How do immune cells recognise infectious pathogens?

Scientists of the University of Heidelberg and the German Cancer Research Centre have clarified the functional principles of an important receptor for bacterial infections: immune cells recognise bacterial and viral pathogens with a receptor known as toll-like receptor 9 (TLR9), which mediates biochemical reaction chains in order to fend off intruders. This discovery made by the Heidelberg researchers paves the way to develop new anti-infective substances and vaccines.

A team of researchers led by Professor Dr. Alexander Dalpke at the Institute of Hygiene at the University of Heidelberg is involved with the "eyes of the innate immune system": tiny protein structures – toll-like receptors (TLRs) – are located on the surface of immune cells. Upon infection, these receptors recognise certain patterns in the genetic material of pathogens, which have persisted over the course of evolution, and subsequently induce defence reactions.

Two contact sites recognise the pathogen

A group of junior researchers led by Dr. Alexander Weber of the German Cancer Research Centre (DKFZ) in Heidelberg also deals with the recognition of these patterns. The young researchers have established a three-dimensional computer model of the TLR9 receptor, which was used as the starting point for the joint project of the two research teams. This rather time-consuming simulation is based on the prediction of individual receptor constituents from published data. Tests with different genetically modified receptor versions, which were designed using this three-dimensional "model", showed that two specific contact sites of the receptor are key for binding to the bacterial DNA.

Vaccines can be improved

The new findings enable the researchers to develop a far more accurate receptor model. This model can then be used in the area of pharmacology. Artificial nucleic acids produced in the laboratory imitate the bacterial genome and, therefore, lead to the activation of the innate immune system by way of the toll-like receptors. These pharmaceutical substances can for example be used for the production of vaccines in order to non-specifically enhance their effect. The new findings help the scientists to adapt these oligonucleotides more accurately than was previously possible.

The Heidelberg scientists will continue their basic research into the communication between pathogens and the immune system. Their next step will involve the transfer of previously gained information to other types of receptors. For example, in contrast to TLR9, TLR7 recognises viral, but not bacterial, genetic material. The researchers hope to be able to clarify previously unknown recognition mechanisms by combining the prediction of three-dimensional structures and experimental tests.

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Literature:

M. E. Peter, A. V. Kubarenko, A. N. R. Weber, A. H. Dalpke, Identification of an N-terminal recognition site in TLR9 that contributes to CpG-DNA mediated receptor activation, The Journal of Immunology, 2009, 182, 7690-7697.

Press release

10-Aug-2009
Source: Universitätsklinikum Heidelberg 05.08.2009 (P)