

# Bat genome provides new insights into the evolution of flight and immunity

December 20 2012

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BGI today announces the online publication in *Science* of the latest findings through genomic analysis of two distantly related bat species, the Black flying fox (*Pteropus alecto*) and David's Myotis (*Myotis davidii*). The work here provides new insight into the genetic mechanisms underlying the evolution of flight and immunity of bats, and also opens the way for addressing major gaps into understanding of bat biology and provides new directions for future research.

[Bats](#) are often characterized as creepy, disease-carrying, and even blood-sucking animals as often depicted in horror movies. The centuries of myths and misinformation make them one of the least studied and most misunderstood animals. However, in recent years, more and more scientists have been irresistibly attracted to their specific traits, such as the capacity for sustained flight, and the feature that bats could coexist

with some of the world's most deadly viruses, such as Nipah, Hendra, [Ebola](#) and SARS.

To identify [genetic changes](#) associated with the development of bat-specific traits, researchers from BGI, CSIRO Australian Animal Health Laboratory, and other institutes, performed whole genome sequencing and [comparative analysis](#) of two different wild-caught bats. They found the two bat genomes were smaller in size than other mammals, but the number of genes was similar to others. This team work yields a valuable genomic resource for unveiling some of the biological mysteries of bats.

The origin of bats has been one of the most discussed topics by scientists in recent years. Until the late 1980s, most researchers assumed that the order Chiroptera was monophyletic and that all bats shared a common flying ancestor. However, another commonly cited hypothesis suggests that megachiropterans (members of the family Pteropodidae) are more closely related to dermopterans (flying [lemurs](#)) and primates than to echolocating microchiropteran bats.

Although the true origin of bats remains unresolved to date, the whole-genome sequencing analysis in this study confirmed that bats do share a common ancestor. Our study also indicated that bats are a member of Pegasoferae, and it diverged from the Equus (horse) lineage approximately 88 million years ago (MYA). Interestingly, the phylogenetic reconstruction with mitochondrial DNA resulted in bats occupying an outlying position in Laurasiatheria. The incongruence between nuclear and mitochondrial trees may reflect rapid evolution of the mitochondrial [genome](#) of the bat ancestor during the evolution of flight.

To identify mechanisms that facilitated the origin of flight in bats, researchers investigated the genes involved in detection and repair of genetic damage. An unexpected concentration of positively selected

genes was found in the DNA damage checkpoint/DNA repair pathway of the bat ancestor, such as the gene ATM, DNA-PKc, RAD50, KU80, and MDM2. They proposed that the changes may be directly related to minimizing/repairing the negative effects of reactive oxygen species (ROS) generated as a consequence of flight. In addition, they also found unique changes in other flight-related genes in the bat ancestor, such as the gene COL3A1, involved in skin elasticity, and CACNA2D1, which has a role in muscle contraction.

Bats have a strong ability to control a variety of deadly microorganisms. When examining the genes associated with the innate immune system of bats, the team identified positively selected genes including c-REL, a member of the NF- $\kappa$ B family of transcription factors. In addition to diverse roles in innate and adaptive immunity, c-REL plays a role in the DNA damage response that has an important function in host defense and is a known target for virus interaction. Researchers inferred that the immune system of bats likely has been influenced by the changes in DNA damage response mechanisms during selection for flight.

Natural Killer (NK) cells provide the first line of defence against pathogenic microorganism and included two families of NK cell receptors, killer-cell immunoglobulin-like receptors (KIRs) and killer cell lectin-like receptors (KLRs, also known as Ly49 receptors). In this study, researchers found KLRs and KIRs were entirely absent in the Black [flying fox](#) and reduced to a single Ly49 pseudogene in David's Myotis. Moreover, KIR-like receptors identified in other species were also absent from both Black flying fox and David's Myotis genomes. According to the findings, researchers suggested that bat NK cells use a novel class of receptors to recognize classical MHC- I molecules, one of two primary classes of major histocompatibility complex (MHC) molecules.

Differences between the Black flying fox and David's Myotis also exist

in the aspects of feeding habit, hibernation and echolocation, among others. In the study, researchers found the digestive enzyme RNASE4 in David's Myotis may be involved in virus resistance, but the gene has acquired a frame-shift mutation in Black flying fox. This finding also relates to the fact that David's Myotis is insectivorous, and Black flying fox feeds on fruits, flowers and nectar. In addition, they observed six candidate genes related to hibernation showing positive selection in David's Myotis relative to non-hibernators, and seven genes related with echolocation had significantly higher dN/dS in the echolocating David's Myotis branch relative to non-echolocating branches.

"The rapid development of genomics greatly enhances our understanding to the mysteries of evolutionary biology, such as the origin, differentiation, and species diversity." said, Guojie Zhang, Project Manager from BGI, "These wonderfully diverse bats are in a special position in the evolutionary processes, and have some fascinating biological characteristics, including sustained flight, hibernation, echolocation, among others. Genomics is one of the approaches to conduct those studies. I believe the data generated in the study will lay a solid foundation for the further functional research. The genomic comparative analysis also will provide important tools for further understanding the autoimmune system of bats and the relevant defense mechanisms against viral infections."

**More information:** "Comparative Analysis of Bat Genomes Provides Insight into the Evolution of Flight and Immunity," by G. Zhang et al. *Science*, 2012.

Provided by BGI Shenzhen

Citation: Bat genome provides new insights into the evolution of flight and immunity (2012,

December 20) retrieved 24 April 2024 from <https://phys.org/news/2012-12-genome-insights-evolution-flight-immunity.html>

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