Press Release

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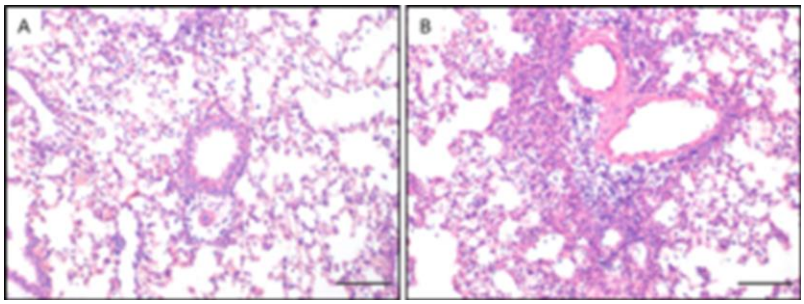
TOO MUCH OF A GOOD THING

SOMETIMES IT IS BETTER TO SLOW DOWN THE IMMUNE RESPONSE

Our immune system fights pathogens, for example to help us make it through an influenza infection. In its eagerness, the immune system sometimes overshoots the mark and damages inherent tissue of the body. This can actually exacerbate the course of disease. In their current publication in the scientific journal, PLOS ONE, scientists from the Helmholtz Centre for Infection Research (HZI) report that activation of a molecule called ICOS, which is situated on the surface of immune cells, limits the extent of lung damage during the infection. It is conceivable that this may be a means to mitigate the course of an influenza infection.



An infection with influenza can lead to severe damages of the pulmonary tissue, which are not only caused by the virus itself but also by cells of the immune system. A targeted activation of the molecule ICOS on immune cells of influenza-infected mice (fig. A) reduces the amount of tissue affecting immune cells in the lung compared to the untreated control group (fig. B) and thus salves the inflammation.

For this year the influenza season is over. For most of us, the classical symptoms of influenza like fever, pain, and tiredness, are a thing of the past for now. No reason to rest, though, for the scientists at the HZI in Braunschweig. Because influenza infections elicited by group A influenza viruses keep causing epidemics and pandemics with a high rate of mortality, in particular amongst infants and the elderly.

Prof Dunja Bruder, who directs research groups at the HZI and the University Hospital of Otto-von-Guericke-University, Magdeburg, and an international team of scientists investigate ways to mitigate the course of the disease in influenza patients. One of the major problems is the damage to lung tissue. "The tissue damage associated with influenza is not only caused by the viruses directly. The immune system fighting the invaders contributes to the damage. It has very effective mechanisms for fighting pathogens, but unfortunately it also destroys body tissue along the way," says Bruder. "We were therefore interested to see how we can prevent this collateral damage without also suppressing the defence against the virus."

In their work, the researchers focussed on a certain group of immune cells, called T cells. Some of these, called cytotoxic T cells, destroy cells that are infected by a virus, but also attack inherent tissue automatically and induce inflammation. For these cells to chase after viruses, they need to be fully activated first, which is done by a molecule called "inducible co-stimulator" or ICOS for short. This molecule resides on the surface of the already pre-stimulated T cells and enhances their activation when it encounters its specific binding partner. This binding partner, in turn, resides on other immune cells, which the T cells encounter in lymph nodes. The researchers simulated this event in the laboratory by specifically treating influenza virus-infected mice with a factor that is similar to the binding partner. With a surprising result: "When we artificially activate ICOS on T cells, we observe less damage to the lung tissue," says HZI scientist Dr Priya Sakthivel. "Under normal conditions, the influenza infection lures many immune cells, including T cells, into the lung. In the treated mice, we find lower numbers of these cells in the lung tissue. We have some initial evidence that the treatment kills many cytotoxic T cells." This reduces the level of damage caused by the immune system itself.

Another contribution is made by another group of T cells, the so-called regulatory T cells. They prevent an immune reaction from getting out of control. They also have the ICOS molecule reside on their surface. Once the molecule is activated, these T cells proliferate and inhibit inflammatory processes. Taken together, the researchers observed fewer cytotoxic T cells and more regulatory T cells. Due to this shift in balance or equilibrium, the inflammation of the lung is less pronounced and influenza infection lasts only insignificantly longer. "The improvements occur right in the phase, in which the tissue damage is most pronounced," says Bruder. It is conceivable for the future to activate ICOS in patients in order to protect them from a particularly severe course of an influenza infection with painful tissue damage.

Original publication:
Priya Sakthivel, Marcus Gereke, Angele Breithaupt, Dietmar Fuchs, Luca Gigliotti, Achim D. Gruber, Umberto Dianzani and Dunja Bruder Attenuation of immune-mediated influenza pneumonia by targeting the inducible co-stimulator (ICOS) molecule on T cells PLOS ONE, 2014

The Immune Regulation research group at the HZI investigates the equilibrium of the immune system in extreme scenarios. This includes, for example, concurrent infection with different pathogens and erroneous attacks on inherent components of the body.

At the **Helmholtz Centre for Infection Research** (HZI) in Braunschweig, scientists are studying microbial virulence factors, host-pathogen interactions and immunity. The goal is to develop strategies for the diagnosis, prevention and therapy of human infectious diseases.
www.helmholtz-hzi.de/en

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