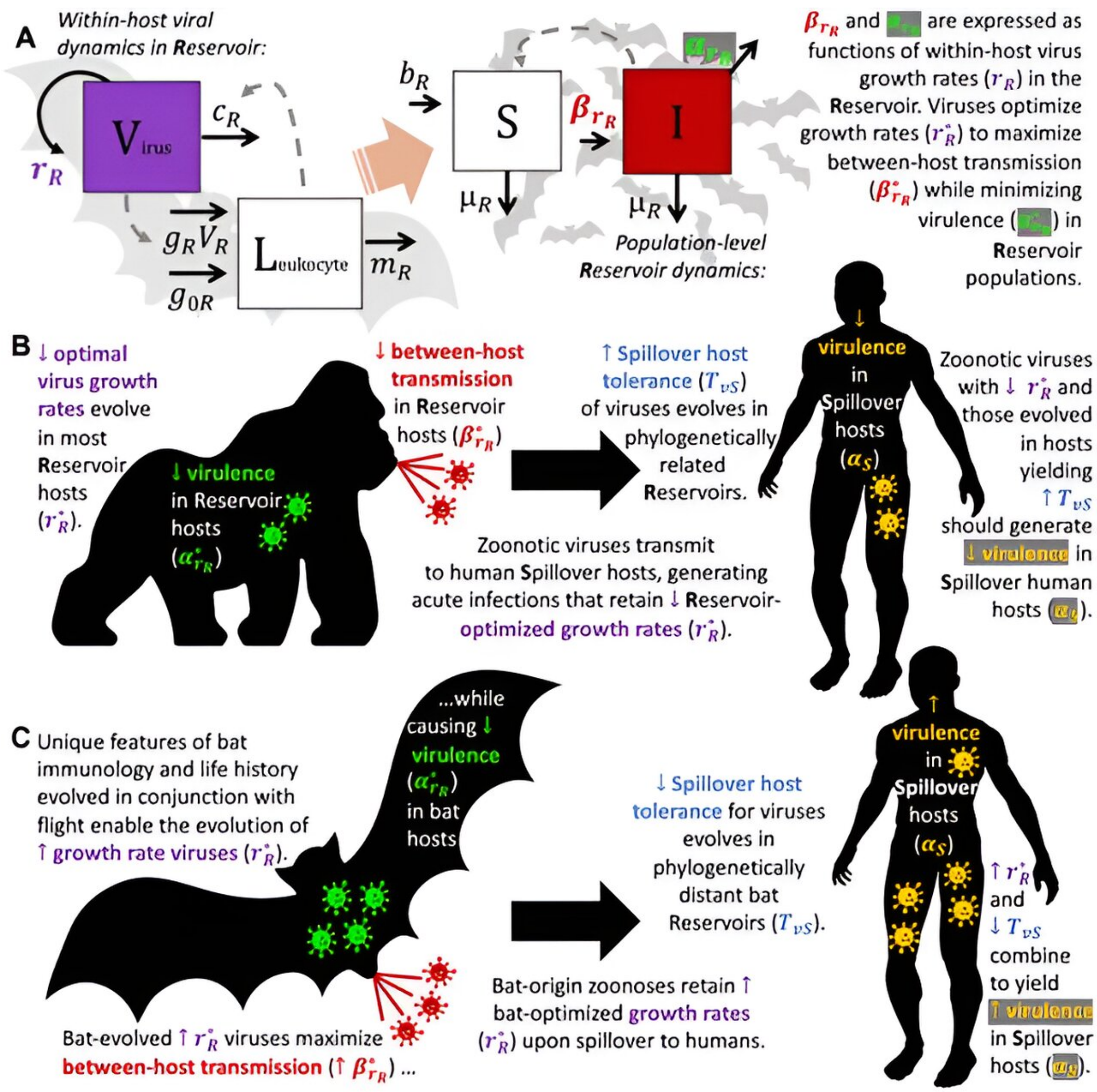
How studying bat viruses can help prevent zoonotic disease

July 3 2024, by Madeline Barron



Work from the Brook Lab suggests that the immunology and life history of a reservoir host shapes the evolution of virulence in zoonotic viruses. Credit: Brook C., et al./Plos Biology, 2023. CC Attribution 4.0 International license

Bats have become the poster child of emerging zoonotic disease. The creatures harbor a vast array of viruses—some of which cause deadly diseases in humans—yet they rarely get sick themselves.

What makes bats such viable viral hosts? Scientists are digging into the question, using what they learn to inform strategies for preventing spillover and mitigating disease.

If you give a bat a virus, it doesn't get sick?

Bats make pretty great hosts for viruses. These mammals live cozily in colonies, which facilitates easy transmission, and they can survive high viral titers in their tissues and sera without showing signs of clinical disease.

According to Cara Brook, Ph.D., an assistant professor in the Department of Ecology and Evolution at the University of Chicago, the latter feature is notable, in part, because of its connection with another batty characteristic: the ability to fly.

