

# STANFORD UNIVERSITY MEDICAL CENTER

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STANFORD -- Scientists have discovered a new class of regulatory genes believed to control specific immune responses of the body to antigens or foreign proteins like viruses and bacteria.

Ten of the regulatory genes were identified by researchers at Stanford and Harvard medical schools, and nearly 20 similar genes were found by other researchers during the past eight years.

This, however, is the first time that discovery of the genes and implication that they may influence predisposition of some people to common viral and bacterial infections has come to public attention.

Genes are units within chromosomes that transmit hereditary characteristics and also govern the development of cell structures.

Scientific interest in immune response genes has increased in recent months because of the growing number of associations between heredity and certain diseases being reported in medical journals and scientific meetings here and abroad.

These genes have, in fact, caused so much excitement in the scientific community that last week leading immunologists and geneticists met in La Jolla to partly pool their knowledge and to talk about development of the best methods for the laboratory experiments needed to confirm this type of link between heredity and disease.

The most exhaustive study of the immune response genes has been made by Dr. Baruj Benacerraf, professor of comparative pathology at Harvard Medical School, and Dr. Hugh O. McDevitt, associate professor of medicine and head of the immunology division at Stanford University School of Medicine. They discussed the long-term implications of the work in a special report in Science, a scientific journal.

In a series of experiments, the scientists injected animals with antigens. Animals which had one of the immune response genes could form a vigorous reaction against the corresponding antigen. This was marked by production of antibody and development of immunity.

Animals lacking such a gene would not become immune and were either totally or partially deficient in their antibody response to the antigen.

Immune response genes, called Ir genes, are believed to be linked to immune response cells which mature in the thymus. The scientists, however, do not know how these genes work. They believe the genes are somehow associated with the same immunological apparatus responsible for rejection of organ transplants.

And this is the intriguing part.

Recent findings suggest a relationship between rejection-triggering antigens in organ transplants and certain types of cancer and other disease, Dr. McDevitt explained in an interview. Among these are Hodgkin's disease, the rare rheumatic disorder systemic lupus erythematosus, and acute lymphocytic leukemia.



Exactly how the tissue rejection antigens, located on the surface of white blood cells, exert an effect on susceptibility to these diseases is unknown.

One possible mechanism, Dr. McDevitt pointed out, is that host antigens may provide a safe receptor site for the attachment of an invading virus. Still another possibility is that the virus "mimics" the biochemical characteristics of host antigens so that the animal cannot identify the invader as foreign and react against it.

A third possibility is that immune response genes located near the genes for transplantation antigens on the host chromosome affect the host's ability to react against antigens on an invading virus.

If a link between hereditary disease susceptibility and transplantation antigens is definitely established, scientists believe it could have great medical significance.

It could lead to development of tests for identifying those who are prone to certain diseases because of hereditary factors, Dr. McDevitt said.

He stressed the studies have dealt so far with mice and guinea pigs. Mapping is under way in laboratories in Maine, Michigan, Montana and Stanford to define the genetic relationship between specific immune response genes and tissue compatibility antigens. But the knowledge gained from animals could ultimately be applied in studies of the immune response of man, he said.

"There is evidence suggesting that specific genes may be one of several factors affecting susceptibility to cancer in both animals and man," Dr. McDevitt said. He cited these examples:

- . Scientists have shown a genetic control of cell susceptibility to the Rous sarcoma virus which causes tumors in chickens.

- . Another researcher has shown that a gene, closely associated with genes for tissue compatibility antigens, influences susceptibility of mice to a type of mouse leukemia.

- . Working with former Stanford geneticist Walter F. Bodmer, now of Oxford University, Dr. McDevitt and his colleagues have identified a statistically significant association between systemic lupus erythematosus and tissue compatibility genes in man.

- . Several laboratories in France, England and Australia have found a similar association between Hodgkin's disease and tissue compatibility genes in humans.

The Stanford immunologist believes studies should eventually be made to detect and type immune response genes in man. But this is not going to be simple.

In the course of their evolution, animals and man have developed a highly sophisticated, complex interplay of different forms of immune responses that simultaneously deal with a variety of needs, Dr. McDevitt commented.

To manipulate these responses, requires a much more precise understanding of how they occur, and what controls them than scientists now have.

Dr. McDevitt's work is sponsored by the National Institutes of Health, the Arthritis Foundation, and the American Cancer Society.

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