



POSTER PRESENTATION

Open Access

A functional inflammasome activation assay discriminates between genetically proven caps patients and patients with low penetrance *NLRP3* variants

Nikolaus Rieber*, Alina Gavrilov, Theresa Endres, Dominik Hartl, Jasmin Kümmerle-Deschner

From 21st European Pediatric Rheumatology (PReS) Congress
Belgrade, Serbia. 17-21 September 2014

Introduction

The cryopyrin-associated periodic syndromes (CAPS) are characterized by recurrent episodes of systemic inflammation. CAPS is caused by mutations in the *NLRP3* gene encoding cryopyrin, an important component of the *NLRP3* inflammasome that activates caspase-1 resulting in inflammation by excessive production of IL-1 β and others. A diagnostic dilemma is often encountered in patients with unspecific inflammatory symptoms like fatigue, muscle pain, arthralgia or slight hearing loss and low penetrance variants in *NLRP3* / *CIAS* with an inconsistent clinical phenotype. The analysis of IL-1 β in the serum did not prove to be a valid diagnostic test in these individuals.

Objectives

In this study we sought to investigate, if a functional inflammasome activation assay discriminates between genetically proven CAPS patients, patients with low penetrance *NLRP3* variants and healthy controls.

Methods

The study population consisted of 16 patients with genetically proven Muckle-Wells syndrome, 9 patients with low penetrance *NLRP3* variants (V198M, Q703K and E627G) and 14 healthy controls. Concentrations of IL-1 β , IL-1 α , IL-18, and Caspase-1 were quantified in cell culture supernatants after inflammasome stimulation with LPS and LPS + ATP for several timepoints.

Results

After 4h of LPS stimulation, secretion of *NLRP3* inflammasome products (IL-1 β , IL-1 α , IL-18) and Caspase-1

were potently increased in MWS patients, whereas there was no increase in low penetrance *NLRP3* variants and healthy controls (for IL-1 β $p < 0.001$ and $p < 0.001$, respectively). Minor differences were still detected at later timepoints and for LPS + ATP stimulation.

Conclusion

Our functional inflammasome activation assay discriminates between genetically proven CAPS patients and patients with low penetrance *NLRP3* variants. This assay might add to the decision, which individuals presumably benefit from an anti-IL-1 therapy.

Disclosure of interest

N. Rieber Grant / Research Support from: Novartis Research Grant, A. Gavrilov: None declared., T. Endres: None declared., D. Hartl: None declared., J. Kümmerle-Deschner Grant / Research Support from: Novartis Research Grant.

Published: 17 September 2014

doi:10.1186/1546-0096-12-S1-P74

Cite this article as: Rieber et al.: A functional inflammasome activation assay discriminates between genetically proven caps patients and patients with low penetrance *NLRP3* variants. *Pediatric Rheumatology* 2014 **12**(Suppl 1):P74.