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Truth about Bats: Transmit so Many Viruses

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Commentary

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A fifth of all current mammal species are bats. And that is incredible, because they help us in many ways. Like, they pollinate many plants; help regenerate forests and control pests, and their excrement is a pretty good fertilizer. Plus, they are really cool. Some of them can sense magnetic fields or use sound to find their food, and of course there is one thing they all have in common: they can really fly. They are the only mammals capable of motorized flight without the aid of machines. But they are also somewhat notorious for something else: being germ flying sacks. You may have noticed that part, with all the talk about zoonotic diseases that has been going on lately. Those are diseases that are transmitted to humans from other animals. And while bats aren't to blame for everything, they have played a role in the transmission of at least 11 viruses, 12 and counting iSARS-CoV-2. These diseases are not the fault of bats, of course. Still, bats in particular carry many viruses. And that's because they have a unique immune system. This means we can learn a lot about these pathogens and their effects by studying bats.

In fact, bat immune systems are so special that what we learn from them may one day help us treat a wide variety of conditions, from cancer to diabetes. And the kick is: bats probably have strange immune systems because they fly! Unlike gliding, flapping flight requires a large amount of energy. So bats have developed ways to boost their cell fuel production at high speed, primarily by putting mitochondria in overdrive. Those are special compartments within cells that convert food into fuel. But there is a catch! When mitochondria convert nutrients into energy, they also create by-products called reactive oxygen species. Basically, the mitochondrial exhaust gases, in the form of truly reactive oxygen-containing molecules. Now these are not all bad but they can also do a lot of damage. They can weaken cell membranes, mess with proteins, and even break DNA, which is why they play an important role in diseases like cancer and arthritis. Cells can try to keep them in check with antioxidants, compounds that essentially neutralize these overly anxious molecules. But those can only do so much, and when balance is lost, cells experience a condition called oxidative stress. This is when most of the DNA damage occurs.

But since bats don't get super cancer immediately after their first flight, researchers have long suspected that they've developed ways to protect themselves from all this flight-related damage. And a few years ago, genetic studies found mutations that increase your ability to detect and repair damaged DNA. Essentially, they have also turbocharged the mechanisms that prevent genetically damaged cells from replicating. Which may also explain why they don't seem to have cancer very often? So bats produce tons of energy without damaging their cells. DNA damage can also be a sign of a viral infection, because viruses need to hijack the cell's genetic machinery to reproduce, and that process generally involves a strategic shutdown.

So naturally, damage to DNA triggers an immune response: inflammation. Basically, when cells detect DNA damage or other signs of infection, they chemically call white blood cells. These cells kill and destroy pathogens using a variety of genetic and chemical tools, and also help control how inflammation develops, for example by introducing additional white blood cells or by changing certain d between them from the elimination of germs to the repair of tissues. Once the invasion is over this immediate or acute inflammatory response helps to get rid of invaders and promotes healing. But remember, thanks to their supercharged mitochondria, bat cells suffer constant damage to DNA. They can repair this damage with these advanced DNA repair tools. But damaged DNA must still ignite an immune flame before it can be repaired.

Then bats would experience super swelling all the time! And prolonged, chronic, and systemic inflammation is not that good. White blood cells and the processes they set in motion can be really destructive to the body's own tissues. In short, too much inflammation can lead to organ failure and even death. Then flight should be a death sentence. Except, bats have also developed some ingenious ways to reduce inflammation. On the one hand, they buffer the activity of STING proteins. These proteins are one of the ways that mammalian cells trigger an inflammatory response when a virus is detected. Furthermore, a genetic analysis of multiple bat genomes showed that they are the only mammals that are completely gene less for PYHIN proteins, another set of inflammation-triggering sensors activated by damaged DNA.

And those are only part of the story. It will still be a while before we fully understand how bats prevent or buffer inflammation in their bodies, because it seems that every time they look, researchers continue to find more of these adaptations. But we know that inflammation is one of the great ways the immune system defends itself against intruders. So doesn't it leave you open to all kinds of real pathogens? And the answer is yes! In the early i21st century, scientists discovered that bats act as a reservoir for many viruses that are extremely dangerous to humans. This includes filoviruses, which cause hemorrhagic fevers, such as Marburg or Ebola. Also, henipaviruses like Hendra and Nipah, which can cause fatal brain infections ... and, of course, coronaviruses, like SARS, MERS, and (most likely) the notorious new coronavirus that started the iCOVID-19 epidemic and there is growing evidence that bats were involved in transmitting these diseases to humans, either directly or indirectly, such as by infecting farm animals.

