Robert-Koch-Stiftung

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Robert Koch Award for 2016 goes to Alberto Mantovani and Michel C. Nussenzweig / Kai Simons receives the Robert Koch Gold Medal

With their outstanding research, laureates lay the foundation for understanding the way in which different immunological mechanisms function

Berlin – The Robert Koch Foundation is jointly awarding this year's 100,000 Euro Robert Koch Award to Professors Alberto Mantovani, Humanitas University, Milan, Italy, and Michel C. Nussenzweig, The Rockefeller University/Howard Hughes Medical Institute, New York, USA. The award honors the pioneering research work conducted by both immunologists, which has resulted in new treatment options, for example in cancer or in the fight against HIV infections.

Professor Kai Simons, Max Planck Institute of Molecular Cell Biology and Genetics in Dresden, receives the Robert Koch Gold Medal for his lifetime achievements, in particular for his characterization of membrane-forming lipids and the development of the Lipid Raft Model.

The awards will be presented at an official ceremony on November 4, 2016 at the Berlin-Brandenburg Academy of Sciences and Humanities in Berlin.

Professor Alberto Mantovani is being recognized for his pioneering work on the link between inflammation and cancer. With his observations that cells of the innate immune system accumulate around certain cancer foci, he opened up an entirely new field of research. Mantovani was able to prove that phagocytes, which are involved in the natural inflammatory response, can be reprogramed in the oxygen-deficient microenvironment of tumors and influence tumor growth. The so-called "tumor-associated macrophages" behave as "corrupted policemen": they promote cancer cell proliferation, release angiogenic factors that encourage new blood vessels to grow into the tumor and, by releasing enzymes, make the surrounding tissue more permeable to tumor cells, which can promote the formation of metastases. They also contribute to taming effective anti-tumor immunity by triggering molecular breaks called checkpoints in lymphocytes. By characterizing the involved chemokines and their receptors, Mantovani was able to demonstrate how a chronic inflammatory response promotes the development and metastasis of cancer. These studies paved the way to a change in paradigm on the nature of cancer, from a tumor cell-centric view to one that includes corruption and taming of immune cells as an essential component of the "ecological niche" of neoplasia. This shift in vision is now reflected in the development of immunotherapy approaches targeting checkpoints and corrupted policemen.

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Michel C. Nussenzweig's groundbreaking work uncovered broad and potent neutralizing antibodies to HIV-1 and established that they are a safe and effective immunotherapeutic for infected humans. Nussenzweig addressed a fundamental issue in immunology – the lack of a detailed understanding of the human antibody response – by developing robust and scalable methods for the cloning of antibody genes from single human B cells. He first applied this approach to define how tolerance develops in normal individuals and later to the HIV-1 antibody problem.

Antibodies that neutralize HIV-1 were first isolated early in the epidemic. Although these antibodies protected macaques from infection, the doses were so high that it led the field to abandon antibody-based vaccines and therapies. Nussenzweig's discoveries of potent anti-HIV antibodies have re-energized the vaccine field and opened the door to new antibody based methods for HIV-1 prevention and therapy.

Nussenzweig made the key breakthrough in this area by applying his antibody cloning techniques to anti-HIV antibodies. His work, and that of others that rapidly adopted his methods, led to the discovery of naturally arising anti-HIV antibodies that were orders of magnitude more potent than previously known antibodies. Moreover, they revealed novel targets of vulnerability. The new antibodies neutralized up to 95% of all HIV-1 strains individually, and nearly all known strains when combined even at very low concentrations.

The antibody cloning experiments revealed that anti-HIV-1 antibodies differ from antibodies to nearly all other pathogens in their high rate of somatic mutation. This observation led Nussenzweig to propose the idea that these antibodies arise by sequential, iterative rounds of antibody mutation, selection, and viral escape. Nussenzweig went on to establish that sequential immunization can elicit such antibodies in mouse models and his ideas are the basis for new vaccination trials in humans.

In addition to his work on vaccines, Nussenzweig established that passive administration of the antibodies he cloned can control infection in humanized mice and in macaques chronically infected with SHIV. Moreover, he showed that a single antibody injection can protect macaques from SHIV infection for up to 23 weeks and he established a relationship between antibody concentration in serum and protective activity.

The results obtained in Nussenzweig's pre-clinical studies led him to conduct phase 1 clinical trials in HIV-1 infected individuals. His groundbreaking studies in humans established that antibodies are safe and effective for HIV-1 prevention and therapy in humans. A single infusion of one of his antibodies, 3BNC117, was well-tolerated, rapidly decreased viral loads in viremic individuals by an average of 1.48 logs, and this effect remained significant for 4 weeks. In addition, the antibody infusions activated endogenous host immune responses against the virus, and accelerated the clearance of virus and infected cells.

Based on his results Nussenzweig proposed that antibodies might be administered on a quarterly or bi-annual basis for therapy or passive protection in humans. Clinical trials to test this idea are currently underway.

Gold Medal for the characterization of membrane-forming lipids and the development of the Lipid Raft Model

Professor Kai Simons receives the Robert Koch Medal in Gold for his impressive lifetime achievements, which took him from Finland via the USA to Heidelberg and to the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden. He is an expert for cell membranes, those wafer-thin membranes made of a double layer

of fat molecules ("lipids") which surround each cell of the human body. It was long thought that these membranes were only a largely uniform fluid matrix. Thanks to Kai Simons, it has been possible to clearly demonstrate the great dynamic and wide range of functions of lipid membrane systems. He discovered island-like structures in the lipid bilayer of cell membranes, which reminded him of the log rafts of Finnish lumberjacks drifting downstream - hence the name "lipid rafts". However, in fact these nanodomains are dynamic. They fluctuate in size and can be clustered to form liquid platforms that play a significant role in signal transduction and many other membrane processes.

The lipid raft model is linked to new therapy approaches, for example in neurological diseases such as Alzheimer's, in which malfunctions in lipid rafts play a role. Kai Simons also found clear evidence that many viruses – including influenza, Ebola, measles and HI viruses – use lipid rafts to invade their host cells or to leave them again, by encasing themselves with rafts from the cell membrane.

Photos of the laureates may be downloaded for editorial use at
www.robert-koch-stiftung.de/Laureates2016

About the Robert Koch Foundation

The Robert Koch Foundation is a non-profit foundation dedicated to the promotion of medical progress and is based in Berlin. It promotes basic scientific research in the field of infectious diseases, as well as exemplary projects that address medical and hygienic issues. Patron of the Foundation, which was founded in 1907, is German President Joachim Gauck.

The Foundation confers a number of distinguished scientific awards each year: the Robert Koch Award – one of Germany's most distinguished scientific awards, the Robert Koch Gold Medal, three awards for young scientists and, since 2013, the Hospital Hygiene and Infection Prevention Award.

Robert Koch (1843 – 1910), after whom the award is named, was the founder of modern-day bacteriology, for which he was awarded the 1905 Nobel Prize for Medicine and Physiology. From 1891 until his retirement in 1904, Koch was Head of the Institute for Infectious Diseases in Berlin.

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