Scientists pinpoint possible reasons for successful cross-species viral spread

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Infectious disease emergence is often the result of a pathogen entering a new host species, as highlighted by COVID-19. However, most cross-species transmissions fail to establish in the newly- infected species.

In a new study—led by a team of researchers at the University of Glasgow and published today in *PNAS*—scientists found disease progression was accelerated, which reduced the chances of onwards transmission, when the original host and the new host were physiologically or genetically more dissimilar.

For diseases to emerge, pathogens not only need to infect a novel host, but also be subsequently transmitted from one individual to another—a critical step. Why some pathogens succeed at this point while others fail is not well understood.

In this study, the researchers analyzed hundreds of published infection experiments involving the transfer of rabies virus—a dangerous pathogen able to infect and cause death in all mammals—from one host species to another.

The study found that rabies virus strains originating in bats—and those transferred from species with warmer body temperatures to those with a cooler body temperature—tended to kill the first infected host too fast for successful onward transmission.

The same was true as the genetic distance between the original and infected host species increased.

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Dr. Nardus Mollentze, Postdoctoral Research Assistant at the MRC-University of Glasgow Center for Virus Research, said: "Our results indicate that rabies virus strains are finely adapted to a specific host environment, and that even subtle mismatches between virus and host can limit the virus' ability to establish transmission in a novel species.

"These findings help to explain why rabies virus is maintained by a rather small subset of mammalian hosts and why emergence in new species is observed only in rare cases."

Dr. Roman Biek, Reader at the University of Glasgow's Institute of

Biodiversity, Animal Health and Comparative Medicine, said: "Our work shows how careful analysis of previous infection experiments can pinpoint small changes in the interaction between pathogen and host that may either help or hinder disease emergence, including emergence of new human infectious diseases.

"This is why investigating the factors which affect the clinical outcomes of cross-species transmission in the first novel host individual infected, the index host, is important, as these outcomes can alter the likelihood of the pathogen spreading further."

Dr. Mollentze added: "As cross-species transmission events are very difficult to observe in nature, we currently remain unable to predict which of them could potentially result in a new epidemic. Studies like ours demonstrate that already-existing experimental infection data can be used to better understand cross-species infections which, if applied to more viruses, may allow us to identify general rules predicting onward spread in the future."

The study, "Virulence mismatches in index hosts shape the outcomes of cross-species transmission" is published in *PNAS*.

More information: Nardus Mollentze et al. Virulence mismatches in index hosts shape the outcomes of cross-species transmission, *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.2006778117

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