Bats are also suspected to have given us other diseases in the past, such as mumps, measles, and hepatitis B! But here comes another magical thing about bats: Even though they are widely infected with notoriously deadly viruses, they don't really seem to get sick of them. As for how is that possible? Well, we still have more questions than answers, but researchers have uncovered some evolutionary quirks about bats' immune systems that help make that happen. In part, this is because active viral infections in bats tend to be short-lived, thanks to their hyper vigilant interferon production systems.

Remember how we said DNA damage is a sign of infection? This is because viruses try to reprogram cells to create copies of them. But the cells are not sitting ducks during this process. In addition to asking for help, which is all that little inflammation we discussed, cells have an internal defense mechanism. They can produce a protein called interferon alpha, which activates genetic and chemical tools that reduce the virus's ability to multiply and spread. Every other mammal we know of activates its interferon system when an infection occurs. But genomic studies suggest that bat cells always have their interferon alpha genes turned ion! All mammalian cells contain an enzyme called ribonuclease L, which, when activated, cuts viral RNA to stop the spread of a pathogen. But, in us and in most other mammals, activating this enzyme requires a complex chain of steps, so it is not super-fast. But bats, on the other hand, can directly activate it with interferons, dramatically accelerating infection containment. Scientists also think that this rapid activation of ribonuclease L helps bats overcome viruses that have evolved to inhibit the enzyme before it can be activated; something that HIV does in humans, for example. Basically, when bats get viruses, they can get rid of them quickly ... for the most part. They can still be victims of at least some, like the rabies virus. And even rapid suppression of a virus can mean that it remains in a group of bats. Bats tend to snuggle together when perching. Furthermore, they fly in the same areas as bats from other colonies, and constantly spray mucus and saliva everywhere when they echolocate. So there is a good chance that, during that window, when a bat has a virus that is actively replicating, it will spread it to another bat. That means that even if each bat only harbors one virus for a short time, it can remain in the population. Instead, research suggests that the viruses themselves have figured out how to lie dormant and undiscovered, such as in the lungs, spleens, or intestines of bats. And then, when the bat becomes stressed, like when it is awakened from hibernation, that stress temporarily cushions its antivirus systems, allowing hidden viruses to emerge. This leads to another period of increased viral replication and elimination. Again, the bat can transfer the infection to other animals.

Still, even when a virus is replicating and getting rid of, bats generally don't look sick, not like a person with the same virus. And that is likely because their inflammation buffers are still working. So they are still suppressing a lot of the immune response that would make them remarkably ill. And that may also be the reason why viruses that are deadly to us are not lethal to them to the body. This includes an extreme systemic reaction called a cytokine storm, in which excessive release of proinflammatory signaling proteins turns a person's immune system of bats.

Basically, they evolved to survive onia host that constantly and aggressively attacks their ability to replicate. So when that assault is suddenly weaker in a new host, they go crazy and produce many little virus babies that send the host's immune system into panic mode. This type of overreaction can also occur to bats. It is simply not in response to viruses. Instead, it appears that their unique immune system may leave them vulnerable to non-viral invaders. The most infamous example of this is White Nose Syndrome, a fungal pathogen that has devastated bat populations in North America. Then, once the bat wakes up, its immune system does react; it just goes too far, which can lead the bat to develop a life-threatening form of systemic inflammation that may mean that the key to saving bats from this fungus (and us, from the deadly viruses they carry) may lie in further bat research. And also, if we are selfish, we have many other diseases characterized by inflammation, such as heart disease and diabetes. Therefore, studying your inflammation system can lead to treatments for our chronic conditions. And the same is true of studies of how bats keep viruses at bay.

Right now, we only have effective antiviral medications for approximately 10 of the more than 200 viruses that can infect humans, and very few broad-spectrum antiviral. If we can discover more tricks about bats, we could use them to develop therapies against the diseases they harbor and other dangerous viruses. Also, all this research could help us live longer. Many researchers think that bats' immune adaptation are also behind some of their other superpowers, such as how they rarely contract cancer or how they live incredibly long lives for animals their size. Small animals generally live fast and die young. But Brandt's bats can live more than 40 years despite weighing only i4-8 grams! So instead of viewing bats as zero species, we should think of them as flying keys to longevity and endurance, and in the end, they will be our allies in health, not our enemies.