

Laudatory speech for Rafi Ahmed and Antonio Lanzavecchia

[Check against delivery.]

The 2017 Robert Koch Award goes to Professor Rafi Ahmed, Director of the Vaccine Center at Emory University in Atlanta and Prof. Antonio Lanzavecchia, Director of the Institute for Biomedical Research in Bellinzona and Professor at ETH Zurich, for their ground-breaking research on immunological memory.

Rafi Ahmed first completed a Bachelor's degree in chemistry at Osmania University in Hyderabad, before transferring to Idaho State University in the USA, where he did a Master's in microbiology. He then completed his doctorate at Harvard University in 1981. He moved to the west coast, first to Scripps Clinic and then to the University of California in Los Angeles. He then worked as Assistant, Associate and, since 1995, Full Professor at the Institute for Microbiology and Immunology. In 2000 he transferred again, this time to Emory University in Atlanta. Since then, he has been Charles Howard Candler Professor of Microbiology and Immunology, and Director of the Vaccine Center and the AIDS Research Center.

Antonio Lanzavecchia studied medicine at the University of Pavia, specialising in paediatrics and infections diseases. From 1981 to 1983 he was Assistant Professor at the University of Genoa, before transferring to the famous Basel Institute of Immunology. He stayed there for 16 years. In 1999, he transferred to the new Institute for Biomedical Research in Bellinzona as its Director and became Professor for Human Immunology at ETH Zurich.

If you ask me, the ability to remember experiences is one of the most fascinating properties of the immune system. Even the ancient Greeks knew about it. In the year 400 BC, Thucydides reported on an epidemic during which those who had overcome the disease and recovered were used to care for the sick, as, in his words, it was known that no-one would get the disease a second time. Our knowledge of how this immunological memory, this received immunity, works is much more recent and is directly connected to Berlin. Robert Koch and his students laid the foundations here. In 1890, Behring and Kitasato were able to show that immunity against tetanus or diphtheria can be transferred with the serum of vaccinated animals, and that protection is specific to the vaccine. In 1897, Paul Ehrlich developed the "side chain theory", which states that the "antibodies" for the serum are produced by special cells, which adjust, or rather "adapt" to the vaccine.

We have only had more precise knowledge of cells that carry immunological memory for roughly 50 years. And Rafi Ahmed and Antonio Lanzavecchia have played a key role in this.

Rafi Ahmed's first major contribution is the proof that there is actually an immunological memory. That means that there are memory lymphocytes, which survive even in the absence of the original pathogen, and are not activated again until the pathogen recurs. In this way, he succeeded in disproving the alternative theory that acquired immunity is a lasting immune reaction.

Rafi Ahmed's second key contribution is the proof that the long-lived activated lymphocytes are exhausted at a certain stage in chronic immune reactions to viruses. They stop working properly, thereby actually facilitating the chronic immune reaction, and cannot remove the viruses. Rafi Ahmed succeeded in showing that it is inhibitory receptor PD-1 that inhibits lymphocytes. If the receptor is blocked, the lymphocytes react strongly again and the viruses are eliminated. With this reactivation of the immune system, Rafi Ahmed developed an effective therapy against chronic infections.

His third significant contribution is his discovery of long-lived plasma cells at the same time as my working group. Plasma cells develop from activated B lymphocytes and they are responsible for secreting the antibodies that protect us against diseases by neutralising pathogens immediately on penetration. It was long thought that plasma cells themselves have only short lifespans, as they disappear rapidly from the organs where they are formed, and that they have to be reformed again and again from activated B lymphocytes. We now know that freshly formed plasma cells permeate the bone marrow and secrete their antibodies into the blood throughout our whole lives. This knowledge that the long-lived plasma cells survive in the bone marrow is important for developing effective vaccination procedures. It is even more important for the development of effective therapies for chronic diseases caused by antibodies, e.g. allergies and many rheumatic diseases. Today, we can refer to this as a new class of diseases, the plasma cell diseases.

Like Rafi Ahmed, Antonio Lanzavecchia has done pioneering research into immunological memory. He laid the foundations for a sophisticated understanding of T lymphocytes of memory by studying their chemokine receptors. He found that the special purposes of T lymphocytes can be identified based on their chemokine receptors. Memory T lymphocytes, which are attracted to inflamed tissue, act on the inflammation there. T lymphocytes attracted to lymph nodes control the activation of B lymphocytes and formation of antibodies there. And so on. These observations were not only original, they were first made on humans and later confirmed in mice, which is rare. This was a fundamental finding with far-reaching significance for biomedicine, as it allows us to determine the quality of the immunological memory and influence it specifically.

Antonio Lanzavecchia then focused on activating T lymphocytes, or rather on the interaction with the cells that present the antigen, thus activating them. These are the dendritic cells on one hand, and the B lymphocytes on the other. He showed that B lymphocytes can present as antigens to the T lymphocytes in an active dialogue, and be activated retroactively by them. Dendritic cells must first mature to competent antigen presenters, and they develop the ability to stop the immune reaction in the course of the immune reaction. Antonio Lanzavecchia's research is of fundamental practical significance. It allows us to control the quality of immune reactions.

Antonio Lanzavecchia himself used his findings on the activation and differentiation of memory lymphocytes to keep them alive, multiply them and investigate their molecular structure outside the body. He developed a method for cloning human B lymphocytes, which he used to produce monoclonal antibodies. Antibodies against pathogens of global significance, as there are no effective vaccinations against them. Antibodies from patients who have developed immunity to these pathogens. Human protective antibodies against influenza, HIV, herpes viruses, malaria and SARS viruses. Antonio Lanzavecchia's approach facilitates a new generation of effective, passive vaccination procedures. And it is a promising approach for understanding why some people become immune while others do not.

Both Rafi Ahmed and Antonio Lanzavecchia have laid the groundwork for our current understanding of immunological memory, the cells that carry it and the antibodies that protect us throughout our lives. Their work has immense practical significance for treatment of infections, chronic inflammations, autoimmune diseases and cancer. We are honoured to present them with the 2017 Robert Koch Award. I congratulate them sincerely.

Andreas Radbruch, for the Advisory Council of the Robert Koch Foundation