Cell response to new coronavirus unveils possible paths to treatments

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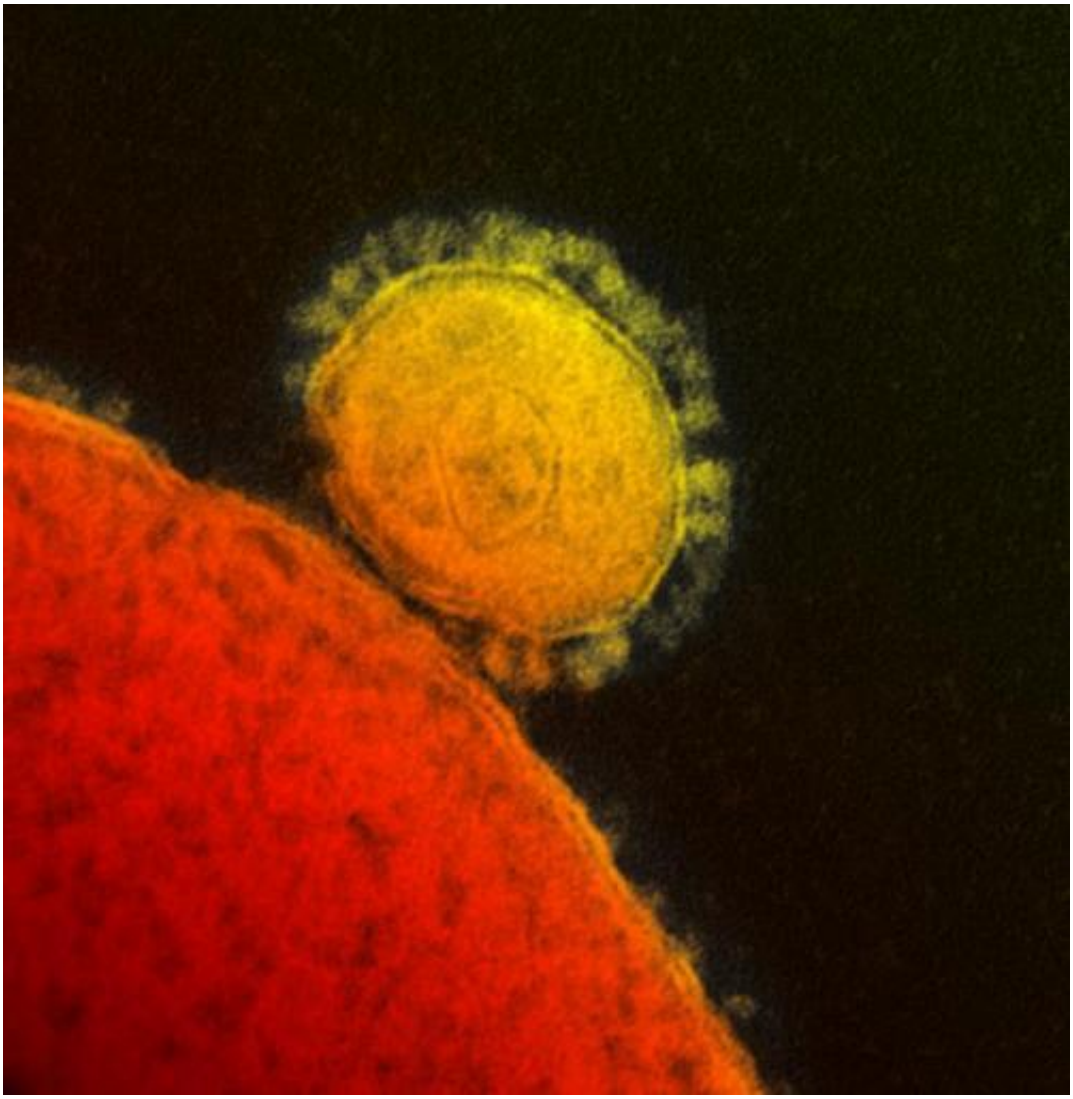

This is the transmission electron micrograph of novel coronavirus. Credit: NIAID/RML

NIH-supported scientists used lab-grown human lung cells to study the cells' response to infection by a novel human coronavirus (called nCoV) and compiled information about which genes are significantly disrupted in early and late stages of infection. The information about host response to nCoV allowed the researchers to predict drugs that might be used to inhibit either the virus itself or the deleterious responses that host cells make in reaction to infection. Since nCoV was recognized in 2012, 17 confirmed cases and 11 deaths have been reported—a high fatality rate that is spurring urgent research efforts to better understand the virus and its effects.

The investigators, led by Michael G. Katze, Ph.D., of the University of Washington, compared cellular gene expression responses to two viruses: the novel coronavirus and a coronavirus that caused a global outbreak of severe acute respiratory syndrome (SARS) in 2003. Although the viruses are in the same family, their effects on human cells are vastly different. In general, nCoV disrupted a greater number of human genes more profoundly and at more time points after infection than the SARS coronavirus. The team identified one set of 207 human genes whose expression differed from normal soon after infection with nCoV and remained disrupted throughout the course of infection. Notably, nCoV down-regulated the activity of a group of genes involved in signaling the presence of an invading virus to the immune system. Such down-regulation may cause a delay in the infection-fighting response.

The researchers used computational approaches to determine that certain classes of drugs, including specific kinase inhibitors and one type of glucocorticoid, act on some of the 207 human genes whose expression was found to be disrupted by nCoV. The team hypothesized that treatment with such drugs might block nCoV replication and disease progression in the host. In their current study, they tested this hypothesis using a kinase inhibitor on nCoV-infected cells grown in test tubes. They found that the drug did inhibit the ability of the virus to replicate.

Additional studies are needed to see if kinase inhibitors could be useful alone or in combination with other drugs to treat nCoV infection in people.

More information: L Josset et al. Cell host response to infection with novel human coronavirus EMC predicts potential antivirals and important differences with SARS coronavirus. mBio DOI: 10.1128/mBio.00165-13 (2013)

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