THE ROLE OF PTX3 IN INNATE REGULATION OF ANTIFUNGAL IMMUNITY IN CHRONIC PULMONARY ASPERGILLOSIS

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INTRODUCTION

Chronic pulmonary aspergillosis (CPA) is an infection with devastating consequences to the lungs, especially for the expanding population of chronic obstructive pulmonary disease (COPD) patients. Susceptibility to CPA differs significantly even among patients with similar predisposing conditions, but the mechanisms that influence the efficacy of individual antifungal immune responses remain almost unknown. Among the many molecules endowed with regulatory properties of antifungal immune responses, the soluble pattern recognition receptor pentraxin-3 (PTX3) has been demonstrated to play a non-redundant role during infection with the fungal pathogen Aspergillus fumigatus. In immunocompromised hosts, genetic variants impairing the expression of PTX3 renders carriers highly susceptible to invasive aspergillosis. Whether PTX3 also influences susceptibility to chronic forms of aspergillosis in otherwise immunocompetent individuals remains unknown.

METHODS

Preparation of A. fumigatus-containing agarose beads
Aspergillus fumigatus-containing agarose beads were prepared according to a previous report (Urb, M., et al., 2015). Briefly, a mixture of 1x106 A. fumigatus conidia with 1% YPD-3% agar was emulsified in pre-warmed liquid paraffin. Beads were filtered to a maximum size of 200 µm diameter and calculated to a concentration of 4x104 conidia per mL.

Experimental protocol for chronic fungal stimulation

PTX3 immunofluorescence
Lung tissue sections were incubated with rabbit anti-PTX3 followed by DyLight 488 donkey anti-rabbit IgG (green) and DAPI (blue) to stain PTX3 and nuclei, respectively. Immunofluorescence analysis was performed by confocal microscopy.

RESULTS

1 Characterization of the in vivo model of chronic fungal stimulation

2 Chronic airway colonization with A. fumigatus hyphae induces PTX3 production

3 Ptx3-deficient mice display increased susceptibility to experimental model of chronic fungal stimulation

4 Cytokine production is defective in the lungs of Ptx3-deficient mice throughout the course of infection

REFERENCES


CONCLUSIONS

The long pentraxin 3 seems to play a crucial role in response to chronic fungal stimulation as revealed by the increased susceptibility of Ptx3-deficient. Interesting, PTX3 also modulates lung inflammation through the regulation of the modulation of several pro- and anti-inflammatory cytokines. Therefore, our results highlight the requisite role of PTX3 to host antifungal response and establish PTX3 as an attractive target for immunotherapeutic strategies to prevent or treat chronic fungal diseases.

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