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DECISIVE FACTOR DISCOVERED IN SARCOIDOSIS PATIENTS

HZI RESEARCHERS DISCOVER IMPORTANT FACTOR FOR THE PROGNOSIS AND THERAPY OF SARCOIDOSIS

Approximately 32,000 to 40,000 people in Germany are suffering from sarcoidosis. This disease usually manifests in the form of nodular tissue changes and mainly affects the lungs. There are two forms of the disease, acute and chronic sarcoidosis, but the cause has not been elucidated for either form. Scientists of the Helmholtz Centre for Infection Research (HZI) in Braunschweig recently identified a molecule that indicates which of the two courses of disease is likely, and the molecule also offers some therapeutic potential. The scientists published their results in the medical journal, "Clinical and Experimental Immunology".



Lung x-ray of a sarcoidosis patient.

Sarcoidosis is an inflammatory disease that may manifest in either of two forms. Although, the disease prevalence varies in different ethnic groups, chronic sarcoidosis represents the more common form. About half of the cases are not associated with overt symptoms. Acute sarcoidosis, also called Löfgren syndrome, manifests very suddenly and mainly in the form of skin changes and swollen lymph nodes. The cause of the disease is not known to date.

"But we have known for several years that patients have a reduced number of regulatory T-cells and a comparatively high number of activated T-helper cells in the lungs," says Prof Dunja Bruder, who directs the "Immune Regulation" research group at the HZI and holds a professorship for infections immunology at the Otto-von-Guericke-University in Magdeburg. "This was the finding on which we based our search for a prognostic marker." T-cells have a number of functions in the immune system aimed at the recognition of and defense against intruders. While the so-called regulatory T-cells prevent an inadvertent attack on intact inherent tissue of the body, T-helper cells support the function of other cells of the immune system.

In cooperation with the team of the other last author Prof Jan Wahlström from the Karolinska Institute in Stockholm, Sweden, Bruder and her team analyzed the expression of the ICOS molecule, which is closely related to T-cell function, in sarcoidosis patients. ICOS enhances the effect of regulatory T-cells and the researchers can recognize this cell type by this feature. "We were able to show that the number of ICOS molecules on regulatory T-cells was increased strongly in the diseased lung, especially of patients affected by Löfgren syndrome, who possess the potential to resolve the disease spontaneously," says Dr Priya Sakhivel, who is the first author of the study and works as a scientist in Bruder's research group at the HZI. "The ICOS level on regulatory T cells from the blood of these patients was identical to that of healthy people though."

Accordingly, the concentration of ICOS on regulatory T-cells being high indicates that the sarcoidosis is the acute form, and there may even be a causal relationship with the spontaneous remission of symptoms of the disease in patients affected by Löfgren syndrome. "We managed for the first time to identify a prognostic marker for sarcoidosis," says Bruder. "This is a first step in improving our understanding of the disease and its manifestation."

Another aspect of ICOS is of interest as well: "In an earlier study with influenza viruses, we showed that ICOS can be specifically activated from outside and that the course of the infection-mediated inflammation and lung tissue damage can be mitigated through

this activation. Following specific therapeutic manipulation, T-cells bearing the ICOS molecule can gain new functions and have a totally new effect on their environment," says Sakthivel. This means that ICOS is of interest for therapeutic purposes as well. It may be possible to specifically activate this molecule to control the effect of regulatory T-cells and, thus, the course of the sarcoidosis disease.

Original publication:

Priya Sakthivel, Johan Grunewald, Anders Eklund, Dunja Bruder and Jan Wahlström. Pulmonary sarcoidosis is associated with high-Level ICOS Expression on lung regulatory T cells-possible implications for the ICOS/ICOS-L axis in disease course and Resolution. *Clinical and Experimental Immunology*. 2015 Sep 28. DOI: 10.1111/cei.12715