Towards novel therapeutic approaches in COPD

INHIBITION OF REGULATED CELL DEATH

This article delves into the groundbreaking research led by Prof. Dr. Ken Bracke (Ghent University), a specialist in Pulmonary Diseases, and his team. Focused on COPD, their work accentuates the intricate interplay between cell death, inflammation, and tissue damage. This research significantly advances the COPD discourse by unraveling molecular complexities, laying the groundwork for novel therapeutic strategies.

The majority of individuals diagnosed with COPD (Chronic Obstructive Pulmonary Disease) are aged 40 or older, and smoking is implicated as the primary cause in the majority of cases, with the risk of developing the disease escalating in correlation with the quantity and duration of smoking. Despite this understanding, the precise trajectory of COPD development remains unclear. While smoking stands out as a primary contributor, other factors, such as prolonged exposure to dust particles in occupational settings and host factors (including abnormal lung development and accelerated lung aging), also play a role.

THE ROLE OF CELL DEATH IN COPD PATHOGENESIS

COPD is characterized by progressive lung damage, leading to respiratory issues. Cell death plays a crucial role in the pathogenesis of the disease. While cell death is a natural process, maintaining a delicate balance between cell renewal and death is crucial. In COPD, there is often excessive cell death, resulting in severe lung damage, especially in the form of emphysema in the lung alveoli and epithelial damage in the airways.

Several forms of regulated cell death have been observed in lungs of COPD patients, including apoptosis and necroptosis. In apoptosis a cell self-degrades, which tends to be non-inflammatory. While necroptosis, activated by molecules such as RIPK1[1], RIPK3[2], and MLKL[3], causes gaps in the cell wall, dispersing its contents into nearby tissues, triggering inflammation, and contributing to tissue damage.

Inhibiting necroptosis activity in lung tissue of specialised COPD mouse models, significantly reduced chronic airway inflammation as well as damage to the lungs[4].

MITIGATING DAMAGE AND INFLAMMATION IN COPD PROGRESSION

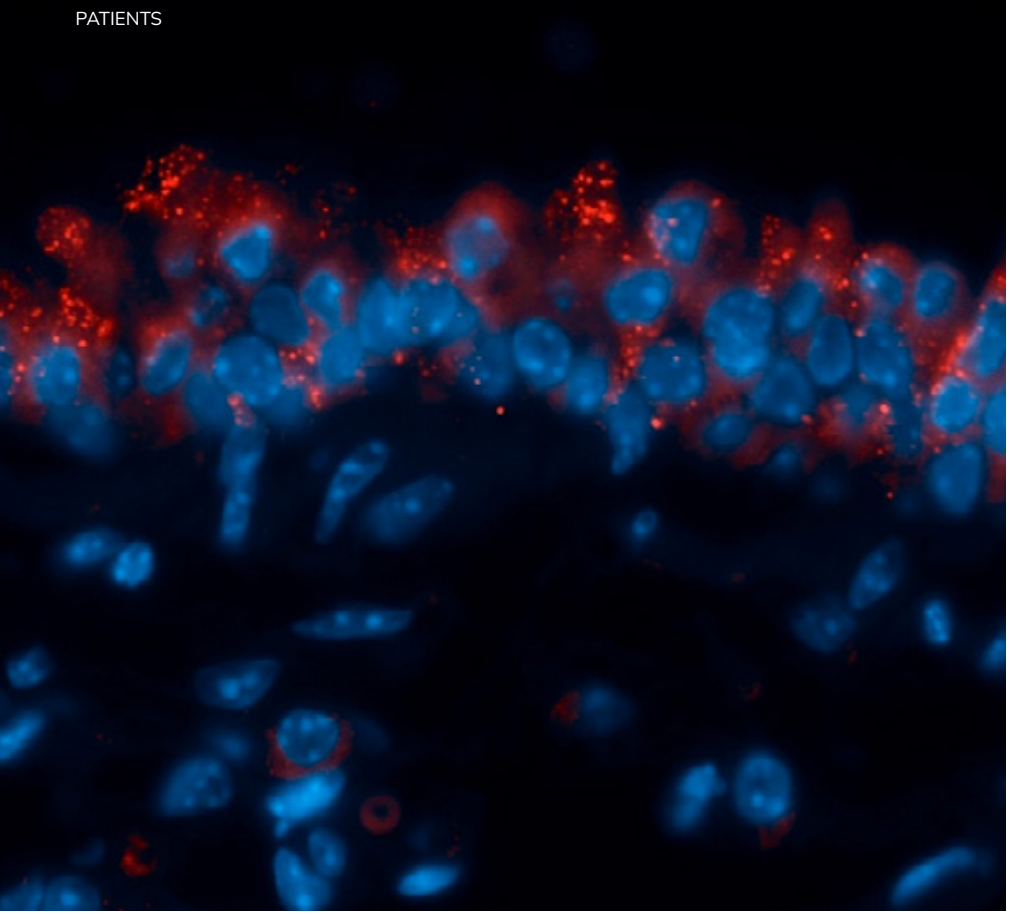
Research into specific forms of cell death is essential, calling for an individualized approach based on the predominant cell death type in a specific COPD patient. Research into

