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:

HAL Id: inserm-00914630
https://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.
PReS-FINAL-2173: Protein kinase C delta deficiency is a new cause of monogenic SLE

A Belot1,2,3*, PK Kasher1, EW Trotter4, AP Foray2, AL Debaud2, E Meffre5, J Brognard4, N Bonnefoy6, Y Crow1

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

Introduction
Systemic lupus erythematosus (SLE) is a prototype autoimmune 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 (PKCδ). Mutation of PRKCD resulted in reduced expression and activity of encoded protein PKCδ. In mouse, PKCδ plays a crucial role in the deletion of autoreactive B cells. As for mice deficient in PKCδ, 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 PKCδ 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, Hopital Femme Mere 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.: PReS-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

© 2013 Belot et al.; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.