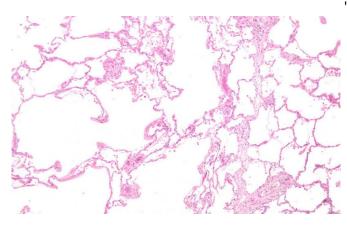


Cell death discovery could lead to new treatment for COPD

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Micrograph showing emphysema (left – large empty spaces) and lung tissue with relative preservation of the alveoli (right). Credit: Wikipedia, CC-BY-SA 3.0

Research shows that inhibiting necroptosis, a form of cell death, could be a novel therapeutic approach for treating chronic obstructive pulmonary disease (COPD), an inflammatory lung condition, also known as emphysema, that makes it difficult to breathe.

Published in the American Journal of Respiratory and Critical Care Medicine, the study by a team of Australian and Belgian researchers, revealed elevated levels of necroptosis in patients with COPD.

By inhibiting necroptosis activity, both in the lung tissue of COPD patients as well as in specialized COPD mouse models, the researchers found a significant reduction in chronic airway inflammation as well as damage to the lung.

Professor Phil Hansbro, Director of the Centenary UTS Center for Inflammation who led the research team, said that necroptosis was a form of cell death known to drive tissue inflammation and destruction.

"Necroptosis, apoptosis and necrosis are all forms of cell death but they operate in distinctly different ways. Significantly, in necroptosis, a cell bursts, dispersing its contents into nearby tissues resulting in an immune and inflammation response."

"Our research suggests that inhibiting necroptosis and preventing this inflammation response may be a new therapeutic approach to treating COPD," said Professor Hansbro.

Joint first author on the study, Dr. Zhe Lu, a researcher at the University of Newcastle, said that their study was the first of its type to be able to distinguish between the roles of necroptosis and apoptosis in COPD.

"Necroptosis is generally pro-inflammatory. Apoptosis, however, tends to be non-inflammatory as it's a more ordered form of cell death—a cell selfdegrades as opposed to bursting and there's no leakage of cell contents. This may explain why, in our study, it's the inhibition of necroptosis and not apoptosis that reduces lung damage and COPD associated inflammation," said Dr. Lu.

A debilitating respiratory condition and a leading cause of death worldwide, there are currently no treatments that halt or reverse the progression of COPD.

"Our research suggests that it is the type of cell <u>death</u> associated with COPD that is important and that the development of new drugs that can interfere or intervene in the necroptosis process could be a new targeted therapy for this common lung disease," said Professor Hansbro.

More information: Zhe Lu et al, Necroptosis Signalling Promotes Inflammation, Airway Remodelling and Emphysema in COPD, *American Journal of Respiratory and Critical Care Medicine* (2021). DOI: 10.1164/rccm.202009-3442OC



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