Team finds potential MERS transmission mechanism between bats and humans

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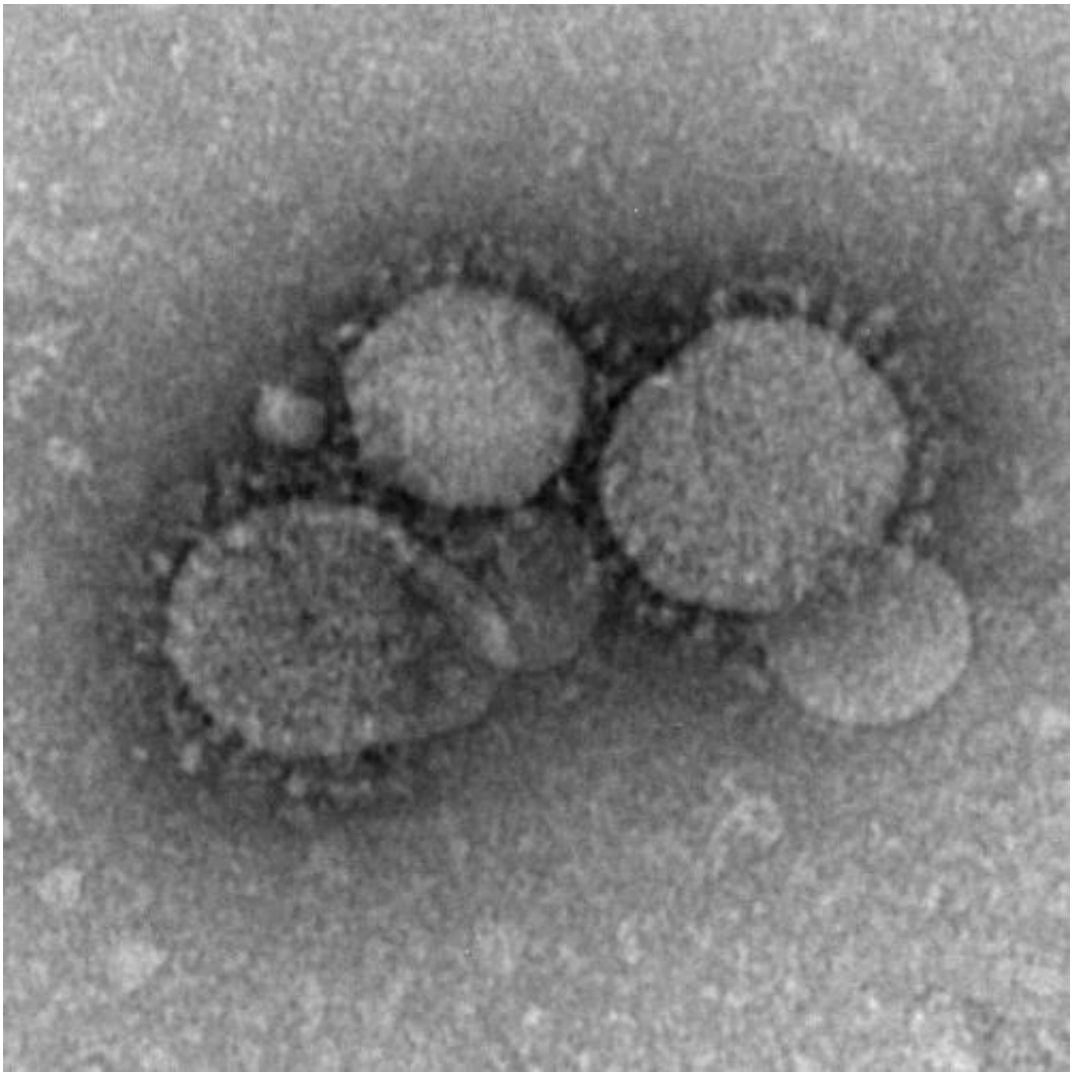

MERS-CoV particles as seen by negative stain electron microscopy. Virions contain characteristic club-like projections emanating from the viral membrane. Credit: Centers for Disease Control and Prevention

Researchers have identified the mechanism used by the deadly MERS virus to transmit from bats to humans. Bats are a native reservoir for MERS and the finding could be critical for understanding the animal origins of the virus, as well as preventing and controlling the spread of MERS and related viruses in humans.

The findings were published in the most recent edition of the *Proceedings of the National Academy of Sciences*.

Leading the research was Fang Li, Ph.D., associate professor of Pharmacology at the University of Minnesota Medical School. Graduate students Yang Yang and Chang Liu from Professor Li's lab participated in the research. The study was conducted in collaboration with Shibo Jiang, M.D., Ph.D. and Lanying Du, Ph.D., from the New York Blood Center, and Ralph Baric, Ph.D., from the University of North Carolina.

MERS (Middle East respiratory syndrome) was first diagnosed in 2012 and has infected over 800 people worldwide since then. About 40 percent of those infected were killed by the disease. Research has linked MERS to the same coronavirus family as the epidemic virus SARS. Both are believed to have originated in bats.

Researchers have known the MERS virus infects human cells by attaching itself to a receptor molecule called dipeptidyl peptidase 4 (DPP4) and then entering human cells. However, it was not known how MERS was being transmitted from bats to humans.

"We wanted to better understand what prompted MERS to jump from bats to humans, and knew we needed to find a virus that was isolated in bats but had the potential to move into a human model," said Li. "HKU4 virus is related to MERS and has, so far, infected bats but not humans. It provided a good model for understanding the bat-to-human transmission process of MERS and related viruses."

After investigating both MERS and HKU4, researchers observed two major indicators MERS had adapted to human cells in a way HKU4 had not done yet.

The first discovery was that HKU4 virus recognizes the same receptor, DPP4, as MERS virus.. However, MERS virus uses the DPP4 molecule from human origin better, whereas HKU4 virus uses the DPP4 molecule from bat origin better. HKU4 also struggles to enter human cells once attached to the DPP4 receptor on the human cell surface. MERS does not have such a problem, though both viruses are able to enter bat cells.

"Overall, our findings suggest that MERS virus has successfully adapted to human cells for efficient infections, and HKU4 virus can potentially infect human cells," said Li. "MERS and MERS-related bat viruses present a constant and long-term threat to human health. So far little is known about these bat viruses that are evolutionary ancestors to human viruses. We need to look at bat viruses carefully, learn how they infect cells and jump species, and then develop strategies to block their transmission to humans."

More information: Receptor usage and cell entry of bat coronavirus HKU4 provide insight into bat-to-human transmission of MERS coronavirus, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1405889111

Provided by University of Minnesota

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