

# How host-cell enzymes combat the coronavirus

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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-ribosylation 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.  
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