

## Preview

# Phylogenomic analyses unraveled the evolution of viral tolerance in bats

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Bats host a range of viruses, exhibiting a coevolution process with many virus genera and a special capacity for viral tolerance. Foley et al.<sup>1</sup> performed phylogenomic analyses for 60 bat species, finding that swarming behavior might facilitate cross-species introgression and the spread of anti-virus immunity gene loci across species.

Bats are the only flying mammals and the longest-lived mammalian species relative to their body size. In addition, bats are also the unique hosts of many highly pathogenic viruses without presenting clinical disease.<sup>2</sup> Previous studies have suggested that bats have adapted to the high-energy consumption required for flight activity by evolving an improved DNA damage repair system, which may also extend their lifespan and improve their immune system by enhancing anti-virus defense and reducing inflammation response to the virus infection.<sup>3-5</sup> The observed viral resistance makes bats natural vectors for interspecific virus transmission,<sup>6</sup> including, it is postulated, the coronavirus causing COVID-19.

Over the past decade, studies have investigated the unique immune system in bats and identified molecular details of how bats balance hosting pathogens versus self-protection from viral infections.<sup>2</sup> This unique immune adaptation has been hypothesized to be involved in bat/virus coevolution, as suggested by studies indicating that bats have evolved a co-phylogenetic relationship with many virus families after the diversification of most extant bat species.<sup>7</sup> Yet, there has been limited research investigating how the diversity of immune genes in bats evolved in the face of the challenge of viral infection. This task has been constrained by the lack of a consensus phylogeny for the bat lineages that have experienced rapid radiation, often involving incomplete lineage sorting and hybridization.

In this issue of *Cell Genomics*, Foley et al. conducted a phylogenomic study on 60 bat genomes from *Myotis*, the

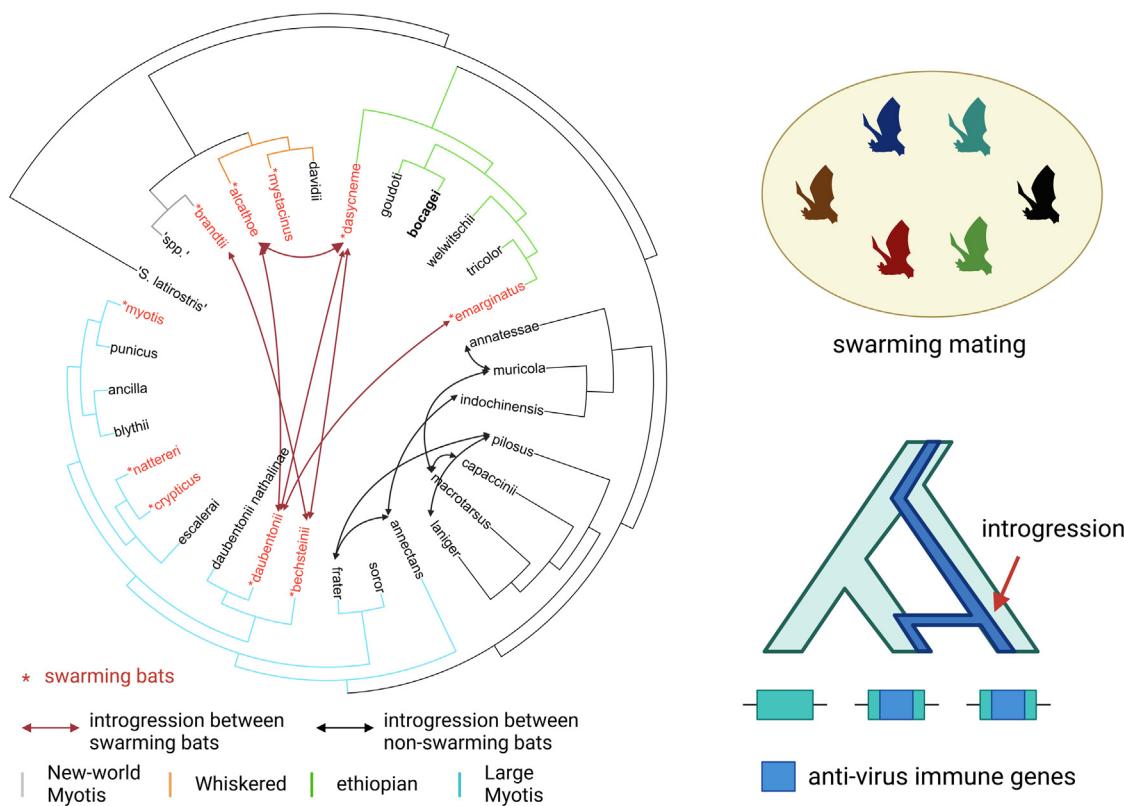
most widespread and species-rich bat genus, examining how hybridization and the subsequent genomic introgression affected the speciation process of the *Myotis* genus and contributed to the evolution of anti-viral immune genes across species (Figure 1).<sup>1</sup> The phylogenetic analysis of *Myotis* species used full-genome data and found a high level of phylogenetic incongruence between the nuclear and mitochondrial topologies. To test whether the post-speciation gene flow might have contributed to this phylogenetic contradiction, the authors implemented a recombination-aware phylogenetic approach for individual gene loci. To achieve this, they inferred the recombination landscape in *M. myotis*, which showed the highest recombination rates and gene richness in the small chromosomes of the *Myotis* genome, a karyotypic feature similar to that found in birds and some other reptiles.<sup>8,9</sup> Then, by computing individual gene trees for 36,264 loci covering 91% of the genome, they discovered widespread discordance between locus trees and asymmetric topological frequencies in the whiskered bat and most *Myotis* clades, a strong signal for the presence of gene flow. In some nodes, over 50% of the genomic region presented the introgression signature. They found that loci supporting the species tree were most clustered in the pericentromeric regions of the three macrochromosomes and the X chromosome—which had the lowest observed recombination rate. D-statistics showed that some clades, such as Muricola, Large myotis, Asian, and Oriental clades, show the most frequent introgression.

