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New trends in the field of immunology

B- and T- lymphocytes along with macrophages have long been regarded as the most important cells of the human immune system and have thus been a major focus of research. This has now changed and it is now the dendritic cells that are regarded as the major components of the adaptive immune system and have become a major focus of scientific interest. Research into innate immune defence mechanisms has also become more important due to the discovery of the role of Toll-like receptors as first-line of defence. The award of Nobel Prizes in Physiology or Medicine to researchers focussed on these aspects is a clear reflection of these new developments.

Although Nobel Prizes are usually awarded for medical and scientific discoveries that were made a long time ago, the award itself is often an excellent indicator of current research and development trends. It often takes many years and decades before a breakthrough discovery is recognised and more than once the researchers behind the groundbreaking discoveries have passed away before their discoveries have been recognised.

Dendritic cells – initially met with scepticism and now a key element in research

On 3rd October 2011, the Nobel Assembly at Karolinska Institutet in Stockholm awarded the Nobel Prize in Physiology or Medicine to the immunologist Ralph M. Steinman "for his discovery of the dendritic cell and its role in adaptive immunity" unaware that Steinman had died from cancer three days before the news of the award would have reached him. In 1973, Ralph Steinman discovered a new strange-looking cell type which, with its long protrusions, looked very similar to neurons. Steinman's dendritic cells are present in tissues in contact with the external environment, such as the skin and the inner lining of the intestines, the lungs and the oesophagus. For a long time Steinman was virtually the only researcher with an interest in dendritic cells and some researchers were even sceptical about their existence. Generations of researchers (including many Nobel Laureates) had previously shown that three cell types were responsible for an adaptive (acquired) immune response: B- and T-lymphocytes (and their subtypes) and macrophages.

Steinman's research fundamentally changed the prevailing view and dendritic cells have since become a key element of immunological research. It has since been shown that it is the dendritic cells rather than the macrophages that are the most important antigen-presenting cells. Mature dendritic cells, i.e. cells that have taken up a bacterium or something similar, migrate to the lymph nodes where they present the pathogen's 'molecular warrant of apprehension' to passing T-cells, resulting in an adaptive immune response.

TLRs recognise the specific pattern of intruders

Model of a Toll-like receptor located in the plasma membrane of an immune cell.
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Toll-like receptors (TLR) are another controversial research topic; they are present on the surface of immune cells (including on the surface of dendritic cells) where they are the first-line of defence against harmful intruders. They recognise molecules that are shared by pathogens but which are distinguishable from host molecules on the basis of specific pathogen-associated molecular patterns. The TLRs got their name from their similarity to a protein coded by the Toll gene identified in Drosophila by Nobel Laureates Christiane Nüsslein-Volhard and Eric Wieschaus in 1985. The Toll receptor was originally known for its developmental role in the early embryogenesis of fruit flies. The immunologist Jules Hoffmann later found that Toll gene mutations led to the death of the flies due to their inability to mount an immune response. This finding boosted research into the immune defence of "simple" invertebrate organisms.

Two years after Hoffmann's discovery, Bruce Beutler discovered TLRs in mice. In the meantime, at least twelve homologous TLRs have been discovered in humans. TLRs are the most ancient conserved components of the innate immune system that induces inflammatory reactions in response to bacterial intruders as well as sepsis, which is a major cause of critical illness worldwide. Alongside Steinman, Bruce Beutler and Jules Hoffmann were awarded the other half of the 2011 Nobel Prize in Physiology or Medicine for their discoveries concerning the activation of innate immunity. Scientists from Baden-Württemberg

universities also play a substantial role in the investigation of TLR-dependent immune responses.

Diverse cross-sectoral field of science

Immunofluorescence image of two dendritic mouse cells with MHC complexes (labelled with red-fluorescent antibodies) on their surface.
© University Hospital Heidelberg

Allergic reactions are also one of the central themes of immunological research with applications in medical practice. Due to their huge and growing importance in our society, allergic reactions are dealt with in a separate dossier on allergies. The dossier also focusses on research into signalling cascades that are involved in the development of allergic disorders and which are triggered by mast cells. It has long been assumed that mast cells are involved in the development of autoimmune diseases; however, recent results obtained by researchers from the German Cancer Research Center suggest that this is not the case. Any organ whatsoever or even the entire body (systemic reactions) can be affected by immune system disorders. Autoimmune diseases and the immune system's ability or failure to detect cancer cells, transplantation immunology and research into immune system stem cells are highly topical issues addressed in the articles in the dossier on immunology.

The Heidelberg immunologist Stefan Meuer has referred to immunology as a cross-sectoral science whose individual branches are not easy for single researchers to work on alone. Immunological findings have an effect on many areas of biology and medicine at the same as being affected by developments in other research disciplines. It is precisely these interactions that make immunology a fascinating, constantly rejuvenating science. More than a hundred years after the first Nobel Prizes in Physiology or Medicine were awarded to the founding fathers of modern immunology – Emil von Behring, Robert Koch, Ilya Mechnikov and Paul Ehrlich – immunological research is always good for coming up with unexpected discoveries worthy of the Nobel Prize.

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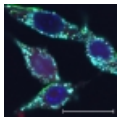
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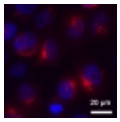
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