



HAL
open science

Inflammasome activation and inflammation in Epidermolysis bullosa

Aphrodite Daskalopoulou, Ioannis Athanasiou, Claire Jumeau, Angela Arenas, Serge Amselem, Dimitra Kiritsi, Sonia A Karabina

► **To cite this version:**

Aphrodite Daskalopoulou, Ioannis Athanasiou, Claire Jumeau, Angela Arenas, Serge Amselem, et al.. Inflammasome activation and inflammation in Epidermolysis bullosa. Assises de Génétique Humaine et Médicale, Jan 2024, Paris, France. inserm-04412170

HAL Id: inserm-04412170

<https://inserm.hal.science/inserm-04412170>

Submitted on 23 Jan 2024

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.



Inflammasome activation and inflammation in Epidermolysis bullosa

Aphrodite Daskalopoulou¹, Ioannis Athanasiou², Claire Jumeau¹, Angela Arenas Garcia¹, Serge Amselem^{1,3}, Dimitra Kiritsi^{2*}, Sonia A. Karabina^{1*}

¹ Sorbonne Université, Inserm, Childhood Genetic Diseases Laboratory, Hôpital Armand-Trousseau, 75012 Paris, France.

² Department of Dermatology, Medical Center- University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany;

³ First Department of Dermatology, Faculty of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece.

* Equally contributing authors

¹ Département de Génétique Médicale, Assistance Publique-Hôpitaux de Paris (APHP), Hôpital Armand-Trousseau, 75012 Paris, France.

Introduction

Epidermolysis bullosa (EB) comprises a group of rare genetic disorders characterized by skin fragility and blister formation due to mutations in genes encoding for the basement membrane proteins or proteins ensuring basement membrane organization or keratinocyte integrity. Inflammasomes are multiprotein complexes, controlling the activation and release of critical pro-inflammatory cytokines, namely IL-1 β and IL-18, *via* caspase-1. The role of cytokines in orchestrating tissue repair and integrity in EB has been poorly studied.

Objective

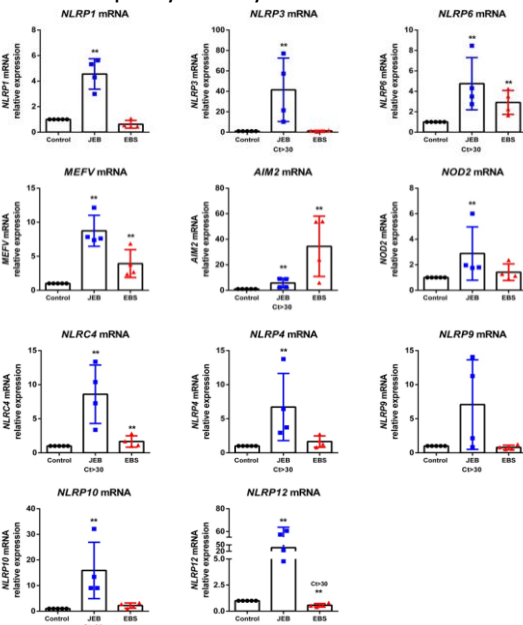
The objective of this study was to investigate the expression and regulation of inflammasome-components and cytokine secretion in keratinocytes of EB patients and controls.

Methods

Primary keratinocytes were derived from biopsies of individuals with 2 different types of EB, specifically junctional epidermolysis bullosa (JEB) (N=4) and epidermolysis bullosa simplex (EBS) (N=4). Normal human epidermal keratinocytes (NHEK) were used as controls. The gene expression of the major inflammasome sensors, members of the caspase family and cytokines was measured using the Mesa Blue qPCR MasterMix Plus for SYBR Assay on a Light Cycler LC480. Cytokine secretion was measured by ELISA.

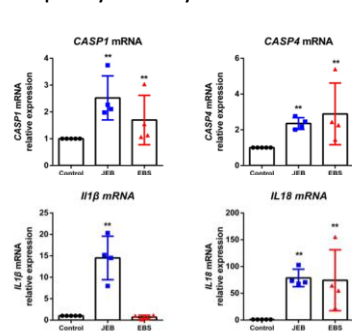
Results

Inflammasome sensors expression in human primary keratinocytes



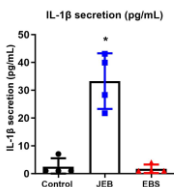
- Elevated mRNA levels of *NLRP1*, *NLRP3*, *NLRP6*, *MEFV*, *NOD2*, *NLR4*, *NLRP4*, *NLRP10*, and *NLRP12* in JEB patient-derived keratinocytes as compared to NHEK.
- The gene expression of *NLRP6*, *MEFV*, *AIM2*, and *NLR4* was increased in EBS patient-derived keratinocytes as compared to NHEK.

Caspase and cytokine expression in human primary keratinocytes



- The gene expression of *CASP1* and *CASP4* was higher in both JEB and EBS patients as compared to NHEK, but did not change significantly between JEB and EBS samples.
- *IL1B* and *IL18* gene expression was significantly higher in JEB patients as compared to controls.

Cytokine secretion in human primary keratinocytes



Data represent the mean \pm SEM of ≥ 3 independent experiments done in human primary keratinocytes of ≥ 4 independent donors.

- IL-1 β secretion was significantly higher in JEB patients as compared to EBS or controls.
- IL-18 secretion was below detection limit for all groups.

Conclusion

In this study, we demonstrated that keratinocytes derived from JEB and EBS patients exhibit increased expression of inflammasome components compared to NHEK suggesting a role of inflammasome(s) in EB pathogenesis. Our data highlight the importance of adhesion of the different skin layers to ensure keratinocyte homeostasis.

As the dysregulation of inflammasome sensors leads to the excessive production of pro-inflammatory cytokines, it could contribute to the chronic inflammation observed in EB.

Further studies on the type of inflammasome(s) implicated in EB and targeted therapeutic interventions to modulate inflammasome activation may hold promise for the development of anti-inflammatory therapies in EB.

Abbreviations: NOD-like Receptors: NLR; interleukin-1 β : IL-1 β ; interleukin-18: IL-18.