MICROBIOLOGY

From our reporter at the Gustav Stern Symposium on Perspectives in Virology in New York

Immune system charged with murder

"Killer T cells," the body's second line of defense against viral infections, may do more harm than good under some conditions. From the results of his recent research, Peter Doherty suggests that the widespread deaths of young, healthy people in the 1918 influenza epidemic were due to a massive action by their own T cells.

Pandemics of influenza are associated with changes in structure of an influenza virus. People's antibody mechanisms, the first line of defense, do not recognize or attack an altered virus. The virus is therefore able to evade the antibodies and infect body cells.

"Recovery from virus infection is not mediated by antibodies but by a T cell response," Doherty explains. "These cells go to the spot where the virus is and do the job of eliminating the virus." The T cells kill any cell that they recognize is infected with a virus.

Although altered viruses get by the antibody defense, they do not fool the T cells, according to recent studies on mice at the Wistar Institute in Philadelphia. Doherty reports, "It seems that at least a proportion of the T cells recognize a group-specific component which is common to all type A influenza viruses." If T cells are exposed to one type A virus, and then to another distinct virus, they react with a rapid, much enhanced response. "The fact that people suffer recurrent attacks of influenza may indicate either that the cell-mediated immune response does not protect, or that T cell-mediated immunopathological process is a significant component of the disease syndrome," Doherty says.

If a massive T cell response kills enough virus-infected cells in a critical organ, it may produce death. That is what Doherty suggests occurred in 1918. The first wave of influenza killed few people but may have primed the cell-mediated immune system. The second and third waves of altered viruses would then have triggered a massive T cell response. Doherty concludes that illness may reflect a balance between cell death caused by a virus and the consequences, beneficial and deleterious, of T cell response.

Cells provide receptors for viruses

Coxsackieviruses infect 30 to 80 percent of the human population and cause a significant amount of disease, ranging from symptoms resembling a common cold to fatal inflammation of heart muscle. No effective drug or vaccine is now available. Research by Richard L. Crowell and June-Sang Siak indicates that specific receptors on human cells make them targets for infection by different types of viruses and that altering these receptors may be the key to curing viral diseases.

Little is known about the cell receptors for most viruses infecting humans. In recent work at Hahnemann Medical College in Philadelphia, Crowell and Siak succeeded in extracting the receptor for one type of coxsackievirus (group B) from human cells grown in the laboratory. Each cell, they found, had about 100,000 of these receptors as integral components of the membrane. The extracted receptors could still bind to viruses and prevent them from infecting other cells. Crowell and Siak are especially optimistic about the medical applications of this work because interfering with the receptors on living cells in the laboratory did not kill the cells or even slow their growth. Analysis of these receptors may also provide a basis for better understanding the early events in virus infection. Why cells would develop receptors for a harmful virus remains an intriguing question.

Virus part can work as vaccine

A new approach to immunization has resulted in a successful experimental vaccine for foot-and-mouth disease. The approach involves injecting swine with only an element of a virus, rather than with intact live or killed agents. Use of isolated components removes the risk of infecting the animal or of causing other diseases and also reduces side effects.

Howard L. Bachrach and co-workers at the Plum Island Animal Disease Center in Greenport, N.Y., have isolated the four major proteins of the virus causing foot-and-mouth disease. When they injected each protein into guinea pigs, one elicited a response by the same antibodies that attack the whole virus. That protein was also effective in immunizing swine. When they were exposed to infected animals, pigs that had received two doses of the protein showed either no sign of disease or only a single sore on the foot.

At present, large amounts of the foot-and-mouth virus protein would be difficult to obtain. The researchers are attempting to find smaller protein fragments that will stimulate the immune response and that can be more easily synthesized in practical quantities.

Wart viruses: A mixed bag

Several types of human warts occasionally convert into malignant skin tumors. Therefore any virus causing warts is a good candidate for a human cancer virus, but research with viruses from warts is difficult, because the viruses will not grow in the laboratory. All wart viruses must be isolated from tissue samples from patients.

Until recently, researchers thought warts were all induced by the same virus. The different appearances of common warts, juvenile flat warts and genital warts were ascribed to their differing locations and hosts. Now Harald zur Hausen of the University of Erlangen-Nürnberg has identified at least five virus types responsible for just common warts. Zur Hausen characterized the viruses from about 400 warts by their DNA and protein and by their interaction with antibodies.

Common warts almost never become malignant, so research must also be done on viruses from other kinds of warts. Whether these viruses play a role in human skin cancer still needs to be clarified, zur Hausen says.

Hepatitis protein and liver cancer

Both clinical and epidemiological studies have suggested an association of primary liver cancer and the presence of a distinctive protein in blood. This protein also appears in the blood of people with hepatitis B and is called the hepatitis B surface antigen.

Jennifer Alexander and co-workers at the National Institute of Virology in Sandringham, South Africa, have evidence that the tumor cells and blood protein are directly linked. Cells grown in the laboratory from a liver tumor removed during an autopsy in 1973 consistently produced material similar to that from patients with hepatitis B.

Alexander's work is the first direct evidence that cancer cells can be the source of the hepatitis B antigen. The persistence of antigen production over so many generations of cells indicates that the hepatitis virus's genetic information is firmly established in the tumor cells, although it is not yet clear whether the virus causes the cells to become malignant. In the laboratory line of cells, it will now be possible to study more extensively the association between the hepatitis B virus and liver cancer.