

OR10-002 - A novel TNFR1 transcript of TRAPS gene

Cécile Rittore, Elodie Sanchez, Stephan Soler, Marieke Albers, Laura Obici,
Michael Mcdermott, Isabelle Touitou, Sylvie Grandemange

► **To cite this version:**

Cécile Rittore, Elodie Sanchez, Stephan Soler, Marieke Albers, Laura Obici, et al.. OR10-002 - A novel TNFR1 transcript of TRAPS gene. *Pediatric Rheumatology*, BioMed Central, 2013, 11 (Suppl 1), pp.A186. <inserm-00881681>

HAL Id: inserm-00881681

<http://www.hal.inserm.fr/inserm-00881681>

Submitted on 8 Nov 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.



MEETING ABSTRACT

Open Access

OR10-002 - A novel TNFR1 transcript of TRAPS gene

C Rittore¹, E Sanchez¹, S Soler¹, M Albers², L Obici³, MF McDermott⁴, I Touitou¹, S Grandemange^{1*}

From 7th Congress of International Society of Systemic Auto-Inflammatory Diseases (ISSAID) Lausanne, Switzerland. 22-26 May 2013

Introduction

Mutations in the *TNFRSF1A* gene encoding the TNF cell surface receptor, TNFR1, cause TNFR-associated periodic syndrome (TRAPS) and polymorphisms in *TNFRSF1A*, including rs4149570, rs767455 and rs1800692, are associated with inflammatory diseases.

Objectives

We describe a novel exon 2-spliced transcript, named TNFR1-d2, and the impact of these 3 SNPs on exon 2 splicing, transcriptional activity of *TNFRSF1A* and TRAPS phenotype.

Methods

Expression of *TNFRSF1A* transcripts was performed by RT-PCR in a range of human cells and tissues. Exon 2 splicing and transcriptional activity were analysed in HEK293T and SW480 cells by *in vitro* alternative splicing and luciferase assays, respectively. We constructed haplotypes containing rs4149570, rs767455 and rs1800692 in controls (n=70), TRAPS (n=111) and TRAPS-like patients (n=450) to compare their distribution and association with clinical features of TRAPS.

Results

TNFR1-d2 was expressed in a tissue-specific manner, whereas TNFR1 expression was ubiquitous. Alternative splicing assays revealed that the T-A-T haplotype at rs4149570-rs767455-rs1800692 showed the highest expression of exon 2-skipping product (p=0.02). Transcriptional activity from the T-T haplotype at rs4149570-rs1800692 was increased compared to the G-C haplotype (p=0.03). In TRAPS patients, rs1800692 T/T homozygotes were excessively rare (p<10⁻⁴) and TRAPS-like patients with this genotype experienced less fever.

Conclusion

Our study provides a novel mechanism of *TNFRSF1A* regulation whereby three polymorphisms in the promoter, exon 1 and intron 4 have a functional and combined effect on exon 2 splicing, via a coupling mechanism between transcription and splicing. These polymorphisms may impact the phenotype of TRAPS and TRAPS-like patients.

Competing interests
None declared.

Authors' details
¹INSERM / CHU A.DE VILLENEUVE, Montpellier, France. ²University Medish Centrum, Utrecht, Netherlands. ³IRCCS Fondazione Policlinico San Matteo, Pavia, Italy. ⁴NIHR-Leeds Musculoskeletal Biomedical Research Unit, Leeds, UK.

Published: 8 November 2013

doi:10.1186/1546-0096-11-S1-A186

Cite this article as: Rittore et al.: OR10-002 - A novel TNFR1 transcript of TRAPS gene. *Pediatric Rheumatology* 2013 **11**(Suppl 1):A186.

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



¹INSERM / CHU A.DE VILLENEUVE, Montpellier, France
Full list of author information is available at the end of the article