillance studies adapted to arboviruses that are yet to emerge. Writing in *Nature Ecology & Evolution*, Pan et al.⁶ expand our knowledge of the general ecology of mosquito RNA viral communities through an metatranscriptomic study of thousands of mosquitos from across China.

The authors trapped 2,438 adult mosquitoes from 81 species across 23 Chinese provinces covering around 4000 km in latitude and longitude. They generated a description of the RNA viral community (the 'virome') from each of the collected individuals by metatranscriptomics. This involves high-throughput sequencing of all RNA material present in a sample, including RNA virus genomes and transcribed DNA viruses genetic material. Metatranscriptomic approaches are biased towards the detection of RNA viruses which include the vast majority of arboviruses, with the exception of the African swine fever virus, which is a double-stranded DNA virus. After *de novo* assembly of non-ribosomal RNA reads, the dataset comprised approximately 10 billion short reads. The authors identified viral genetic material among this by similarity searches using hallmark proteins found in a wide range of RNA and DNA viruses.

After discarding diet-content viruses, such as plant viruses, and bacteriophages, the authors focussed on 393 putative virus species likely to infect mosquitoes that were identified based on their phylogenetic relatedness and high abundance and prevalence in samples. The majority of these viruses might belong to new species, including 3 novel potential arboviruses which were detected at low prevalence.

The authors then focussed their ecological analyses on the most abundantly collected mosquito species. They studied virus sharing across mosquito species and geographical distance using networks of similarity and connectivity of viral communities.

They identified several viruses that were likely shared among multiple mosquito species or genera, with very similar viral genome sequences. Overestimation of virus sharing due to cross-contamination during sample processing, which is commonly reported in metatranscriptomic studies⁷, cannot be ruled out. Nevertheless, the results presented seem to robustly imply that there is a spectrum of host specificity of mosquito-infecting viruses. As emerging viruses tend to have a broad host range, a better understanding of the general principles that determinate virus-mosquito specificity would be important for arbovirus prevention⁸.

Furthermore, Pan and colleagues' data reveal that, even when two individual mosquitos were separated by thousands of kilometres, they could share a wide range of virus species with highly similar genomes showing no spatial influence. Virus dispersion across large geographical distances may be caused by recent long-distance spreading of mosquitos, which has been documented for the Asian tiger mosquito (*Aedes albopictus*) and that can be facilitated by winds or human activities, such as trade⁹. However, the geographical circulation timescale of mosquito viruses warrants further study, as the low evolution rate of the mitochondrial *cox1* gene Pan et al. used to speciate mosquitos did not permit this hypothesis to be tested.

The authors finally assessed the relative explanatory power of host phylogeny and environmental factors (here climate and land use characteristics) on virus distribution using generalized linear models. This provided the most impactful result of their study: they found that, although a large number of generalist viruses were shared among mosquito species or even genera, the number of shared viral species decreased sharply with increasing phylogenetic distance. Indeed, host phylogeny had a major effect on virome composition (around 17% of the explained data variance), followed by minor effects of climate (4%) and land-use characteristics (1%) (**Fig. 1**). These results mean that, although some mosquito populations were spatially close, the number of shared viruses between them was primarily determined by the genetic distance of the mosquitos. Consequently, the authors identified mosquito species that contained a higher virus richness and abundance (including *Armigeres subalbatus* and *A. albopictus*), and emphasised that such species could represent hotspots of virus diversity (in congruence with previous studies based on a lower number of individuals^{10,11}), thereby potentially posing a higher risk of arbovirus emergence. Complementarily, although more studies are needed to confirm these results, the authors identified geographical hotspots of viral diversity that may differ among mosquito species, encompassing areas with high mammal richness, relatively low temperatures, and high precipitation.

Interestingly, a considerable portion of mosquito viromic data variance (around 78%) obtained from this study remained unexplained. A relatively low explanatory power of tested variables is the norm in high-dimensional datasets, and could either reflect stochasticity in virus assemblages or unmeasured environmental or host covariates^{12,13}. Immunity has the potential to play a pivotal role in shaping virome composition, and highly competent vector species could show enhanced immunological tolerance to viruses. Moreover, the interplay between mosquito immunity and its microbiome (which includes viruses) has been shown to affect the success of viral infections¹⁴. The results obtained by

Pan et al. in this general ecology study trigger exciting hypotheses for further investigation using immuno-ecological approaches.

We are witnessing the increasing impacts of global climate change and human activities on the expansion of mosquito geographical distribution, which also increases the risk of the emergence of novel arboviruses¹⁵. The study conducted by Pan et al. represents a promising step towards our comprehension of the key factors shaping the distribution of viruses in mosquitoes, which is essential for prioritising policies for surveillance of pathogens in hotspot mosquito species.

Fig. 1 Relative effects of mosquito species and environmental factors on mosquito virome composition. Pan et al.⁶ determined that mosquito host phylogeny had a greater impact on mosquito virome composition than climate (temperature and precipitation) or land use characteristics (ecosystem type, human density and mammal richness), which accounted, respectively, for around 17%, 4% and 1% of the explained variation between analysed mosquito viromes. The authors also identified hotspot mosquito species of viral diversity (represented by the dark red on the left panel).

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Competing interests

The author declares no competing interests.

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