

PReS-FINAL-2173: Protein kinase C delta deficiency is a new cause of monogenic SLE

Alexandre Belot, Pk Kasher, Ew Trotter, Ap Foray, Al Debaud, E Meffre, J Brognard, N Bonnefoy, Y Crow

► **To cite this version:**

Alexandre Belot, Pk Kasher, Ew Trotter, Ap Foray, Al Debaud, et al.. PReS-FINAL-2173: Protein kinase C delta deficiency is a new cause of monogenic SLE. *Pediatric Rheumatology*, BioMed Central, 2013, 11 (Suppl 2), pp.O8. <inserm-00914630>

HAL Id: inserm-00914630

<http://www.hal.inserm.fr/inserm-00914630>

Submitted on 5 Dec 2013

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

PRoS-FINAL-2173: Protein kinase C delta deficiency is a new cause of monogenic SLE

A Belot^{1,2,3*}, PK Kasher¹, EW Trotter⁴, AP Foray², AL Debaut², E Meffre⁵, J Brognard⁴, N Bonnefoy⁶, Y Crow¹

From 20th Pediatric Rheumatology European Society (PRoS) Congress Ljubljana, Slovenia. 25-29 September 2013

Introduction

Systemic lupus erythematosus (SLE) is a prototype auto-immune disease. Infectious triggers, genetic background, immunological abnormalities and environmental factors are all supposed to interact in disease development. Rare causes of monogenic SLE have been described, (e.g. complement deficiencies, interferonopathies and FasL deficiency) providing unique insights into fundamental mechanisms of immune tolerance.

Objectives

Our objective was to identify the cause of an autosomal recessive form of SLE in an inbred family with three affected siblings.

Methods

We investigated three siblings and used next generation sequencing to identify mutations in the disease-associated gene. We performed extensive biochemical, immunological and functional assays to assess the impact of the identified mutations on B cell biology.

Results

Genetic mapping and targeted exome sequencing lead to the identification of a homozygous mutation in PRKCD, encoding protein kinase C delta (PKC δ). Mutation of PRKCD resulted in reduced expression and activity of encoded protein PKC δ . In mouse, PKC δ plays a crucial role in the deletion of autoreactive B cells. As for mice deficient in PKC δ , we demonstrated that B cells display a resistance to calcium-dependent apoptosis and a higher proliferation rate associated with an increase of immature B cells in affected patients, and a developmental shift toward an immature phenotype of naïve B cells.

Conclusion

Our findings indicate that PKC δ is crucial in regulating B cell tolerance and preventing self-reactivity in humans.

Disclosure of interest

None declared.

Authors' details

¹Faculty of Human and Medical Sciences, Genetic Medicine, University of Manchester, Manchester, UK. ²U1111, INSERM, France. ³Pediatric Nephrology, Rheumatology & Dermatology Department, Hôpital Femme Mère Enfant, Hospices Civils de Lyon, Lyon, France. ⁴Paterson Institute for Cancer Research, Cancer Research UK, University of Manchester, Manchester, UK. ⁵Department of Immunobiology, Yale University, New Haven, USA. ⁶IRCM, Institut de Recherche en Cancérologie de Montpellier, U896, INSERM, Montpellier, France.

Published: 5 December 2013

doi:10.1186/1546-0096-11-S2-O8

Cite this article as: Belot et al.: PRoS-FINAL-2173: Protein kinase C delta deficiency is a new cause of monogenic SLE. *Pediatric Rheumatology* 2013 11(Suppl 2):O8.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit



¹Faculty of Human and Medical Sciences, Genetic Medicine, University of Manchester, Manchester, UK
Full list of author information is available at the end of the article