How host-cell enzymes combat the coronavirus

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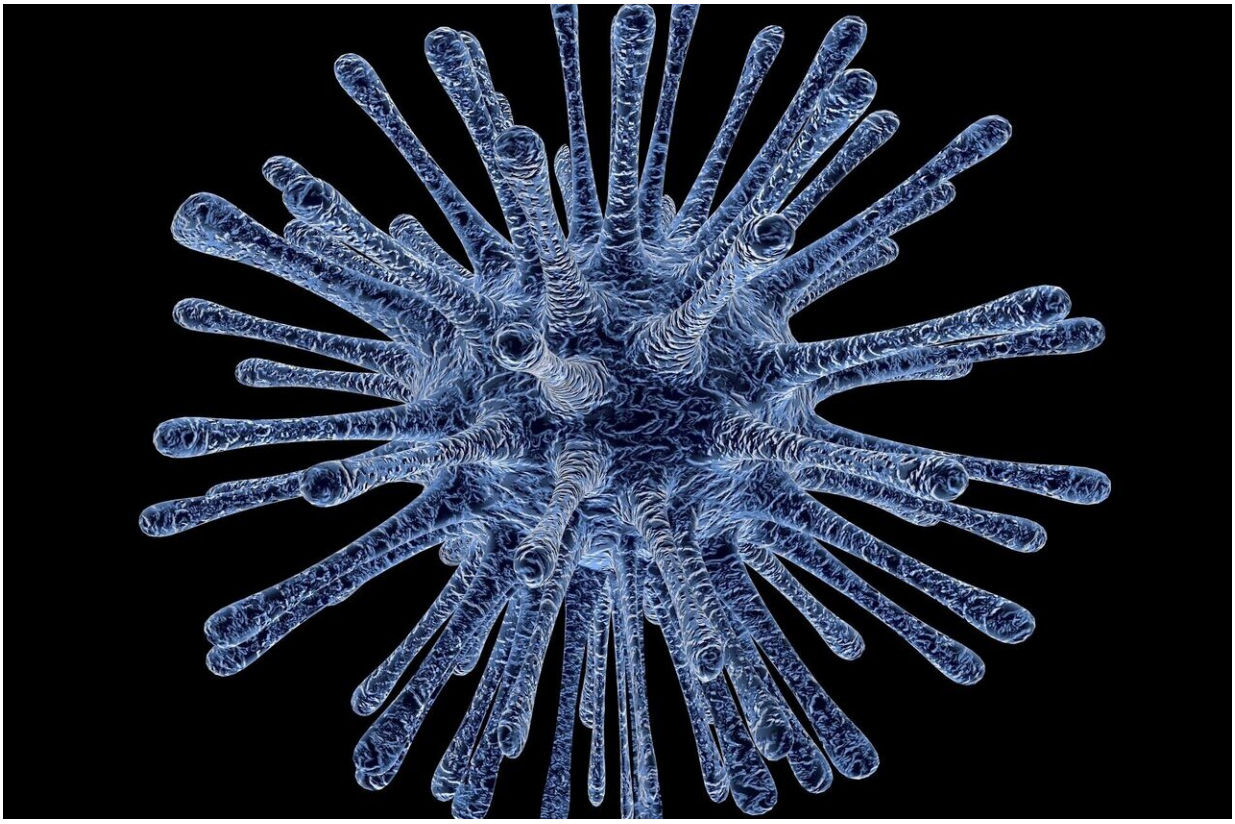

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Host-cell enzymes called PARP12 and PARP14 are important for inhibiting mutant forms of a coronavirus, according to a study published May 16 in the open-access journal *PLOS Pathogens* by Stanley Perlman

of the University of Iowa, Anthony Fehr of the University of Kansas, and colleagues.

A biochemical process called ADP-ribosylation facilitates the host response to virus infection. This process is catalyzed by enzymes called poly(ADP-ribose) polymerases (PARPs). Several viruses, including all members of the coronavirus family, which cause severe disease in agriculturally important and companion animals as well as humans, encode a macrodomain to reverse ADP-ribosylation and combat this immune response, facilitating viral replication and virulence. As such, viruses with mutations in the macrodomain are highly attenuated and cause minimal disease in organisms. These results suggest that macrodomains counter cellular ADP-ribosylation, but the potential role of PARPs in this process has not been clear.

In the new study, the authors used macrophage cells and mice infected with a coronavirus to identify PARPs, specifically PARP12 and PARP14, as host-cell ADP-ribosylating enzymes important for the attenuation of macrodomain-mutant viruses. The findings showed that the macrodomain is required to prevent PARP-mediated inhibition of coronavirus replication, and enhancement of the production of antiviral proteins called interferons. According to the authors, the results demonstrate a broad strategy of virus-host interactions, unveil previously unknown mechanisms of immune regulation, and indicate that the macrodomain may be a useful target for antiviral therapy.

The authors add, "ADP-ribosylation has increasingly been recognized as a host cell strategy to combat virus infections and viruses have learned how to counter this modification. Here we describe a previously unidentified interaction between the specific host cell enzymes that effect ADP-riboslylation and a viral protein that evades this host response."

More information: Grunewald ME, Chen Y, Kuny C, Maejima T, Lease R, Ferraris D, et al. (2019) The coronavirus macrodomain is required to prevent PARP-mediated inhibition of virus replication and enhancement of IFN expression. *PLoS Pathog* 15 (5): e1007756. doi.org/10.1371/journal.ppat.1007756