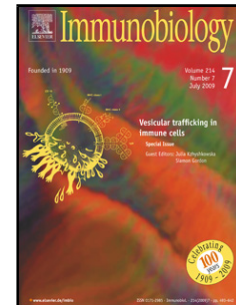


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Epistatic interaction between TLR4 and NOD2 in patients with Crohn's Disease: relation with risk and phenotype in a Spanish cohort

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Highlights:

- An epistatic relation between TLR4 and NOD2 has been described.
- Mutation both in TLR4 and NOD2 increases the risk to develop Crohn's Disease
- TLR4 variants are associated with a stricturing behavior and gut perforation
- TLR4 contributes to ileal location in patients carrying a NOD2 variant

Abstract

Crohn's Disease is one of the two major forms of the Inflammatory Bowel Diseases and, although the etiology is not completely understood, the confluence of environmental and genetic factors has been demonstrated. The aim of this study was to determine the distribution of *TLR4* variants in a Spanish cohort of Crohn's Disease patients and their relation with phenotype and common *NOD2* variants. A total of 371 Crohn's Disease (CD) patients and 636 healthy controls (HC) were included. Single Nucleotide Polymorphisms (SNPs) in *TLR4* (*D299G* and *T399I*) and *NOD2* (*R702W* and *G908R*) detection was performed by a Taqman[®] Allelic Discrimination Assay. *1007insC* *NOD2* variant was analyzed using a PCR combined with fluorescent technology and the different alleles were determined depending on the PCR products size. *D299G* and *T399I* were related to CD only in patients carrying *NOD2* variants (*NOD2*+/*TLR4*+ haplotype) ($p=0.036$; $OR=1.924$), increasing the risk to develop CD when *1007insC* and *TLR4* variants were both present ($OR=4.886$). We also described a

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