Why bats don't get sick from the deadly diseases they carry

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Black-headed flying fox (right) among a grey-headed colony. Credit: CSIRO/Michelle Baker, Author provided

Bats are a natural host for more than 100 viruses, some of which are lethal to people. These include Middle Eastern Respiratory Syndrome (MERS), Ebola and Hendra virus. These viruses are among the most dangerous pathogens to humans and yet an infected bat does not get sick or show signs of disease from these viruses.

The recent Ebola outbreak in West Africa showed the devastating impact such diseases can have on human populations.

As treatments in the form of therapeutics or vaccines rarely exist for emerging diseases, future outbreaks of disease have the potential to result in similar outcomes.

Understanding disease emergence from wildlife and the mechanisms responsible for the control of pathogens in their natural hosts provides a chance to design new treatments for human disease.

The path to discovery

Until recently, bats were among the least studied groups of mammals, particularly in regard to their immune responses.

But even early studies of virus-infected bats provided clues that there may be differences in the immune responses of bats. It was observed that some bats were capable of clearing viral infection in the absence of an antibody response.

Antibodies are one of the hallmarks of the immune response and allow the host to respond more rapidly to subsequent infection when the same pathogen invades the body. The absence of a detectable antibody response within the bat was striking and drew our attention to the earliest stages of the immune response, called the innate immune system.

The recent sequencing of the first bat genome provided some of the first clues that the innate immune system may be key to the ability of bats to control viral infection. There is intriguing evidence for unique changes in innate immune genes associated with the evolution of flight, and bats are the only mammal capable of sustained flight.

Flight is energetically expensive and results in the production of oxygen radicals. In the research we speculated that bats have made changes to their DNA repair pathways to deal with the toxic oxygen radicals.

A number of innate immune genes intersect with the DNA repair pathways. These genes have also undergone changes, so it appears that the evolution of flight may have had inadvertent consequences for the immune system.

Bat super immunity

In humans and other vertebrates, infection with viruses triggers the induction of special proteins called interferon.

This is one of the first lines of defence following infection. It starts the induction of a variety of genes, known as interferon-stimulated genes. These genes play specific roles in restricting viral replication in infected and neighbouring cells.

Humans and other mammals have a large family of interferons, including multiple interferon-alpha genes and a single interferon-beta gene. People have 17 type I interferons, including 13 interferon-alpha genes.

Analysis published today of the interferon region of the Australian black flying fox reveals that bats have fewer interferon genes than any other mammal sequenced to date. They have only ten interferon genes, three of which are interferon-alpha genes.

This is surprising given that bats have this unique ability to control viral infections that are lethal in people and yet they can do this with a lower number of interferons.

Although interferons are essential for clearing infection, their expression is also tightly regulated. This is to avoid over-activation of the immune system, which can have negative consequences for the host.

The expression of interferon-alpha and interferon-beta proteins, which account for the majority of the antiviral response generated following viral infection, is normally undetectable in the absence of infection. It is rapidly induced following detection of a pathogen.

Yet we again see a difference in bats. The three interferon-alpha genes are continuously expressed in bat tissues and cells in the absence of any detectable pathogen. Bats appear to use fewer interferon-alpha genes to efficiently perform the functions of as many as 13 interferon-alpha genes in other species. And they have a system that is constantly ready to respond to infection.

Continual activation of the interferon response in other species can lead to over-activation of the immune response. This frequently contributes to the detrimental effects associated with viral infection, including tissue damage. In contrast, bats appear able to tolerate constant interferon activation and are continually primed for viral infection.

The bat approach in others

We are familiar with the important role bats play in the ecosystem as pollinators and insect controllers. They are now demonstrating their worth in potentially helping to protect people from infectious diseases.

The ability of bats to tolerate a constant level of interferon expression is poorly understood at the moment. But the identification of the unique expression pattern of interferons in bats is a first step in identifying new ways of controlling viruses in humans and other species.

If we can redirect other species' immune responses to behave in a similar manner to that of bats, then the high death rate associated with diseases such as Ebola could be a thing of the past.

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