Cold viruses enter cells without knocking

Two research teams have found the structure of a key part of a protein that common cold viruses use as a doorknob to enter cells.

The protein protrudes from the membranes of cells that line the inside of blood vessels. Ordinarily, it functions as a receptor, binding white blood cells as part of a local immune or inflammatory response. However, rhinoviruses, which cause 70 percent of colds in humans, use the receptor to weasel their way inside cells.

Knowing the structure of the receptor, called ICAM-1, may help scientists find new ways to combat the common cold by stopping rhinoviruses from binding to it. Even though about 100 different types of rhinoviruses exist, says Jordi Bella of Purdue University in West Lafayette, Ind., most of them enter cells the same way—via ICAM-1.

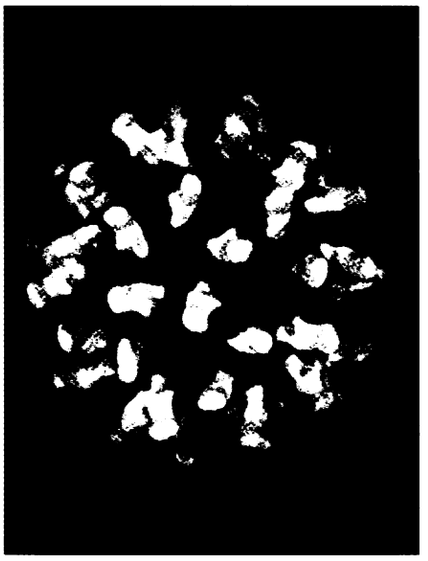
The two groups, one led by Michael G. Rossmann of Purdue and the other by Timothy A. Springer of Harvard Medical School in Boston, used X-ray crystallography on purified samples of the receptor to deduce the shape of two crucial sections of the molecule. Reports from both groups appear in the April 14 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

Overall, the findings are quite similar, says Springer, but the groups differ in their descriptions of the paired structure that the receptor molecules assume in the cell membrane.

ICAM-1 is a long protein with five segments. One end is embedded in the cell membrane, and the other binds rhinoviruses. Examining the two segments farthest from the cell membrane, the Purdue and Harvard teams found that the protein strand of the outermost segment forms loops to which the virus attaches. Another portion of the segment binds white blood cells, says Bella.

Because rhinoviruses and white blood cells attach to different parts of the receptor, potential therapies could conceivably block the action of the virus without harming the normal function of the receptor, he adds.

The Purdue group is now trying to produce an image of the virus and the receptor linked together. Learning how the virus and ICAM-1 stick to each other is only the first step in understanding how rhinoviruses infect cells, says Bella. In terms of developing therapies, "maybe it will be more powerful to intervene on the subsequent steps." —*C. Wu*



Rossmann et al./Purdue Univ.

This computer model shows 60 sites on a rhinovirus (sphere) where cell receptor tips (yellow) can attach.

Stress hormone may speed up brain aging

For 20 years, studies of rats and other nonhuman animals have suggested that sustained exposure to high concentrations of stress hormones provokes cell loss in the hippocampus, a brain structure integral to memory and spatial navigation.

A new study indicates that cortisol, the major human stress hormone, can provoke hippocampal deterioration and cognitive declines associated with aging in healthy people.

Elderly individuals with fairly high cortisol concentrations that rose further over a 5-year period displayed substantially smaller hippocampal volume than folks of the same age who had moderate, gradually declining concentrations of cortisol in their blood over the same period, reports a team of neuroscientists headed by Sonia J. Lupien of McGill University in Verdun, Quebec.

Moreover, members of the group with higher cortisol concentrations—which nonetheless fell within the normal range—performed much worse on memory tasks that rely on a functional hippocampus. These tests consisted of memory for pictures of common items seen the day before and immediate recall of walking paths from one location to another in an experimental maze. The findings appear in the May NATURE NEUROSCIENCE.

"Lupien and colleagues provide substantial evidence that long-term exposure to adrenal stress hormones may promote hippocampal aging in [healthy] elderly humans," state Nada M. Porter and Philip W. Landfield of the University of Kentucky in Lexington in an accompanying commentary.

Eleven elderly men and women between the ages of 63 and 80 participated in the investigation. Cortisol measurements were taken annually for 5 years. During home visits, the six volunteers who displayed high and rising cortisol concentrations reported more intense feelings of stress in their lives than the five people whose cortisol readings started out moderate and then declined.

After 5 years, magnetic resonance imaging scans revealed that hippocampal volume was markedly smaller in the participants with the highest cortisol measurements and the largest cortisol jumps from year to year.

By driving up concentrations of adrenal hormones in the blood, chronic stress may contribute to brain cell destruction and interfere with the generation of new hippocampal neurons in adults' brains (SN: 3/21/98, p. 180), Lupien and her coworkers propose.

The new findings complement preliminary evidence of smaller-than-average hippocampal volume among people who develop long-lasting stress reactions to traumatic events, such as military combat or childhood sexual abuse (SN: 6/3/95, p. 340).

It's unclear whether adrenal hormones directly affect the hippocampus and, if they do, how they alter cellular activity, say Porter and Landfield. —*B. Bower*

My mother, the clone?

Children of celebrities often face a rough time growing up. Does the same hold true for the offspring of celebrated barnyard animals?

The answer to that pressing question may soon be at hand. This week, the Times of London reported that the world's most famous sheep, Dolly, is pregnant. The Roslin Institute in Edinburgh, where scientists initiated Dolly's development from an adult ewe cell (SN: 3/1/97, p. 132), had not made an announcement when SCIENCE NEWS went to press.

Beyond providing fodder for farmers' tabloids, Dolly's pregnancy would confirm that she is fertile, further evidence that the cloned animal is normal, despite her unconventional means of conception. Because Dolly was created using DNA from a 6-year-old animal, biologists have wondered if she would suffer premature aging or other problems. To determine whether Dolly is fertile, investigators mated her last year. No official due date has been released, but Dolly is in partial quarantine to minimize the risk of miscarriage, according to the Times.

Roslin Institute scientists are conducting further tests to confirm that Dolly's DNA matches that of the donor ewe and not that of a fetus the ewe may have been carrying. Several scientists have raised the latter possibility, noting that no other research group has yet duplicated the cloning of an adult animal. —*J. Travis*