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Built-in molecular brakes curb the sniffles

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Researchers at Johns Hopkins have discovered how our anti-infection machinery turns itself down and limits the sniffles, congestion and fevers that are a side effect of the campaign against invading viruses. The discovery seems to solve part of the mystery of why the misery of the common cold lasts only so long.

The key to curbing any excess activity by the immune system apparently rests with Carabin, a newly discovered protein made by the specialized white blood cells that march in when a virus attacks.

Results of a study published online this week at *Nature* show that Carabin "acts like an internal brake to dial down the speed and intensity of an immune response so that it doesn't go too fast or too far, or careen out of control and attack healthy cells," says Jun O. Liu, Ph.D., professor of pharmacology, neuroscience and oncology at Hopkins.

Searching for proteins that control immunity, Liu and his team homed in on those that latch on to parts of cells that are active during an infection. "Carabin popped out," says Liu.

To see what Carabin could do, the research team added it to white blood cells already primed and ready for anti-infection action. The more Carabin in the cells, the less active the cells became.

When people are infected with a cold virus, for example, the virus enters cells and hijacks its works so that the cells become viral factories. The immune system's white blood cells go after these infected cells not only

by fielding chemicals that kill them directly, but also by turning on genes that help out. When Liu and his group added Carabin to cells and then studied such genes, they discovered that Carabin disabled the "on" switches, keeping the genes off.

"By now we were pretty convinced that Carabin can turn down the immune system, so the next question was, 'what controls Carabin?'" Liu noted.

Tracking Carabin to its origins, the researchers said they were surprised to learn that viral infection not only turns on the immune system machinery, but also triggers the making of Carabin, which in turn shuts off the immune response.

"It's like having a built-in timer to keep the immune system in check," says Liu.

If Carabin turns out, after further study, to be a keystone natural inhibitor of immune responses, Liu added, it may prove useful in stopping such unwanted immune reactions as the rejection of transplanted organs.

Source: Johns Hopkins Medical Institutions