MedicalXpress

The cellular protein shredder is impaired by cigarette smoke and in COPD patients

January 13 2016

Scientists at Helmholtz Zentrum München, together with an international team and colleagues from the University Hospital of the University Munich (LMU) and the German Center for Lung Research (DZL), have shown for the first time that cigarette smoke reduces the activity of the immunoproteasome. In addition, patients with chronic obstructive pulmonary disease (COPD) display reduced immunoproteasome levels. This might contribute to the COPD patients' increased susceptibility to airway infections, as recently published in the *American Journal of Respiratory and Critical Care Medicine*.

The immunoproteasome is a defined structure in mammalian cells that is specialized to degrade protein molecules that are foreign to the cell, such as upon virus infection. Its function is comparable to a cellular shredder. Protein shreds (peptides) are then presented to the immune system on the outside of the cell to evoke a specific immune response against the virus-infected cell. A research team headed by PD Dr. Silke Meiners from the Institute of Lung Biology and Disease (iLBD) / Comprehensive Pneumology Center (CPC) at the Helmholtz Zentrum München has now discovered that smoking crucially impairs this protective response of the immune system.

"We observed that cigarette smoke reduces the activity of the immunoproteasome in human cells," explains first author Ilona Kammerl. "As a result, the presentation of the degraded protein shreds to the immune system does not function properly and thus weakens the specific immune response." Importantly, lungs of COPD patients

displayed reduced immunoproteasome activity.

"COPD patients frequently experience acute worsening of pulmonary function ("exacerbations") during a viral infection, and often do not completely recover from these. This suggests that the specific immune response to viral pathogens is reduced in COPD patients. Our data provide the first indications that this is due to cigarette smoke-induced reductions in immunoproteasome activity," emphasizes study leader Silke Meiners. Cigarette smoke is a primary risk factor for COPD.

Use as biomarker conceivable

The scientists now want to investigate whether lower immunoproteasome activity can serve as a biomarker for increased susceptibility to viral infections in COPD. Further studies should clarify whether changes in immunoproteasome levels are detectable in blood cells and this is associated with increased susceptibility to airway infections.

The immunoproteasome could also be suitable as a therapeutic target structure. "A targeted increase of immunoproteasome activity would be advantageous to elicit a more efficient immune response to virus infections in COPD patients and thus counteract a decline in pulmonary function," explains Prof. Dr. Oliver Eickelberg, Vice-Director in the DZL, chairman of the CPC, and director of the iLBD.

More information: Impairment of Immunoproteasome Function by Cigarette Smoke and in COPD. *Am J Respir Crit Care Med*. 2016 Jan 12. [Epub ahead of print]

Provided by Helmholtz Association of German Research Centres