Rhinovirus receptor found; colds carry on

Researchers last week reported identifying and cloning the molecular receptor that enables rhinoviruses to infect human nasal-passage cells. Because rhinoviruses cause roughly half the cases of common cold, the accomplishment was widely reported as a breakthrough toward finding a cure for that most unpopular illness.

The new findings, reported in the March 10 CELL, have indeed generated excitement among virologists. Along with another paper in the same issue, in which researchers report cloning the poliovirus receptor, the work practically doubles the number of well-characterized virus receptors. But while an improved understanding of viral infectivity is sure to follow, researchers insist that reports of the common cold's death have been greatly exaggerated.

Virologists have sought since 1986 to learn the details of the "major" rhinovirus receptor—the cell-membrane docking site to which the great majority of rhinoviruses bind. But beyond the receptor's size and general characteristics, researchers had learned precious little about the molecule's amino acid sequence or its primary function on healthy cells.

Working separately, cell biologists and immunologists over the same period investigated a class of cell-surface molecules called intercellular adhesion molecules, including one known as ICAM-1. Among other things, ICAM-1 appears to play a role in concentrating white blood cells during episodes of inflammation. Last week's big news, reported by two teams working from opposite directions, is that ICAM-1 and the major rhinovirus receptor are one and the same.

The identity was reported by Timothy A. Springer of the Harvard Medical School in Boston and his colleagues, working on ICAM-1, and Jeffrey M. Greve and his co-workers at Molecular Therapeutics, Inc., in West Haven, Conn., who had been investigating the rhinovirus receptor. Vincent R. Racaniello at Columbia University in New York City and his colleagues also reported cloning the cell receptor for poliovirus, a rhinovirus relative responsible for paralytic polio.

The unexpected identity of ICAM-1 as the major rhinovirus receptor makes sense, at least in retrospect, researchers say. In response to cellular secretions characteristic of inflammatory reactions, the number of ICAM-1 molecules on the surfaces of some mucosal cells increases many fold, to as many as 350 million per cell. Thus in "choosing" ICAM-1 as their route of cellular infection, rhinoviruses—which themselves initiate an inflammatory response—guarantee themselves many new docking sites once they wedge a foot in the cellular door. "This explains a lot about the epidemiology of the common cold," says Ann Palmenberg, a virologist at the University of Wisconsin, Madison.

As headline writers were quick to note, an understanding of rhinovirus receptors may someday lead to a nasal-spray drug to block rhinovirus binding and infection in people. But keeping those sites blocked will be far from simple, researchers say, in part because the nose clears most substances from its lining every 15 minutes. Moreover, at least seven other types of viruses with different binding sites also cause colds.

"The new and exciting thing about these receptors is not so much that it's going to cure the cold," Palmenberg says. Rather, the well-defined ICAM-1 now provides researchers with an invaluable tool for viral receptor research. Only the receptors for the AIDS virus, the Epstein-Barr virus and the influenza virus are as well characterized. The new research, she says, "has the implication that other cellular adhesion molecules may well be major receptors for other, much more pathogenic viruses. You're going to see a lot of virologists suddenly catching up on all the literature about adhesion molecules." —*R. Weiss*

Acid highs and lows in Adirondack lakes

Ecologists studying 274 lakes in New York's Adirondack area report 80 percent have acidified over the past 50 years, probably due to acid rain. This study, which the researchers say is the first to profile regional lake acidification by elevation, also identified several factors apparently predisposing the area's high-altitude lakes to greater acidification.

The ecologists compared water-chemistry measurements made between 1929 and 1934 with data collected from the same lakes between 1975 and 1985. In the March ENVIRONMENTAL SCIENCE AND TECHNOLOGY, they describe the half-century changes in Adirondack alkalinity as "significant" and as a more "robust and accurate" gauge of regional acidification than a largely pH-based 1986 analysis by the National Academy of Sciences (NAS). The NAS study had concluded that possibly no change occurred.

Alkalinity is essentially a measure of water's acid-buffering capacity, whereas pH measures hydrogen ions. Because pH can vary with the amount of dissolved carbon dioxide in water, "it is not a reliable way to measure additions of strong acids—like the sulfuric and nitric acids found in acid rain," says Mark D. Mattson, at the New York Botanical Garden's Institute of Ecosystem Studies, in Millbrook, a coauthor of the new study. Moreover, he says, pH is very difficult to measure with methods used during the 1920s and '30s. For these reasons, his group focused on alkalinity.

The researchers found a median alkalinity decrease of 50 microequivalents per liter (μequiv/l) in Adirondack lakes—a value suggesting the annual addition of about 6×10^{17} hydrogen ions of strong acid per liter. For lakes measured at 250 μequiv/l in the 1930s, a 50-unit drop would hardly change either their pH or their biology. But such a drop—the norm at around 582 meters elevation—could easily prompt major changes, such as fish kills, in high-elevation lakes that measured only 50 to 100 μequiv/l in the 1930s, Mattson says.

Geology and weather contribute to increased acid sensitivity at high altitude, the researchers found. Since rainfall and a lake's collection of rain runoff tend to increase with altitude in the Adirondacks, higher lakes generally receive more acid rain. Moreover, high-altitude lakes are more likely to sit near acid-fostering crystalline bedrock and thin acid soils.

The short stay of water in Adirondack lakes also fosters acidification, says Charles Driscoll, a civil engineer at Syracuse (N.Y.) University. Many researchers over the past several years have shown sediment-dwelling microbes can neutralize acid added to lakes. However, he notes, this process can take up to five years. Driscoll says his own research has shown that Adirondack lakes, unlike Midwestern ones, tend to flush water through their system far too quickly—from once to 10 times per year—to allow much in-lake buffering of acid.

Noting that the NAS couldn't decide if acidification occurred in Adirondack lakes, Mattson says, "We wanted to set the record straight" and show that the ambiguity is due to "unreasonable" assumptions about interpreting the older data.

"There are a lot of problems with those historical data [used by both groups]," Driscoll says. "But I think [Mattson and his co-workers] have done as good a job as could be done—much better than the NAS."

James R. Kramer at McMaster University in Hamilton, Ontario, disagrees. Head of the NAS team, he charges that the new report contains serious errors—such as its authors' claim to have used, for comparison, the same pH method as the NAS group. Kramer also challenges those researchers' understanding of historical pH-analytical methods and says they underestimated what the NAS team knew about limitations in the New York lake data. "The bottom line," he says, "is that there are too many unknowns to make a definitive statement" about Adirondack acidification. —*J. Raloff*