

Immunoproteasome inhibits healing function of macrophages

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Scientists of Helmholtz Zentrum München, a partner in the German Center for Lung Research (DZL), have observed that the immunoproteasome inhibits the repair function of alveolar macrophages. This opens up new therapeutic options. A specific inhibition of the immunoproteasome may promote healing processes of the lung. The results have now been published in the journal *Cell Death & Differentiation*.

The macrophages recognize and eliminate foreign materials and pathogens and alert the immune system to invaders by sending out numerous inflammatory signals. When the inflammation has run its course, the macrophages also help cleaning up and thus play a specific role in wound healing. For this clean-up function of macrophages, which is referred to as alternative activation, interleukin 4 (IL-4) is of key importance.

Immunoproteasome regulates alternative macrophage activation

The team led by PD Dr. Silke Meiners and Dr. Tobias Stöger of the Institute of Lung Biology and Disease (iLBD) / Comprehensive Pneumology Center (CPC) at Helmholtz Zentrum München has now found that the immunoproteasome regulates the IL-4 stimulation of the macrophages. It inhibits the IL-4 <u>signaling pathway</u> and thus reduces alternative macrophage activation.



"In experiments with alveolar macrophages, we showed that in cells lacking the immunoproteasome, a specific receptor for IL-4 is augmented," said Ilona Kammerl, who shares the first authorship of the publication with Shanze Chen. The immunoproteasome inhibits the IL-4 signaling pathway and thus limits its effect.

Effect can be influenced by specific antiimmunoproteasome drugs

To confirm these results, the research team used a pharmacological immunoproteasome inhibitor. The aim was to block the IL-4 signaling pathway and thus allow the macrophages to increasingly switch to the repair and clean-up mode. "As hypothesized, when we added the inhibitor we observed a significantly stronger alternative activation of the <u>alveolar macrophages</u>," said study leader Tobias Stöger.

The <u>scientists</u> now want to determine in animal models whether targeted treatment with specific inhibitors of the immunoproteasome accelerates the healing processes in the <u>lung</u>, for example, after acute pneumonia. Corresponding preliminary experiments are already underway.

More information: S Chen et al. Immunoproteasome dysfunction augments alternative polarization of alveolar macrophages, *Cell Death and Differentiation* (2016). DOI: 10.1038/cdd.2016.3

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