



K O N I N K L I J K E N E D E R L A N D S E  
A K A D E M I E V A N W E T E N S C H A P P E N

**Dr A.H. Heineken Prize for Medicine 2010 awarded to Professor Ralph Steinman of the Rockefeller University**

Your Royal Highness,

Members of the Board of the Dr H.P. Heineken Foundation

and the Alfred Heineken Fondsen Foundation,

in particular their chairwoman, Mrs. De Carvalho,

Esteemed laureates,

Ladies and gentlemen,

Professor Steinman,

The jury has awarded you the 2010 Dr. A. H. Heineken Prize for Medicine for your discovery of the dendritic cell and its role in the immune response system.

I still remember the fierce debate that raged at the Mononuclear Phagocyte Conference in Leiden in 1978, when you presented this relatively rare, odd-looking cell. It was not only difficult to find and isolate, but it also did a few things better than ordinary macrophages. Looking back, we must conclude that you were right and that your discovery was very important for our understanding of biology and medicine. Indeed, researchers have studied dendritic cells extensively in recent years as a cancer treatment.

Ladies and gentlemen,

What are these cells? Dendritic cells are cells that sense invasion by foreign material, also called antigens. As sentinels, they are present in all the tissues of our body. We find them in the skin, inside the nose, lungs and intestines. and in the lymph nodes and spleen. They are able to enlarge their surface by growing projections called dendrites – not to be confused with the dendrites of the nervous tissue.

Before the discovery of the dendritic cell, it was not clear how the major cells of our immune system, the T lymphocytes or ‘T cells’, were able to react to abnormal cells such as infected cells, cancer cells or transplanted cells. How did T cells detect these abnormal cells? At the time, it was thought that macrophages performed the initial handling, and that they would process the material and then present it to the T cells.

In 1978, together with the late Zanzvil Cohn, Professor Steinman discovered a completely new cell type, the dendritic cell, by means of microscopy. In the years to follow, he demonstrated that the dendritic cell is the initiator of T cell responses. Virtually single-handedly, he placed the dendritic cell at the heart of T cell response: this unique, tiny set of cells recognises and captures



the antigens of foreign invaders, processes them and presents them to the T cells. Steinman was the first to show that activated dendritic cells act in small numbers with extraordinary potency. Furthermore, dendritic cells regulate the functioning of other cells in our immune system, such as the B lymphocytes (the cells that produce antibodies).

Steinman's work taught us that dendritic cells are crucial in the defence against infectious diseases, in allergic disorders such as asthma, in autoimmune diseases, but also in cancer and transplantation.

In 1980, Steinman and his group described the first specific marker on the surface of the dendritic cell. He took another crucial step forward in 1985, when he studied the Langerhans cells in the skin. Although it had been reported earlier that Langerhans cells are important in contact allergy, he performed the crucial investigations establishing that the Langerhans cells in the skin are dendritic cells.

Steinman's assertion that dendritic cell maturation is needed to induce robust T cell responses is now universally accepted. He was also the first to propose the concept of dendritic cell maturation. Matured dendritic cells stimulate the immune response, while a lack of maturation turns off the immune response, as is needed to tolerate the body's own cells. These concepts have led to rational protocols to induce tolerance or immunity by interventions such as vaccination. Since the days of Jenner and Pasteur, vaccination has largely been an empirical field. Steinman has taught us that vaccination works by virtue of proper functioning dendritic cells.

Professor Steinman, you are widely recognized as a major contributor to immunology. Your discoveries, which were obtained during a long and often difficult scientific journey, have become essential components of all modern textbooks of immunology. The 2010 Heineken Prize for Medicine acknowledges your discovery of the dendritic cell, its nature, and its function; you have used this knowledge to advance our understanding of the causes of human disease, and cleared the way to developing therapies that will – no doubt – benefit patients.