Leukemia: Promising Antisera

C-type RNA tumor viruses are widely implicated not only as causes of various animal tumors, but also of some human cancers, notably leukemia. A closely collaborating group of German and American scientists sought to find some component of one of these viruses that would be highly antigenic. Such a component would provoke a strong immune response in mammals (due to the presence of an antigen, a foreign protein) and thus be capable of being used as a vaccine or immunotherapy against virally induced leukemia. They succeeded for the first time, in curing and preventing viral-induced leukemia in mammals using purified viral antigen or viral antiserum. The discovery opens the way to possibly curing leukemia patients and vaccinating people against leukemia.

The advance was reported at the Seventh International Symposium on Comparative Leukemia Research in Copenhagen last week. Many at the meeting, attended by 300 of the world's top cancer scientists, regard the research as a significant achievement in the fight to understand, cure and prevent cancer.

The principal investigators of the two teams are Werner Schäfer of the Max Planck Institute for virus research in Tübingen, Germany, D.P. Bolognesi of Duke University Medical Center in Durham, N.C., P.J. Fischinger of the National Cancer Institute in Bethesda, Md., and Fernando de Noronha of Cornell University. According to one colleague at the meeting Schäfer is the world's expert in "stripping viruses down into parts and putting them back together again."

The researchers were especially eager to obtain a molecule from the surface of the virus rather than from inside the virus. Such a molecule would be expected to react maximally with the immune defense mechanism of the host. Furthermore, such a molecule would be free of genetic material from the virus that might cause infection.

They chose as their model the Friend murine leukemia virus, a C-type RNA tumor virus which causes leukemia in mice. They selected this virus because it can be grown in large amounts. They broke the virus into various surface components so that they could see which parts might work as a vaccine. That is, they gave different components to different mice. One of the viral surface molecules, a sugar protein, was particularly effective in preventing leukemia in the mice.

Having thus found a viral molecule that could work as a leukemia vaccine, they made antiserum (antibodies) to it to see whether the antiserum might be used as immunotherapy in leukemic mice. They gave the viral antisera to ten leukemic mice. Twenty others did not receive the antiserum. This latter group of mice continued to show viral infection and leukemia and died three months later. The treated mice stopped showing viral infection, overcame their leukemia and are still alive after eight months.

As Schäfer reported at the meeting, "To our knowledge, this is the first demonstration that vaccination with a purified viral component or immunotherapy with the corresponding viral antiserum can prevent or control virally induced leukemia."

Since C-type RNA tumor viruses are closely related, the German-American team is now trying to see whether their mouse viral antigen and antigen antiserum can protect other mammalian species as well. Indeed, they have preliminary findings that their antiserum can be used to cure cats of leukemia. They will now try to see whether the antiserum can also cure primates that have leukemia.

Their ultimate goal, of course, is to use the antigen and antiserum to prevent leukemia in people and to cure leukemic patients. To do this, however, they have to make sure that human leukemia cells contain viral antigen that is identical to that in the other mammalian species. Preliminary evidence that human leukemia cells do, in fact, contain the same antigen was presented at this meeting by Richard S. Metzgar of Duke University Medical Center. Metzgar reported that a portion of the mouse antigen could be detected on human leukemia cells. Other investigators who participated in the German-American team effort include M. Claviez, H. Frank, G. Hunsmann, H. Schwarz and H.J. Thiel of the Max Planck Institute in Tübingen and R.W. Green and A.J. Langlois of Duke University.

Leukemia in the test tube

For the first time, bone-marrow cells that give rise to the body's blood cells and immune system can be maintained in the test tube for extended periods. This new bone-marrow culture system opens the door to understanding how bone-marrow cells differentiate into blood cells and immune cells and, most critically, how blood cells and immune cells become leukemic.

The culture system has been developed by T.M. Dexter and L.G. Lajtha of Christie Hospital and the Holt Radium Institute in Manchester, England. Dexter reported on it at the Seventh International Symposium on Comparative Leukemia Research. The symposium is sponsored by the Leukemia Society of America and by the U.S. National Cancer Institute. The chairman of the session during which Dexter spoke, Donald Metcalf of Royal Melbourne Hospital in Melbourne, Australia, told SCIENCE NEWS that he considered the test-tube system "an important advance."

The bone-marrow cells that give rise to red blood cells and immune cells are called stem cells. Stem cells are known to go through several stages of development before they become well defined blood or immune cells. First they become committed cells, that is, cells committed to be a special type. Then the committed cells become blast cells, that is cells which are primitive and still undifferentiated into a particular blood or immune cell. Finally they become specialized blood or immune cells. What prompts stem cells to go through these several stages, however, has been largely a mystery. Now Dexter's and Lajtha's culture system should allow researchers to unlock some of the secrets of development.

"The nice thing about this system," Dexter says, "is that it is a cell population in a culture bottle, and you can monitor any changes that occur in those cells." Why their particular system works, and others tried in the past have not, however, is yet to be determined.

The Manchester investigators, Metcalf says, "have also made leukemia occur in the test tube, which has not happened before either." What they do essentially, is treat mice with a special hand-synthesized chemical known as MNU (methylnitrosourea). They remove bone-marrow cells from the animals and put them in the test tube for several months until they become blast cells. Then, if they inject the blast cells back into mice, the mice develop leukemia.

This elegant test-tube, live-animal method, Dexter points out, "allows us to follow changes leading to leukemia development." Although many cancer scientists believe that cancer is a condition wherein differentiated blood and immune cells revert to their former, primitive stage, Dexter does not think so. Rather, he suspects that leukemia is triggered by some defect that occurs along the way as stem cells become committed cells, blast cells and finally blood or immune cells. The new laboratory techniques should help the other team and other reseachers determine whether this really occurs. □