



Activation of immune cell proteasomes in peripheral blood of smokers and COPD patients: implications for therapy

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This study demonstrates distinct activation of immunoproteasomes in peripheral blood cells of young smokers and COPD patients. Specific inhibition of the immunoproteasome might represent a novel therapeutic concept for COPD treatment. <https://bit.ly/3rEwaU7>

Cite this article as: Kammerl IE, Hardy S, Flexeder C, *et al.* Activation of immune cell proteasomes in peripheral blood of smokers and COPD patients: implications for therapy. *Eur Respir J* 2022; 59: 2101798 [DOI: 10.1183/13993003.01798-2021].

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This article has an editorial commentary:
<https://doi.org/10.1183/13993003.02557-2021>

Received: 22 March 2021
Accepted: 19 July 2021

Abstract

Background Immune cells contain a specialised type of proteasome, *i.e.* the immunoproteasome, which is required for intracellular protein degradation. Immunoproteasomes are key regulators of immune cell differentiation, inflammatory activation and autoimmunity. Immunoproteasome function in peripheral immune cells might be altered by smoking and in chronic obstructive pulmonary disease (COPD), thereby affecting immune cell responses.

Methods We analysed the expression and activity of proteasome complexes in peripheral blood mononuclear cells (PBMCs) isolated from healthy male young smokers as well as from patients with severe COPD and compared them with matching controls.

Results Proteasome expression was upregulated in COPD patients as assessed by quantitative reverse transcriptase-PCR and mass spectrometry-based proteomic analysis. Proteasome activity was quantified using activity-based probes and native gel analysis. We observed distinct activation of immunoproteasomes in the peripheral blood cells of young male smokers and severely ill COPD patients. Native gel analysis and linear regression modelling confirmed robust activation and elevated assembly of 20S proteasomes, which correlated significantly with reduced lung function parameters in COPD patients. The immunoproteasome was distinctly activated in COPD patients upon inflammatory cytokine stimulation of PBMCs *in vitro*. Inhibition of the immunoproteasome reduced pro-inflammatory cytokine expression in COPD-derived blood immune cells.

Conclusions Given the crucial role of chronic inflammatory signalling and the emerging involvement of autoimmune responses in COPD, therapeutic targeting of the immunoproteasome might represent a novel therapeutic concept for COPD.

