

Role of IL-1b in NLRP12-associated autoinflammatory disorders and resistance to anti-IL-1 therapy

Isabelle Jeru, Véronique Hentgen, Sylvain Normand, Philippe Duquesnoy, Emmanuelle Cochet, Adriana Delwail, Gilles Grateau, Sandrine Marlin, Serge Amselem, Jean-Claude Lecron

► **To cite this version:**

Isabelle Jeru, Véronique Hentgen, Sylvain Normand, Philippe Duquesnoy, Emmanuelle Cochet, et al.. Role of IL-1b in NLRP12-associated autoinflammatory disorders and resistance to anti-IL-1 therapy. *Pediatric Rheumatology*, BioMed Central, 2011, 9 (Suppl 1), pp.O31. inserm-00624792

HAL Id: inserm-00624792

<https://www.hal.inserm.fr/inserm-00624792>

Submitted on 19 Sep 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



ORAL PRESENTATION

Open Access

Role of IL-1b in NLRP12-associated autoinflammatory disorders and resistance to anti-IL-1 therapy

Isabelle Jeru^{1*}, Véronique Hentgen², Sylvain Normand³, Philippe Duquesnoy¹, Emmanuelle Cochet⁴, Adriana Delwail³, Gilles Gâteau⁴, Sandrine Marlin⁴, Serge Amselem¹, Jean-Claude Lecron³

From 18th Pediatric Rheumatology European Society (PReS) Congress Bruges, Belgium. 14-18 September 2011

Background

A new class of autoinflammatory syndromes called *NLRP12*-associated disorders (*NLRP12AD*) has been associated with mutations in *NLRP12*. Conflicting data on the putative role of *NLRP12* in IL-1b signaling have been generated *in vitro*.

Aim

This prospective study was undertaken to assess the secretion of IL-1b and three IL-1b-induced cytokines (IL-1Ra, IL-6 and TNF-a) in patients' PBMC cultured *ex vivo* and to evaluate the patients' response to recombinant IL-1 receptor antagonist (IL-1Ra, anakinra), a major drug in the treatment of autoinflammatory disorders.

Methods

Patients' disease manifestations and cytokine measurements were recorded before anakinra treatment was started, during 14 months of therapy, and after discontinuation of anakinra treatment.

Results

Spontaneous secretion of IL-1b by patients' PBMC was found to be dramatically increased (80 to 175-fold) compared to controls. Consistently, anakinra initially led to a marked clinical improvement and to a rapid near-normalization of IL-1b secretion. However, a progressive clinical relapse occurred secondarily, associated with an increase in TNF-a secretion, persistent elevated levels of

IL-1Ra and IL-6 and a reactivation of IL-1b secretion. Anakinra was discontinued after 14 months of therapy.

Conclusion

Our findings provide *in vivo* evidence of the crucial role of IL-1b in the pathophysiology of *NLRP12AD*. This is the first time anakinra has been used to treat this disorder. This study provides new insights into the mechanisms underlying resistance to anti-IL-1 therapy observed in few patients with autoinflammatory syndromes. Our data also point to the potential interest of cytokine *ex vivo* measurements as predictors of response to treatment.

Author details

¹INSERM, Paris, France. ²Centre Hospitalier de Versailles, Versailles, France. ³Université de Poitiers, Poitiers, France. ⁴Assistance Publique - Hôpitaux de Paris, Paris, France.

Published: 14 September 2011

doi:10.1186/1546-0096-9-S1-O31

Cite this article as: Jeru *et al.*: Role of IL-1b in *NLRP12*-associated autoinflammatory disorders and resistance to anti-IL-1 therapy. *Pediatric Rheumatology* 2011 **9**(Suppl 1):O31.

¹INSERM, Paris, France

Full list of author information is available at the end of the article