



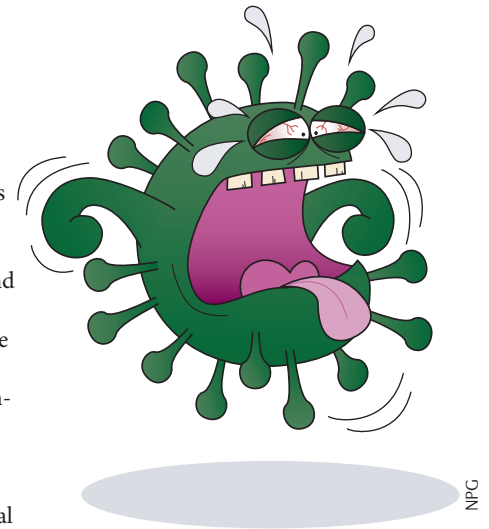
Animal viruses in pieces

The genomes of RNA viruses can be remarkably varied in their molecular composition: single or double strands of RNA that can be positive or negative sense, linear or circular, and segmented or non-segmented. Some segmented RNA viruses package each genome segment into a different virus particle; however, although common for RNA viruses that infect fungi or plants, a multi-component composition has not yet been observed in animal viruses. Now, Ladner *et al.* describe a multi-component RNA virus that infects mosquitoes and report genomic analyses that suggest that other animals, including primates, can also be infected by multicomponent RNA viruses.

The authors isolated a novel RNA virus, which they named Guaico Culex virus (GCXV), from *Culex* spp. mosquitoes and sequenced the genomes of six isolates from locations in Trinidad, Peru and Panama. All six isolates had segmented genomes, with either four or five segments. Genetic experiments showed that the fifth segment that was present in some of the isolates was dispensable for both infection and replication. Importantly, an assay that measures packaging demonstrated that GCXV is a multicomponent virus, which is the first such report for an animal virus. The uneven distribution of virus segments between cells was also consistent with a multicomponent composition of GCXV. Genome

analyses showed that GCXV is a Jingmenvirus (Jingmenviruses are recently described flavivirus-like viruses), and that the two largest segments of GCXV encode proteins that exhibit homology to Flavivirus NS5 (an RNA-dependent RNA polymerase) and NS3 (a helicase and serine protease), respectively. The other two ubiquitous segments were each composed of three ORFs that are suspected to encode capsid components, partly based on evidence from proteogenomic experiments that assayed the protein content of GCXV particles. Finally, biochemical analyses showed that GCXV is an enveloped virus, similarly to flaviviruses, and is thus the first known virus to be composed of separate enveloped packages.

Although the host range of GCXV seems to be restricted to mosquitoes, several recent studies have isolated Jingmenviruses from a range of animal hosts, and Ladner *et al.* report the presence of a Jingmenvirus in primates. Genome segmentation is a universal feature of all sequenced Jingmenviruses, although multicomponent viruses had not previously been reported for this family. To examine the origins of Jingmenviruses, the authors performed phylogenetic analyses of NS3 and NS5 homologues, which suggested that Jingmenviruses form a monophyletic group that is a sister clade to flaviviruses, which are non-segmented; this suggests that



segmentation is an innovation that has occurred in the Jingmenvirus lineage, although the authors could not rule out an alternative evolutionary scenario in which a segmented common ancestor became non-segmented in the *Flaviviridae* lineage. The authors propose that the multicomponent composition of GCXV is likely to be shared by other Jingmenviruses, although confirmation of this hypothesis will require experimental investigation. The authors also note that their findings raise interesting questions regarding the fitness benefits and costs of a segmented genome and multicomponent composition.

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ORIGINAL ARTICLE Ladner, J. T. *et al.*
A multicomponent animal virus isolated from
mosquitoes. *Cell Host Microbe* <http://dx.doi.org/10.1016/j.chom.2016.07.011> (2016)

“ [GCXV is] ... the first known virus to be composed of separate enveloped packages ”