The right response to every pathogen

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In the event of an infection, the immune system releases messenger substances. These molecules can either activate immune cells to defeat invading pathogens, or inhibit them to prevent an excessive immune reaction. For this, the immune system has to decide very quickly what mixture of activating and inhibiting messenger molecules leads to a successful defence.

Researchers from the Helmholtz-Centre for Infection Research in Braunschweig, Germany, have now been able to show that hitherto underrated immune cells, so-called mast cells, decide at a very early stage of an infection which way the defence has to go. They only produce the crucial messenger substance beta-interferon during a viral infection, not during a bacterial infection. The reason for this: While on the one hand the molecule always helps to defeat viruses, it hinders on the other hand important immune cells to kill bacteria - and thus impairs the defence. The group's results have now been published in the scientific magazine *PNAS*.

Mast cells play a central role during allergic reactions, a function researchers have concentrated on until now. They reside directly under the skin and mucosae, and react immediately when an allergenic substance enters the body. As a result, reddened mucosae, swelling, runny eyes and a runny nose occur. However, mast cells also seem to have a crucial, but only superficially understood, function during pathogenic defence. "They wait precisely at that position where pathogens enter the body," says Nelson O. Gekara, researcher in the group "Molecular Immunology" at the HZI, "and thus belong to the very

first line of immune defence."

To investigate how mast cells react when they come in contact with bacteria and viruses, the HZI-researchers incubated mast cells and pathogens together in a petri dish. Then, they measured what messenger substances the cells produced. As soon as a virus infection occurred, the scientists were then able to detect beta-interferon, produced by the mast cells. Conversely, during a bacterial infection, no beta-interferon was found. "Until now it has been unknown that mast cells can virtually decide whether they produce beta-interferon or not," says Nicole Dietrich who did research on the mast cells. "During a viral infection, beta-interferon helps because it activates mechanisms in surrounding cells that support the virus defence."

The researchers found the reason for why mast cells do not produce beta-interferon during bacterial infections in the defence line that follows mast cells: "Beta-interferon inhibits precisely those cells that quickly eliminate invading bacteria," says Nicole Dietrich. Thus, mast cells determine very early which direction the immune defence is taking.

Important for this decision making are receptors on the surface of all immune cells: So-called "Toll-like receptors" activate mast cells as soon as a pathogen enters the body. When the receptors are triggered, mast cells produce a number of messenger substances that attract cells or keep them at distance, activate or inhibit them and thus regulate an optimised immune response.

"To produce beta-interferon, immune cells have to absorb the receptors and transport them into the cell interior. During a bacterial infection, mast cells refuse to incorporate the receptor and thus do not produce beta-interferon", says Nelson O. Gekara. This is another step towards understanding the complex network of messenger substances, immune cell and pathogen defence. "It seems as if every line of defence can

precisely decide which step will be the next and best."

More information: Dietrich Nicole; Rohde Manfred; Geffers Robert; Kröger Andrea; Hauser Hansjörg; Weiss Siegfried; Gekara Nelson O. Mast cells elicit proinflammatory but not type I interferon responses upon activation of TLRs by bacteria. Proceedings of the National Academy of Sciences of the United States of America 2010;107(19):8748-53

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