Flu Vaccine Aims at Constant Target

Like a shape-shifter in a science fiction novel, the virus that causes influenza can morph into new forms. Mutations that alter the structure of proteins on its surface enable the virus to evade its host's immune system. Host antibodies search in vain for the flu virus versions that they had encountered previously.

A new study points to an unchanging viral feature that the immune system might be trained to detect.

The conserved protein, called M2, is dwarfed by its neighbors, hemagglutinin and neuraminidase. These capricious, larger molecules have made the flu virus a moving target. Scientists track changes in these proteins to redesign the flu vaccine annually, so they can reeducate immune cells to prepare for a new onslaught. The vaccines, however, only represent health authorities' best guess at what form the flu virus will take as it spreads in Europe and the Americas.

The viruses that cause all forms of influenza A, the most severe flu, display the same M2 surface protein. By bonding the little M2 to a protein from a hepatitis B virus, Belgian scientists have built a molecule that attracts the attention of the immune system in mice. Confronted by this combination protein, immune cells make antibodies that stand ready to glom on to the M2 protein and hamper the virus' attempts to infect a host.

In theory, whether or not the immune system recognizes the hemagglutinin or neuraminidase proteins the virus contains, it would still attack the virus' M2 site, says study coauthor Walter Fiers, a molecular biologist at the University of Ghent.

In the Belgian experiments, all the mice contracted the flu, as evidenced by weight loss and a temperature drop, when exposed to five times the amount of flu virus needed to cause illness. Of 36 mice previously given various doses of the M2-based vaccine, 30 survived the flu, but 9 of 11 unvaccinated mice died.

In a second experiment, all 14 mice receiving a uniform, moderate dose of vaccine survived, whereas 16 unvaccinated animals all died within 9 days, the researchers report in the October NATURE MEDICINE. In later tests, the vaccine provided immunity against additional influenza A strains.

"It's a very interesting study," says Jeffery K. Taubenberger, a molecular pathologist at the Armed Forces Institute of Pathology in Washington, D.C. "Clearly, they show that under these circumstances, they can ameliorate the disease—not preventing infection, but making it milder."

A separate test demonstrated that the vaccinated mice retained their immunity to the flu for 6 months, says Fiers. Antibodies in vaccinated mice hobble M2 and keep the virus from spreading from cell to cell, he says.

While scientists can often develop a strong flu vaccine by tracking the hemagglutinin protein, their guess is sometimes off target, rendering the vaccine much less effective. Incorporating a more consistent—if less potent—M2-based component into the vaccine might prove useful in years plagued by bad guessing, Fiers says.

"It seems probable that a combination of old and new [vaccines] will be required to develop a truly 'universal' vaccine for influenza," says Edwin D. Kilbourne of the New York Medical College in Valhalla in the same issue of NATURE MEDICINE.

An M2 component that moderates the severity of the flu could be especially valuable in a pandemic, such as the devastating outbreaks that occurred in 1918, 1957, and 1968, says Frederick G. Hayden, a clinical virologist at the University of Virginia in Charlottesville. In those years, flu strains incorporating abrupt changes in their large surface proteins hit populations worldwide.

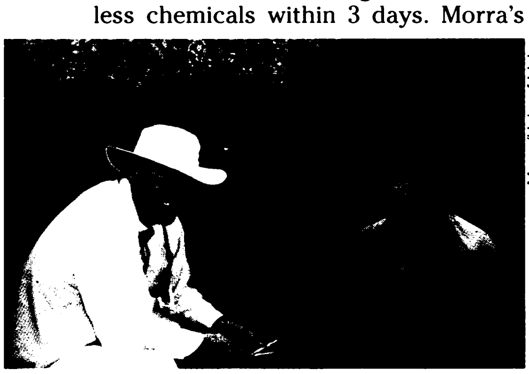
The new study is "a very interesting initial set of experiments," Hayden says. He adds that the real value of an M2 vaccine won't become certain until it's tested in larger mammals. —*N. Seppa*

Coming: A new crop of organic pesticides

Because many plant pathogens hide out in the soil, growers have learned to counter the pests' dirty tricks by pumping toxic chemicals into the ground shortly before planting. Now, scientists report promise for an alternative—fumigating soils with a living mulch.

Plants in the brassica family—which includes cabbages, mustards, and the rapeseed plants from which growers harvest canola oil—produce compounds called glucosinolates. Enzymes in the soil or in other organisms can transform the glucosinolates into compounds toxic to a wide range of creatures. Brassicas themselves contain such enzymes, which are released when the plant is chewed.

Matthew J. Morra of the University of Idaho in Moscow and his colleagues now show that as they grow, brassica plants infuse the soil with these toxins. If farmers then plow the plants into the soil, the pesticidal chemicals flood the root zone. These toxins tend to degrade to harmless chemicals within 3 days. Morra's team describes its findings in the just-published September JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY.



Morra/Univ. of Idaho

Kirkegaard (left) and Morra (right) examine roots of Humus, an Idaho-pioneered rape now undergoing tests as a living fumigant in Australia. Back home, Morra is testing two new hybrids.

Most of a brassica's glucosinolates develop in its stems and leaves, notes coauthor James B. Gardiner, now of the University of Vermont in Burlington. However, his Idaho data show that even when the entire plant is plowed under, only the root glucosinolates give rise to measurable toxins in the soil. Gardiner also found another surprise. Rapes in the field release a different mix of toxins than do those produced in indoor experiments.

As brassica mulches stabilize soil, they offer "a softer, greener approach" to pest control, says John A. Kirkegaard of the Commonwealth Scientific and Industrial Research Organization in Canberra, Australia. He has linked improved wheat yields to toxins released by an earlier crop of rape. Yet "it's not a silver bullet," he says, since some pests are immune to the toxins—at least in the concentrations now made by rapes.

Ironically, Gardiner notes, breeders have traditionally worked to reduce a rape's glucosinolates, since they can render it unpalatable as a forage and impart a pungent flavor to cooking oils. With a potential market for high-glucosinolate brassicas, Jack Brown at the University of Idaho has been crossing distantly related species of winter-hardy rapes with glucosinolate-rich mustards.

He's just created two fertile hybrids. Unlike mustards, the new species are hardy to well below freezing, allowing their use as an erosion-controlling winter cover, he says. Field tests are just getting under way to compare their crop-protection value against that offered by traditional rapes and commercial soil fumigants. —*J. Raloff*