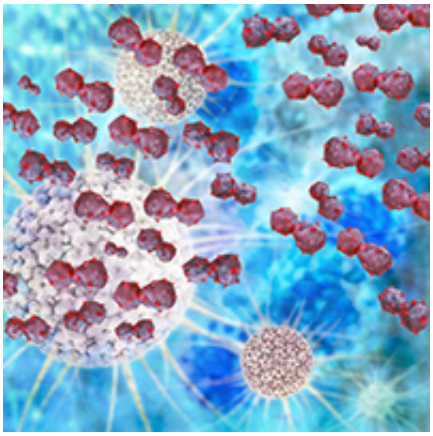
Additional immune dysfunction related to cystic fibrosis discovered

September 4 2014



Credit: fotolia

Cystic fibrosis (CF) is a frequent genetic disease affecting the lung and the gastrointestinal tract. Scientists from the Helmholtz Zentrum München now have shown that many of the adult patients with CF in addition lack a cell surface molecule, which is important for immune defence. The results have been published recently in the 'Journal of Molecular Medicine'.

Cystic fibrosis (mucoviscidosis) is due to a mutation of an ion channel which leads to highly viscous mucus and to dysfunction of the lung and the gastrointestinal organs. Since these patients frequently suffer from chronic infections, Dr. Thomas Hofer and Professor Dr. Loems Ziegler-Heitbrock from the Comprehensive Pneumology Center (CPC) at

Helmholtz Zentrum München - together with colleagues at the Klinikum der Universität München and the University of Leicester, UK - investigated, whether these patients might have an additional immune defect. The scientists found that the immunological cell surface molecule HLA-DQ is reduced or absent in many of these patients.

Defect is seen in all relevant leukocyte populations

HLA-DQ belongs to the MHC class II molecules, which can present crucial parts of invading microbes to immune cells such that the latter are activated leading to specific elimination of the pathogens. The class II molecules are strongly expressed on primary immune cells such as monocytes, macrophages and so-called dendritic cells. The study showed that HLA-DQ is reduced or absent in all these cell types in the blood and in the lung. Hence, all of the relevant antigen-presenting cells of the immune system are affected.

First insight into the molecular mechanism

In order to uncover the molecular mechanism behind this defect, the team studied the different steps in the molecular regulation In patients with a defect of HLA-DQ, the inflammatory messenger interferon-gamma was unable to induce the transcription factor CIITA along with a failure to increase HLA-DQ. What remains unclear is the cause of the deficient interferon response and the contribution of defective HLA-DQ to the course of the disease. In further studies the scientists aim to develop a rapid test system for the immune dysfunction that may be of great importance for diagnosis and treatment of cystic fibrosis. The research conducted at Helmholtz Zentrum München focuses on major common diseases such as metabolic and lung diseases. The aim is to develop new approaches to the diagnosis, treatment and prevention.

More information: Hofer, TPJ et al (2014). "Decreased Expression of HLA-DQ and -DR on cells of the monocytic lineage in cystic fibrosis," *Journal of Molecular Medicine*, DOI: 10.1007/s00109-014-1200-z