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, Switerland. 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.

 $^{\overline{1}}$ INSERM / CHU A.DE VILLENEUVE, Montpellier, France Full list of author information is available at the end of the article

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 Fundazion Policlinico San Matteo, Pavia, Italy. ⁴6.NIHR-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

) Bio Med Central

Submit your manuscript at www.biomedcentral.com/submit



© 2013 Rittore 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.