Smoking is implicated as the primary cause of COPD in the in the majority of cases, with the risk of developing the disease escalating in correlation with the quantity and duration of smoking. Photo by Andres Siimon on Unsplash.

1. Receptor-interacting serine/threonine-protein kinase 1 (RIPK1)
2. Receptor-interacting serine/threonine-protein kinase 3 (RIPK3)
3. Mixed lineage kinase domain like pseudokinase (MLKL)
4. Van Eeckhoutte et al, Eur Respir J, 2023.
Lu et al, Am J Respir Crit Care Med, 2021.

MY PULMONARY RESEARCH

PATIENTS



Positive immunofluorescent staining of phosphorylated MLKL – the executioner of necroptosis – in airway epithelium of cigarette smoke-exposed mice.

Inhibitors of RIPK1, RIPK3, and MLKL offers hope for personalized therapies, mitigating cell death regulation and pro-inflammatory reactions in COPD. In summary, reducing damage and inflammation, eliminating excess cells, and targeted drug treatments, are crucial considerations for optimizing COPD care.

FURTHER RESEARCH

COPD represents a diverse spectrum of conditions, encompassing various phenotypes, thereby complicating our understanding and treatment approaches. Identifying COPD subgroups, such as those with type 2 inflammation, will unlock potential for precise and targeted treatments. Furthermore, strengthened collaboration with the pharmaceutical industry, and a continued exploration of diverse forms of cell death stand out as promising directions for advancing COPD knowledge and treatment methodologies.

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About Prof. Dr. Ken Bracke

Ken Bracke is Associate Professor at the Department of Respiratory Medicine of the Ghent University, Belgium. He obtained a Master's degree in Biotechnology in 1999, a Master of Science in Biomedical and Clinical Engineering Technology in 2001 and a PhD in Medical Sciences in 2007, all at Ghent University. Working at the 'Laboratory for Translational Research in Obstructive Pulmonary Diseases', his research is focused on unraveling the immunological pathways that lead to the initiation and persistence of Chronic Obstructive Pulmonary Disease (COPD), combining experimental models with academic and clinical research on human samples. He has an H-index of 48 and is author or co-author on 121 publications, published in peer-reviewed international journals. He received several academic awards, including the 'AstraZeneca Foundation Award on Clinical and Translational Research in Pneumology' of the Fund for Scientific Research Flanders in 2011, the 'Prof. Romain Pauwels Award' of the Belgian Respiratory Society, for the best internationally peer-reviewed paper by a Belgian researcher in 2013 and the 'Dr. G. Schamelhout-Koettlitz Award for Pneumology' of the Belgian Royal Academy for Medicine in 2015.

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