University of Zurich[UZH]

Rolf Zinkernagel

Nobel Prize in Physiology or Medicine 1996

Nobel Prize in Physiology or Medicine 1996 for "discoveries concerning the specificity of the cell mediated immune defense"

* 6 January 1944 in Riehen

1979–2008 Professor of Experimental Immunology at the University of Zurich

Tell-Tale Proteins

The original plan was to specialize in tropical medicine in Africa, or to practice winter-sports medicine in some alpine valley. For Rolf Zinkernagel, studying medicine at the University of Basel opened up possibilities to satisfy his taste for adventure – but in the end he chose the adventure of research. Zinkernagel said that his motivation and enthusiasm for research was about "finding out something that no one before me had known."

It was a continuing education course in experimental medicine in 1970/71 that first brought Zinkernagel to Zurich and set him on a career in research. At the time, he had no idea that, nine years later, he would return to the University of Zurich, this time as an associate professor. After earning his doctorate, Zinkernagel had applied to participate in this prestigious course in order to gain clarity on his professional ambitions. He was selected as one of ten students from the whole of Switzerland. The course gave him insights into the new and fascinating possibilities of immunological research as well as the opportunity to make important contacts.

The theoretical part of the course was followed by practical work at the University of Lausanne. In the department of biochemistry, Zinkernagel became acquainted with the joys and frustrations of working with microorganisms in the laboratory. In doing so, he was following a family tradition: His father was a biologist at the Basel chemical company J. R. Geigy AG, and his mother, who came from La Chaux-de-Fonds, was a laboratory assistant.

The next step was to be a period of research abroad. But where? By now, Rolf Zinkernagel was no longer on his own. During his studies, he had met Kathrin Lüdin, who had specialized as an ophthalmologist. Together, they wrote over 50 applications for research positions. Finally, through Henri Isliker, his boss in Lausanne, Zinkernagel came into contact with the head of the Department of Microbiology at the Australian National University in Canberra. And so, in 1973, the family moved with their two small children and a scholarship from the Swiss National Science Foundation to the other end of the earth. In his new laboratory, Zinkernagel installed himself in the only free place: "It was a small room that I had to share with Peter Doherty, an Australian veterinarian." What started as the chance sharing of workspace evolved into a successful team of two friends.

The two researchers began studying the body's immune response to a virus that causes meningitis in mice with the aim of discovering exactly how this mechanism functions. Zinkernagel turned this work into a second doctorate. Using the only mouse cell line available to them in Canberra, they tested the immune response in various mouse strains. To their surprise, they found that the virus-immune cells of certain genetically defined mouse strains could destroy the virus-infected cell line, while others could not. Thus, fate had handed them a major discovery: Zinkernagel und Doherty pursued this discrepancy – and learned how the immune system recognizes the cells that are infected with viruses. It was immediately clear to both researchers that they had entered new scientific territory. Zinkernagel remained

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modest, however: "The mix for my subsequent Nobel Prize was 50 percent luck, 49.5 percent hard work and 0.5 percent inspiration." He also saw his medical training as an advantage for research: "A physician is used to complex thinking."

After its publication in the scientific journal *Nature*, Zinkernagel and Doherty's discovery spread very rapidly throughout the scientific world, which increasingly effected the researcher's private life. This was dramatically brought home to the Zinkernagels in December 1974. Kathrin Zinkernagel, heavily pregnant with their third child, was already in the maternity hospital while Rolf Zinkernagel had to discuss his findings at a conference in Canberra. Immediately after his presentation, he jumped on his bike and pedaled the ten kilometers to the hospital as fast as he could. But he arrived "ten minutes too late at the hospital, and 'das Buschi' had already arrived," as he wrote to a Swiss friend. "Buschi" is the Basel German word for baby.

A brief stay in Switzerland was followed by a move to California in July 1975. Rolf Zinkernagel had for some time had an invitation from the Scripps Clinic in La Jolla in his pocket. In the Scripps laboratory, he was able to research into the role of the thymus in immune responses. Here, too, he achieved spectacular results. Then, in 1976, he received an offer from the University of Zurich: The chair for toxicology at the Department of Pathology was vacant. Zinkernagel had long given up hope of a suitable position in Switzerland, but now he suddenly saw the possibility of returning and building a bigger research group. This involved, however, difficult and protracted negotiations with the Zurich authorities. The Zinkernagels required strong nerves: The signed contract reached him just ten days before he was scheduled to commence work. In fall 1979, Rolf Zinkernagel began work as associate professor of experimental pathology at the University Hospital; he was appointed full professor in 1988.