Considering the high genetic distance between the investigated species, these results suggest that ancient interspecific hybridization involving multiple clades has depleted the species tree across the macrochromosomes and almost completely replaced the speciation phylogenetic signal with an introgression signature.

Such a high frequency of gene flow across the genomes involving multiple clades is exceptional compared to other mammals. It leads one to wonder about the underlying ecological drivers of the surveyed admixture. A previous study identified widespread promiscuous mating among swarming *Myotis* species.<sup>10</sup> Foley et al. examined whether there was a link between introgression and annual swarming behavior. Indeed, high levels of introgression have been observed in swarming species, from both the same clade and different clades, particularly in the Ethiopian clade. In contrast, no introgression was detected in *M. bocagii*, a species from the same clade that does not exhibit swarming behavior.<sup>1</sup>

A large assemblage of swarming bats during mating also increases the chances of virus transmission, which may pose a significant challenge to the hosts. Foley et al. hypothesized that viral tolerance in *Myotis* might be enhanced by gene flow on immune gene loci between species at swarming sites. Comparing the expression data from the virus challenge experiment in *M. daubentonii*, they showed that genes corresponding to virus infection were enriched in microchromosomes and located in the most frequently introgressed regions. Remarkably, some





**Figure 1. Phylogenetic analyses revealed a high-frequency interspecific introgression among bat species from the *Myotis* genus**

This exceptionally high occurrence rate of cross-species hybridization might be promoted by the promiscuous mating during the annual assemblage in the swarming season. A high frequency of gene flow following the introgression might have led to the spread of anti-virus immune loci between swarming bat species and contributed to shape the evolution of unique immunity system in swarming bats.

introgressed genes, such as *OAS1*, *OAS3*, and *OASL*, exhibited up to a 6-fold change in response to viral challenge, implying that the alterations in immune gene expression induced by hybridization may be adaptive. In addition, some of the large introgressed haplotypes that have been maintained over a long time also include genes involved in regulating adaptive and innate immune systems.

Interspecific hybridization provides a crucial source of novel genetic variation that drives species diversification and local adaptation. By performing a phylogenomic analyses for several *Myotis* species, Foley et al. reported data supporting that annual swarming may have driven the frequent adaptive gene introgression in immune loci and thus may contribute to the evolution of viral resistance across bat species. The phylogenetic relationships identified and the pattern of genetic introgression produced in this study provide a valuable reference for further investigation of the bat/virus co-evolution and

how introgressed genes shape host defense systems. This may be how bats evolved a unique ability to serve as ideal reservoir hosts for many viruses. Further investigation into the immune systems of *Myotis* species could help us understand the mechanisms bats use to balance virus defense against tolerance and the origin of genes crucial to their longevity and resistance to cancer.

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#### DECLARATION OF INTERESTS

The authors declare no competing interests.

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