Protective Chemistry: Sensitive Cell Control

A cell's defense against viruses can switch on at the prod of a single molecule. That biochemical armor, a protein called interferon, protects the cell from certain death. No one knows just how interferon works, but because its protective action confounds a wide range of viruses, the protein is being investigated clinically as a possible "pan-vaccine" (SN: 2/28/76, p. 130).

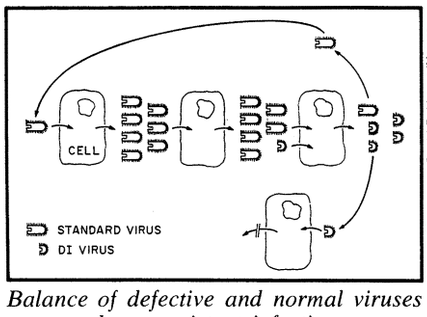
The most potent substance so far discovered for turning on production of interferon is described in the April 28 NATURE. Although all viruses will stimulate interferon synthesis, Philip I. Marcus and Margaret J. Sekellick of the University of Connecticut demonstrate that a single short segment of double-stranded RNA from a defective virus works best.

Defective viruses arise naturally when viruses are grown in cells in a laboratory. These agents consist of the same protein coat as the normal virus, but they contain only a fraction of the genetic material. This defect prevents them from successfully infecting cells alone, but they can reproduce in the presence of normal viruses. Virologists call these viruses defective interfering (DI) particles because they eventually interfere with the normal viruses' reproduction.

Defective interfering particles are likely to play a role in persistent infections. Alice S. Huang and David Baltimore suggested in 1970 that a balance of normal and DI viruses could explain infections that don't immediately either spread or heal. Marcus and Sekellick now propose that for a certain group of DI particles, interferon is involved in preventing viruses from killing cells.

Marcus and Sekellick studied DI particles that arise from vesicular stomatitis virus, which causes a cattle disease. The genetic material in that virus is a single strand of RNA, and most of the DI particles contain shorter pieces of that RNA. One set of DI particles, however, contains RNA consisting of two regions that can bind together into a double-stranded structure.

DI viruses with the single-stranded RNA have no measurable effect on a cell's interferon production, Marcus and Sekellick report. DI viruses with the double-stranded RNA, however, stimulate a burst of interferon production in the experimental cells, chick embryo cells grown in the laboratory. The double-stranded RNA did not need to be functional for reproducing or making protein in the cells. It could stimulate interferon production even if its other functions were destroyed by heat or ultraviolet light. After the double-stranded RNA enters a cell, it seems that a cellular gene for interferon is activated. New cellular RNA and protein appear to then be required for interferon production.



Alice S. Huang and David Baltimore/Nature

Balance of defective and normal viruses may produce persistent infections.

This action of double-stranded RNA fits well with experiments showing that interferon production can be stimulated, but less effectively, by an artificial double-stranded RNA. The difference in efficiency can be explained by the packaging. The RNA molecule in a DI particle is designed to be delivered into a cell, and the viral coat is designed to deliver its contents. The artificial RNA, on the other hand, has to find its own way through the cell membrane and is susceptible to various destructive enzymes. Researchers have to treat cells with thousands of artificial molecules in order to get just a few in, but the DI particle successfully delivers a single molecule, Andrew Ball, a colleague of Marcus and Sekellick explained to SCIENCE NEWS.

Treatment with DI particles that produces interferon allows laboratory-grown chicken and human cells to survive an otherwise lethal dose of the parent vesicular stomatitis virus. The researchers report that it also protects cells against a dose of the unrelated virus that causes Newcastle disease. Laboratory cells derived from the kidneys of green monkeys are a type of cell that does not respond to any inducers of interferon and was not protected by the DI particles.

There are currently no plans to use these defective viruses clinically, although trials have been run using the artificial double-stranded RNA. The toxicity of that material should make new approaches to stimulating human interferon production welcome.

To the scientists the most striking aspect of these experiments is the sensitivity of the cells. "This is the most dramatic demonstration that we've got yet that a single molecule of anything can affect a cell," says Ball. "When you compare the size of a molecule and the size of a cell, it's like a pea up against the Cathedral of Notre Dame." □

The big apple: Better for your psyche

Fifteen years ago, the results of the now-famous Midtown Manhattan Study shocked behavioral scientists and laymen alike by reporting that 23 percent of New York City's East Side residents were in need of psychiatric treatment. At the time, the report was greeted by some "with skepticism, flat disbelief or questions about the mental competence of the study's scientists," recalls Columbia University's Leo Srole, the sociological researcher who directed the study. Since then, the figure has come to be accepted as realistic for New York and other cities, and has added fuel to the argument that big cities are indeed unhealthy "jungles" for the human psyche.

Now, in a 20-year follow-up of 695 original interviewees (the 1962 report was based on data from 1,660 persons interviewed in 1954), Srole reports that the mental health of New Yorkers is about twice as good as it was in 1954. Moreover, in combining these latest results with survey data from the United States, Canada and elsewhere, Srole concludes that big city residents appear to have substantially fewer mental health problems than their rural and small town counterparts. "Mental health overall," he states, "is more favorable in big population centers, including New York as the biggest, than in smaller ones." The results, he emphasizes, "offer no support whatsoever to the antique presupposition of the superiority of rural mental health."

Srole presented his findings at the annual meeting of the American Psychiatric Association last week in Toronto.

In the 1974 reinterviews, the Manhattan follow-up subjects answered the almost identical battery of 92 symptom items they had answered 20 years before. Srole compared the results of persons from 40 to 60 years old with those of respondents in the same age ranges in 1954. In the original and follow-up studies, he notes, the samples are representative of both rich and poor persons living in the predominantly white population area.

Over the two-decade period, the percentage of those with "impaired" mental health in the 40 to 49 age category dropped from 16 to 8.4 percent. Persons between 50 and 59 went from 21.7 percent impaired to 10.3 percent. Srole attributes much of the improvement to changes in upbringing that occurred years ago. In the original survey, for example, the respondents in their 50s were brought up by parents who grew up in the late 1800s, Srole notes, whose attitudes and socio-ec-