The laboratory for immunological research had to be built from scratch. Machinery and equipment were acquired, and space installed for the accommodation of the experimental animals – particularly mice. Rolf Zinkernagel himself drew up the plans for the "mouse hotel." He was greatly helped by his friend Hans Hengartner, a biochemist who moved from Basel to Zurich and became a professor at both the University and ETH. Together they established the Institute of Experimental Immunology, which they led together for almost thirty years. With their team, they observed viruses in mouse strains in order to learn more about the functions and development of the immune system. Young scientists from all over the world came to the Institute to learn the latest immunological techniques.

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When Rolf Zinkernagel left the Institute in the evenings, the University Hospital's park already offered him a taste of his own garden in Zumikon, where his family lived in an old farmhouse in spacious surroundings. Kathrin Zinkernagel had her own practice as an ophthalmologist – indeed, the parents' professions clearly influenced their children: All three would later study medicine.

In October 1996, the news of Zinkernagel receiving the Nobel Prize was akin to a bomb going off in the normality of everyday life and work. Rolf Zinkernagel was then 52, and the telephone call from Stockholm came as a surprise. He was suddenly exposed to the full glare of publicity: Well-wishers and journalists waited in throngs outside his little office at the University Hospital, and bottles of champagne were uncorked. But the next day, the professor turned up to start work at seven o'clock as usual. Then, in Stockholm in December, the Zinkernagels celebrated with Peter Doherty, their Australian friend and Zinkernagel's co-laureate, what the researcher still happily recalls as a "great party."

Zinkernagel used the sudden popularity deriving from the "halo of the Nobel Prize," as he termed it, to realize an unusual idea: He called the editor-in-chief of the Swiss tabloid *Blick* and offered to write a regular column for the paper. His aim was to make the case for basic research. And Zinkernagel inspired many of his colleagues to present the results of their research in easily accessible language in the pages of *Blick*. Week after week, his column explained to a broad readership how scientific findings affect our everyday life and health, or how researchers come to their conclusions. During this period, which lasted about five years, he became one of the most popular scientists in Switzerland.

In 2008, after nearly three decades of research in Zurich, Rolf Zinkernagel

retired, at the same time as his colleague Hans Hengartner. Despite officially retiring, he has kept his little office in the University Hospital, where he can still often be found. His daughter, Annelies, works as a senior physician at the same hospital.

His weekly column in *Blick* made Rolf Zinkernagel one of the most popular scientists in Switzerland.

As professor emeritus, Zinkernagel continues researching today. But he does now have more time for his garden in Zumikon, and for music – he loves opera and has begun to play the cello. Zinkernagel has also been a member of the Rorschach Section of the Swiss Alpine Club since his youth, just like Tadeus Reichstein before him. There he has yet one unfulfilled wish: Climbing Mont Blanc, the highest mountain in the Alps. *Margrit Wyder*

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Honored in Zurich:

New Insights into Our Immune System

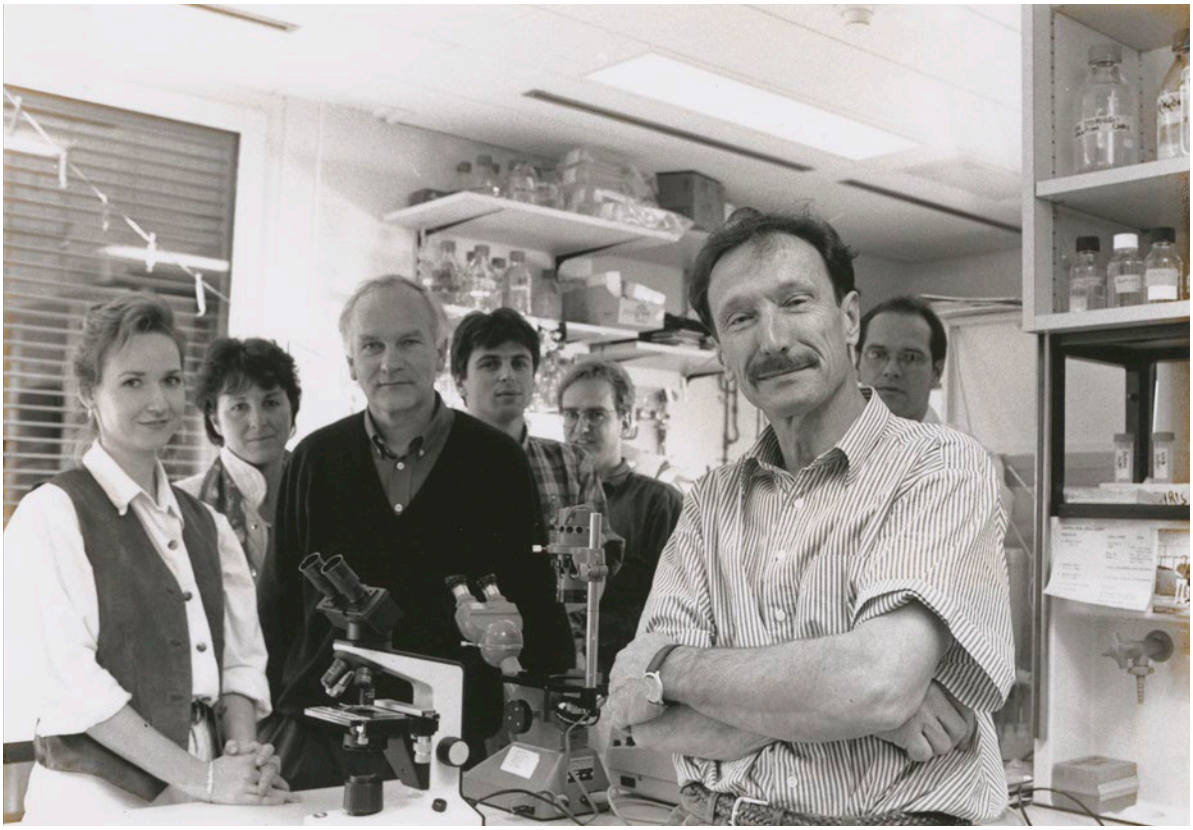
When a virus penetrates a body cell, the cell will produce viral DNA or RNA. This is how the virus can multiply and spread through the body; illness is often the result. Our immune system, which consists of a complex network of various organs, cells, and molecules, protects us from such attacks by microorganisms. Special white blood cells, known as T lymphocytes, or T cells, circulate in our bodies, acting as immune cells. They originate in the bone marrow, as do all blood cells, and then mature in the thymus, an organ located behind the breastbone. (The letter T indicates that they stem from the thymus.) It is the job of these lymphocytes to identify and destroy cells infected with viruses.

But how can these T-cells distinguish infected cells from healthy ones? This was the discovery made by Rolf Zinkernagel and Peter C. Doherty in their research with genetically different mouse strains at the Australian National University in Canberra: The body's cells possess protein extensions that protrude from the cell walls and are monitored by the T-cells. If a cell is infected by a virus, foreign proteins also reach the surface of the cell. It is precisely this mix of foreign proteins with the cell's own proteins that the specialized immune cells recognize as dangerous. They then dock on to the infected cells and kill them.

Zinkernagel and Doherty's discovery is instrumental in the treatment of infectious diseases and the strengthening of the immune system. But cancer research, too, is looking with hope to the work of these "killer cells." Both in the laboratory and recently in clinical practice, scientists have succeeded in demonstrating that specially prepared T cells can identify cancer cells as dangerous, and then destroy them.

Zinkernagel and Doherty's findings are also significant for transplant surgery. In such cases, it is particularly dangerous for the cells in a transplanted organ to be attacked by the body's immune system. The targeted shutting down of immune defenses is therefore a major objective.

Several Nobel Prizes have been awarded for research into the immune system. In this area of medicine, the practical benefits of the prize-winning discoveries or inventions can be easily verified, a factor Alfred Nobel expressly stipulated in his testament. Already the first winner of the prize for medicine, German doctor Emil von Behrings, received the honor on this basis: He developed a vaccination against diphtheria, which often has fatal consequences for children. *(MW)*



The biochemist Hans Hengartner (third from left) and Rolf Zinkernagel led the Institute for Experimental Immunology at the University of Zurich for nearly 30 years.

Peter Doherty and Rolf Zinkernagel in Stockholm in 1996 upon receiving the Nobel Prize for their research on the body's immune response to viruses.