Novel neutrophil elastase isoform suggests new approach to pulmonary emphysema

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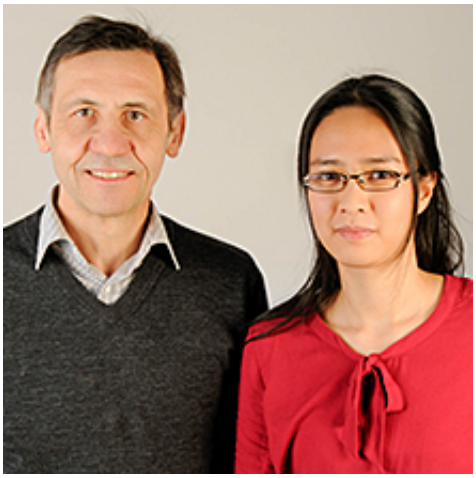

Dr. Dieter Jenne, Dr. Therese Dau; Credit: HMGU

Elastases of white blood cells are involved in tissue destruction and can thus cause various diseases. Scientists from the Helmholtz Zentrum München have discovered a new isoform which could be involved both in the pathogenesis of diseases such as pulmonary emphysema as well as in the failure of some therapy approaches. The results of the study have just been published in the journal *Nature Communications*.

A delicate balance of elastases and elastase inhibitors provides for regular tissue formation and destruction in the body. A perturbation of this balance can lead to excess elastase activity – and as a consequence, increased tissue damage. This is also the case in pulmonary emphysema:

Here elastases are no longer sufficiently inactivated, and the lung tissue is destroyed.

Cleaved neutrophil elastase "aggressive and resistant"

The research team of Dr. Therese Dau, Dr. Ali Önder Yildirim and PD Dr. Dieter Jenne of the Comprehensive Pneumology Center (CPC) at Helmholtz Zentrum München has now discovered a novel elastase isoform and has studied its properties. The elastase produced by neutrophil granulocytes (the largest group of white blood cells) may be present in a cleaved (two-chain) state. It also leads to tissue damage; at the same time it appears to react less to inhibitors.

"Our results show that the cleaved elastase is particularly aggressive and resistant," said study leader Jenne. "That is why we suspect that it contributes to the development of pulmonary emphysema – especially when an inhibitor deficiency is present as a cause of disease, such as in congenital alpha-1-antitrypsin deficiency.

Basis for improved drugs

Elastase inhibitors have long been claimed as a useful therapeutic approach to neutralize the excess elastase in pulmonary emphysema, but their results did not meet expectations. "The reduced effect of inhibitors on cleaved elastase explains why some inhibitors remain ineffective," said lead author Dau. "Based on our studies, however, new inhibitory substances may be developed in the future that are effective against different elastase isoforms and thus achieve better efficiency."

More information: "Auto-processing of neutrophil elastase near its active site reduces the efficiency of natural and synthetic elastase

inhibitors," *Nature Communications*. DOI: 10.1038/ncomms7722