Common cold viruses reveal one of their strengths

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Common cold season is back, which has people wondering why we catch the same virus, year after year. Why don't we ever develop immunity against the common cold? Professor Pierre Talbot at INRS has known about the incredible variability of coronaviruses for some time. They're responsible for the common cold as well as many other infections, including neurological diseases. Along with his research associate Marc Desforges, Professor Talbot worked on a study recently published in *Nature Communications* about the ways in which coronaviruses adapt and evolve, becoming ever more effective at infecting hosts without being defeated by the immune system.

The small, spiky spheres, the coronaviruses are closely monitored by public health agencies, since they're able to be transmitted between species and some have a high potential mortality rate. Both SARS and MERS are caused by coronaviruses. Their ability to adapt to new environments seems due in part to the spikes on the surface of the virus —more specifically, a small, strategic part of the proteins that form those spikes.

The spikes are made up of S proteins (S for spike). A specific part of the spike seems to allow the virus to attach itself to host cells. The spike's RBD (receptor binding domain), which initiates the interaction between cell and virus, is essential for infection. But RBDs are targeted by antibodies that neutralize the virus and allow the immune system to flush it out of the host's system.

Coronaviruses are thus faced with an evolutionary problem. They can't infect cells without an RBD, which needs to be exposed so that it can latch onto cells. But the RBD needs to be masked to avoid being targeted by antibodies.

In response, the coronavirus has developed a mechanism that helps it survive, and thrive. The RBD is made up of three parts that vary widely between strains. Thanks to this variation, antibodies are unable to detect new strains, whereas RBDs retain—and even improve—their affinity for the target cell. Plus, RBDs alternate between visible and masked states.

To gain this insight, a group of researchers including Professor Talbot studied the alphacoronavirus HCoV-229E and, more specifically, the interaction between its RBD and aminopeptidase N (APN)—the host cell protein the RBD latches onto. The team crystallized the multiprotein complex and then analyzed the structures of both proteins.

By observing the RBD's structure up close, the team was able to identify the three long loops that latch onto APN. As analyses of these viruses over the last fifty years have shown, these loops are virtually the only thing that varies from one strain to the next.

The experiments demonstrate that the changes observed in the loops modulate an RBD's affinity with APN. The variants that have the greatest affinity are also likely to be better at infecting host cells, which helps them spread. Six different classes of HCoV-229E have popped up over the years, each with a greater RBD-APN affinity than the last.

This discovery adds to our understanding of the evolution of coronaviruses and could lead to similar analyses of other coronaviruses. Although there are many elements left to explain, the RBD seems to be an important feature that must be monitored as we follow the adaptive evolution of these viruses and assess their ability to infect.

More information: Alan H. M. Wong et al, Receptor-binding loops in alphacoronavirus adaptation and evolution, *Nature Communications* (2017). DOI: 10.1038/s41467-017-01706-x