"Flight is the most physiologically [and] metabolically costly form of terrestrial locomotion," Brook said during a scientific session at ASM Microbe 2024. "It appears that bats compensate for the metabolic demands of flight through a number of unique molecular adaptations," including dampened recognition of cellular damage, a unique anti-inflammatory phenotype and upregulated DNA damage repair pathways.

While these bat adaptations evolved for flight, "they have cascading consequences on [bats'] longevity, their resilience and resistance to cancers, as well as their resistance and tolerance to virus infection," Brook explained.

The same pathways that tamp down the negative effects of flight also dampen the impacts of viral infection and facilitate greater viral tolerance. This heightened tolerance is balanced with enhanced antiviral immune responses, which together make bats exceptionally good at coexisting with viruses.

And bats host thousands of different viruses, spanning hundreds of bat species. Many of these viruses belong to families with members that cause human disease, including Paramyoxiviridae (Nipah virus), Filoviridae (Marburg virus), Rhabdoviridae (rabies virus) and Coronaviridae (SARS-like viruses).

It is this cocktail of viruses found within bats, and their links with known zoonoses, that have placed them under the spotlight of scientific inquiry. New viruses related to existing threats are routinely detected in the soaring mammals. As a result, bats are popularly viewed as powder kegs of viruses with the capacity to wreak havoc in human populations.

How concerning are bats, really?

Researchers debate whether bats really harbor a particularly vast and dastardly collection of viral threats; some argue this perception is a product of confirmation biases. It's a numbers game: if one looks for many new viruses in many bats, they will, on average, find many new viruses in bats—and the more one finds, the more one will look.

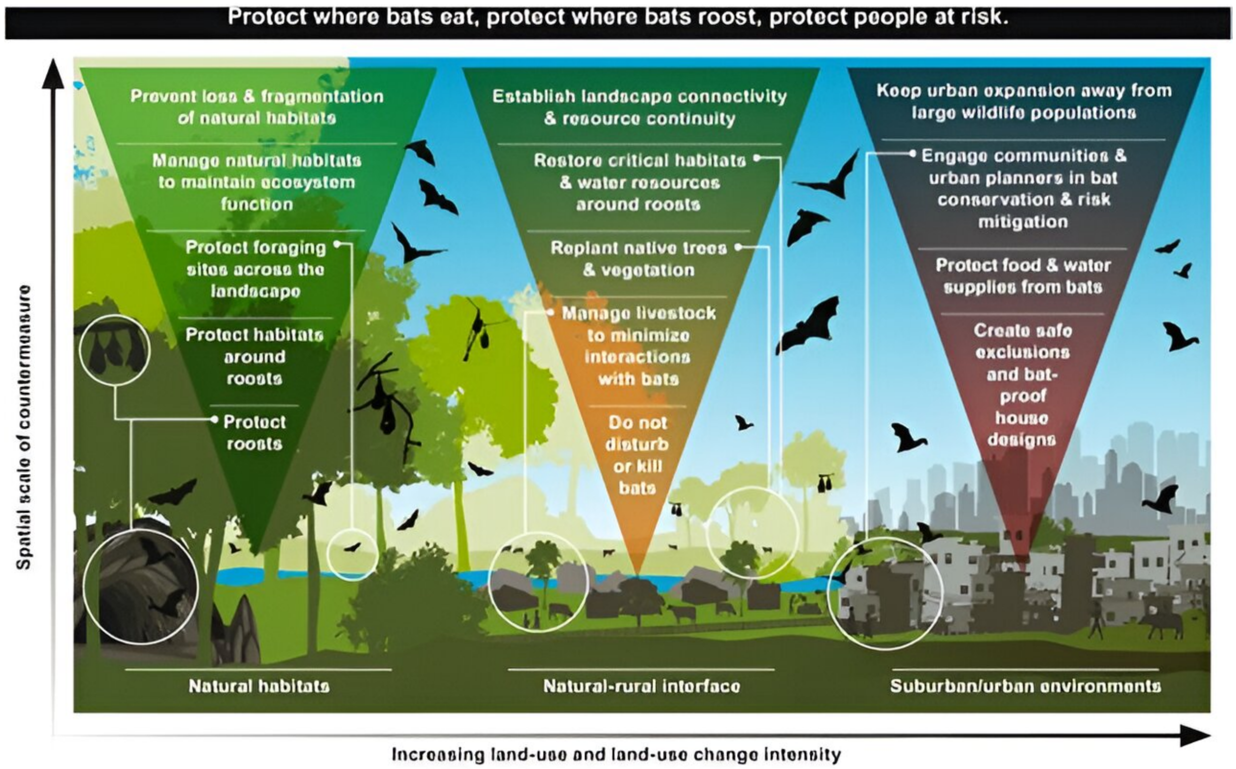
One study reported that the number of human-infecting viruses in bats (or any animal) is proportional to the number of species that exist (more than 1,400). That is, bats aren't any more virus-rich than would be expected based on how many of them there are.

