

## Cell-Mediated Immune Response

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### 1996 Nobel Prize Medicine

Peter Doherty and Rolf Zinkernagel were awarded the 1996 Nobel Prize in Physiology or Medicine for their discovery of the specificity of the cell-mediated immune response mounted by our immune systems against viruses. They were particularly able to identify the mechanism behind the recognition of self molecules against foreign and harmful organisms.

Doherty and Zinkernagel discovered how white blood cells, especially T-lymphocytes, recognize and kill virus-infected cells. Their discovery offered a great deal of information to clinical medicine especially in the field of immunology and virology.



The banner features a bright orange background. At the top center is a white icon of a flask with a flame, followed by the word "EXPLORABLE" in a white, sans-serif font. Below this, the phrase "Quiz Time!" is written in a white, cursive script. Underneath, there are three white-bordered boxes, each containing a different image and a quiz title. The first box shows a pair of red roller skates on a wooden deck, with the text "Quiz: Psychology 101 Part 2". The second box shows a fan of colorful pencils, also with the text "Quiz: Psychology 101 Part 2". The third box shows a Ferris wheel at sunset, with the text "Quiz: Flags in Europe". In the bottom right corner of the banner, the text "See all quizzes =>" is written in white.

## Background

Try to imagine the environment that we live in. We are surrounded by a wide array of microorganisms that are always present in our environment. Our only defense from these harmful microorganisms is our immune system.

Our immune system is basically composed of various interdependent cells that act to protect our body from parasitic, bacterial, viral and fungal infections. Their main purpose is to eliminate foreign and harmful microorganisms along with infected cells and keep all self-molecules safe from infection. To be able to perform this task, the immune system must be able to detect, recognize and differentiate molecules from the harmful microorganism from normal self molecules. The immune system cannot simply destroy everything in its path regardless of the nature of the target cells and tissues.

Lymphocytes are one of the primary components of our immune defense. There are two types of lymphocytes, the B-cells and the T-cells. B-cells are responsible for our humoral immune response while T-cells are responsible for our cell-mediated immune response. B-cells were already widely understood during the 1970's. Scientists have already discerned how antibodies work against foreign bodies such as bacteria. The less understood topic during that time was cell-mediated immune response and how cellular immune effectors recognize and kill virus-infected cells without harming normal healthy cells.

## **The Winners**

Peter Doherty was born on the 15th of October 1940 in Brisbane, Queensland. He attended the Indooroopilly State High School. He earned his BVSc (Bachelor in Veterinary Science) in 1962 from the University of Queensland. He also received his MVSc master's degree in veterinary science in 1966 from the same university. He then attended University of Edinburgh in Scotland for his Ph.D. which he finished in 1970. After receiving his Ph.D., he went back to Australia and conducted research on immunology at John Curtin School of Medical Research in Canberra.

Rolf Zinkernagel was born on the 6th of January, 1944 in Riehen, a village near Basel, Switzerland. At an early age, his mind was already set to pursue medicine and become a doctor. He studied medicine in the University of Basel and earned his M.D. in 1970. He became a visiting fellow in the Department of Microbiology in John Curtin School of Medical Research from 1973-1975. It is during this time that he collaborated with Peter Doherty. It was also due to their scientific interaction that he chose to enroll as a Ph.D. student at the age of 28 at ANU. He received his Ph.D. from Australian National University in 1975.

## **The Specificity of Cell-Mediated Immune Response**

The main goal of the research conducted by Peter Doherty and Rolf Zinkernagel was to study how the immune system, particularly T-cells which are involved in cellular immune response, could protect mice from a virus that causes LCM or Lymphocytic Choriomeningitis. Doherty and Zinkernagel injected LCM-immune T-cells into immunosuppressed, virus-infected recipients. The T-cells home equally well to lymphoid tissue of mice from the same strain and mice from another strain. Surprisingly, they found that the T-cells continue to multiply only in the mice from the same strain. This means that replication is not triggered by the virus, but is dependent on the thymus-derived lymphocytes exposed to histocompatible, virus-infected target cells.

In a similar study, they also found that the T-lymphocytes, despite their reactivity with the virus, were not able to kill the virus-infected cells from a different strain of mice. This means that being infected with the virus is not the only factor considered by the T-cells for them to attack the virus-infected cells. The virus-infected cells must also be histocompatible with the T-cells. This means that T-cells from a strain of mice will not attack virus-infected cells of another strain of mice because they are not histocompatible.

The next logical question is how does the T-lymphocyte recognize histocompatible virus-infected cells? The answers to their question were proteins encoded by the Major Histocompatibility Complex that are expressed on the surface of cells which displays self antigens. This histocompatibility antigen enables the T-cells to recognize self molecules. Integrating all the results that they were able to gather, they concluded that

the [cellular immune response](#) [1] needs to simultaneously recognize both foreign molecules and self molecules via histocompatibility antigens.

Succeeding researches conducted by other scientists showed that if a cell is infected by a virus, a small part of that virus is displayed bound to the cell's histocompatibility antigen on the cell's surface. The complex formed by the virus and histocompatibility antigen serves as the signal for the T-cell receptors to recognize the virus-infected cells.

## Clinical Relevance

The most immediate impact of this discovery was on the field of research. As mentioned above, the discovery of the virus-histocompatibility antigen complex was triggered by this discovery. Our increased knowledge concerning the specificity of cellular immune response enables us to strengthen beneficial immune reactions. On the other hand, that same knowledge also enables us to diminish or change unwanted immune reactions towards the body's own tissue, such as those occurring in rheumatic diseases. This discovery also triggered the development of new vaccines that will protect us against all these infectious diseases.

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### Links

[1] <http://www.medicinenet.com/script/main/art.asp?articlekey=6172>