Learning from bats to fight inflammation in humans

May 11 2023, by Federico Graciano

Concept art representing the study and its findings developed by the study team. Credit: Qi Su

By studying the unusual ability of bats to host viruses without significant illness, scientists at Duke-NUS Medical School have discovered a protein that could unlock new strategies for fighting inflammatory diseases in humans.

"Bats have attracted great attention as a likely reservoir of the SARS-CoV-2 virus responsible for the COVID-19 pandemic," said Professor Wang Lin-Fa, from Duke-NUS' Emerging Infectious Diseases (EID) Program, the senior author of the study published in the journal *Cell*. "But this unique ability to host yet survive viral infections could also have a very positive impact on human health if we can understand and exploit how they achieve this."

The research is focused on multi-protein complexes called inflammasomes that are responsible for the overactive inflammation that causes serious symptoms in many diseases. Inflammasomes are also implicated in functional decline in aging.

The Duke-NUS team discovered that a bat protein called ASC2 has a powerful ability to inhibit inflammasomes, thereby limiting inflammation.

"This suggests that the high-level activity of ASC2 is a key mechanism by which bats keep inflammation under control, with implications for their long lifespan and unique status as a reservoir for viruses," explained Dr. Matae Ahn, first author and co-corresponding author of the study, who is an Adjunct Research Fellow with the EID Program and the SingHealth Duke-NUS Medicine Academic Clinical Program. Dr. Ahn

is also a full-time clinician in SingHealth's Postgraduate Year One (PGY1) Residency Program after graduating from Duke-NUS in 2022.

Vivian Chen, co-first author of the study and an MD-Ph.D. candidate in Duke-NUS, highlighted that the team was able to demonstrate the potential for exploiting the powers of the bat protein in humans by showing it could also be effective in mice. She elaborated, "Expression of the bat protein in genetically-modified mice dampened inflammation and reduced the severity of the diseases driven by various triggers, including viruses."

Examination of the ASC2 protein in detail identified four amino acids in the molecule that were key to making the bat protein more effective at dampening inflammation than its corresponding human protein. This provides valuable insight for the development of drugs that can mimic the anti-inflammatory effect of the bat protein.

The next step for the team is to investigate the potential of their findings for treating humans. Prof Wang said, "We have filed patents based on this work and are exploring commercial partnerships for drug discovery. We are hoping to develop a new class of anti-inflammatory drugs for inflammasome-driven human diseases."

Prof Wang strongly believes that it is time to focus on the more promising aspects of what makes bats special "to help fight the human diseases of the future."

Duke-NUS' Senior Vice-Dean for Research, Professor Patrick Casey, commented on the study, "Even as COVID-19 begins to recede from the public's attention, Professor Wang and his team continue to break new ground with their basic research into bat biology, yielding unique insights that can potentially strengthen global pandemic preparedness. This is a prime example of the immense value basic scientific research

brings to solving major public health challenges."

More information: Matae Ahn et al, Bat ASC2 suppresses inflammasomes and ameliorates inflammatory diseases, *Cell* (2023). DOI: 10.1016/j.cell.2023.03.036

Provided by Duke-NUS Medical School

Citation: Learning from bats to fight inflammation in humans (2023, May 11) retrieved 11 August 2024 from https://medicalxpress.com/news/2023-05-inflammation-humans.html

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