Yet, work from Brook's lab suggests bats are, in fact, special, viral reservoirs deserving of attention. Her group discovered that, compared to other mammalian and avian reservoirs, bats harbor the most virulent zoonotic viruses (i.e., have capacity to cause severe disease within humans) with the highest case fatality rates (they're particularly deadly). Why might this be? Brook circled back to the bat immune system.

Bat defenses select for viruses with high growth rates

It appears that the antiviral properties of bats are likely to select for high growth rate viruses that we expect would be pathogenic upon spillover to non-bat hosts," she said. During replication in a reservoir host, viruses must grow at adequate levels to facilitate transmission while minimizing virulence (i.e., if their reservoir host dies, they can't spread).

Bats' ability to tolerate high viral loads, coupled with their anti-inflammatory phenotype, means that viruses can replicate at high densities to maximize transmission between animals. In less tolerant hosts, these supercharged viruses may trigger extensive damage—indeed, modeling and empirical data suggest that virulence in humans partly depends on a virus's reservoir-adapted growth rate.



Bats have a number of important ecosystem functions; protecting them requires small and large-scale interventions across natural and urban environments. Credit: Plowright, R.K., et al./Nature Communications, 2024. CC Attribution 4.0 International license.

Bat-borne viruses are less likely to establish sustained human transmission

This isn't the whole story, though. "It's important to note that [these findings don't] account for the probability of zoonotic spillover, which we know is inversely related to phylogenetic distance," Brook said.

While bat-borne viruses may be virulent, they are less likely to establish sustained human-to-human transmission; those viruses hail from reservoir host groups closely related to people (e.g., primates). This is not trivial, as viruses with pandemic-causing potential are often associated with high human transmissibility.

In other words, hosts with a shorter phylogenetic distance from humans contain viruses with lower morbidity and mortality, but a higher potential for endemic establishment in human populations; the opposite is true for bat-borne viruses. Moreover, whether a virus causes a high death burden in humans depends not on the type of animal it came from, but rather a compilation of viral traits, the animal host population and its interactions with humans.

Studying bat-borne viruses informs spillover prevention

The image that emerges from these data is that a complex mix of factors dictate a virus' zoonotic risk, with roots in immunology, ecology and epidemiology. Humans have the most active role in boosting the chances of spillover, due to activities and impacts like deforestation and climate change that facilitate greater human-wildlife interaction.

If a virus is detected in bats, it doesn't automatically spell doom for the human population. There is often an intermediate animal host (e.g., dogs, pigs, horses) where a bat-borne virus may hang out and evolve before hopping into people. This chance of secondary spillover is a paramount concern, and highlights that there are other animals that require attention in the fight against zoonotic disease.

Nevertheless, Brook emphasized the value of understanding the transmission and persistence of bat-borne viruses, as doing so can identify potential points of early intervention to prevent spillover from happening in the first place.

Over the last decade, she and her collaborators have investigated viruses in three endemic species of fruit bats in Madagascar. By tracking bats and analyzing samples collected from the creatures over time, the scientists have gained insights into how viruses move through the population, and how bats respond.

For instance, they've illustrated that there are four clades of Henipavirus (a genus whose most famous members are Nipah and Hendra viruses) persisting at low levels in the fruit bats. The animals develop lifelong immunity to the viruses, but short-term antibody responses, suggesting there are other (e.g., T cell) immune mechanisms at play.

Additionally, through their virus discovery efforts, Brook and her colleagues have uncovered new henipaviruses that do not bind the same cell receptors as known zoonoses, like Nipah virus. She highlighted that delineating the receptors these viruses do bind would help determine their potential tropism.

The research crew's goal is to use these collective findings to develop a multivalent vaccine to potentially eradicate henipaviral infections in bats prior to zoonotic emergence.

"Our primary interest in understanding the transmission dynamics that maintain these viruses in wild bats links to our interest in identifying opportunities for interventions to prevent spillover to human populations," Brook said, reiterating, however, that "zoonosis is a multi-layered challenge, scaling from the cell to the ecosystem."

Save the bats

Understanding where bats fit on the spectrum of zoonotic risk is important because bats are dying. It is estimated that over half of bat species in North America alone are at risk of severe population decline in the next 15 years due to scourges like white nose syndrome and climate change. Framing bats through a lens of fear, and the belief that they are inherently harmful to humans, undermines efforts to protect them.

And they're worth protecting, not least because of their ecosystem value (e.g., pollination, controlling insect populations).

Scientists can learn a lot from bats, including how to combat the very viruses that make them a concern. Delving into the mechanisms of the bat immune system—the particularities of which differ among the vast number of bat species—could be useful for understanding the transmission and evolution of possible viral threats they harbor, as well as how we can better tackle them.

Bats have something to offer in other research areas, too, like in the fields of cancer and aging (when adjusted for body size, 18 of the 19 mammal species that are longer-lived than humans are bats).

When all is said and done, the creatures are more than the viruses they host—they also hold clues to advance and maintain human health.

Provided by American Society for Microbiology