Behçet's disease and genetic interactions between HLA-B*51 and variants in genes of autoinflammatory syndromes

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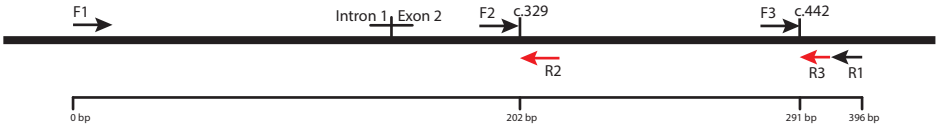
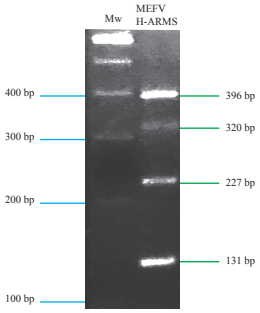
Supplementary Table 1. List of primers used in H-ARMS PCR analysis

Assay	Primer Name	5' – 3' sequence
MEFV Leu110Pro and Glu148Gln H-ARMS	F1	CGCCCGGCCCGTTGTTTTCCTCAATTTC
	R1	GCAGGGCCGGGCTCCGGGTCCGAGGCTT
	F2	CCCTGGGGGAGAACAAGCCCAGGAGACC
	R2	CCCCTCGGGGTGGTCTGGAGTCTGCA
	F3	CTGCCAGCCTGCGGTGCAGCCAGCGCC
	R3	GGGCTTCCTCGACAGCCCCCTCCCGGCGTC
NOD2 Arg311Trp and Arg703Cys H-ARMS	F1	TGGAGGAGCTCTTCAGCACCCCTGGCCA
	R1	CAGGCCACGTGCAGCCTTCCGAGCCAGCC
	F2	CAGTGGCAAGAGCACGCTCCTGCCGC
	R2	ACCCGGTGCAGCTGGCGGGATGGAGGGA

A)

MEFV

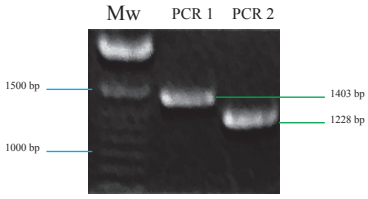




MEFV H-ARMS	
***cis*: ab + AB haplotypes**	***trans*: Ab + aB haplotypes**
396	396
321	320
227	227
131	131
No band	145*

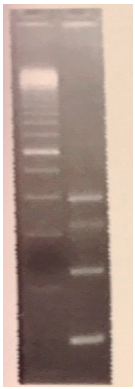
B)

NOD2

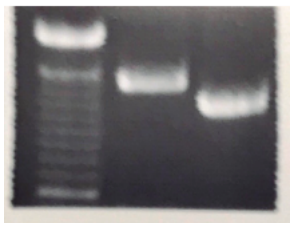


	NOD2 H-ARMS	
	***cis*: ab + AB haplotypes**	***trans*: Ab + aB haplotypes**
PCR 1 (F1 and R1 primers)	1403	1403
PCR 2 (F2 and R3 primers)	No band	1228*

C)



D)



Supplementary Figure 1. Schematic representation of the H-ARMS PCR carried out in order to know the *cis*/*trans* configuration of two pairs of rare variants in *MEFV* and *NOD2* found in two BD patients. A) *MEFV* Leu110Pro and Glu148Gln analysis, uncropped electrophoresis gel showing all available bands. B) *NOD2* Arg311Trp and Arg703Cys analysis, electrophoresis gel cropped at 800 bp band of the molecular weight marker. C) Untouched A gel electrophoresis. D) Untouched B gel electrophoresis

Supplementary Table 2. Type I error estimations.

		Unadjusted significance level (α)	
		0.05	**0.01**
Parameter	**SKAT P-value**	0.088	0.013
	FRG P-value	0.014	<0.01

For estimation of type I error, a simulation was used. A total of 2596 rare variants of the genomic region hg19 chr22:17000000-31400001 were retrieved from 107 IBS and 107 TSI individuals from 1000 genomes database and HLA-B51 status was determined with OptiType software. Phenotype (case/control) was randomly assigned. Simulation data were analysed as it was done for samples using SKAT and FRG.

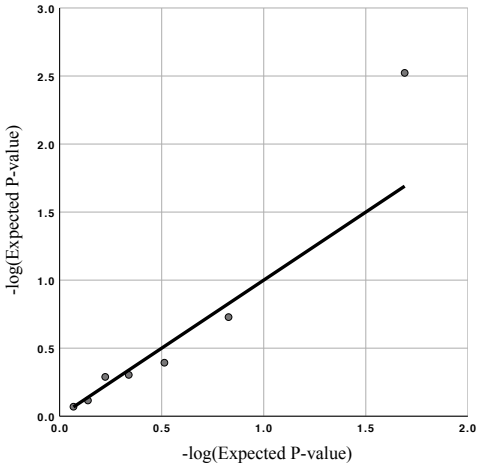
Supplementary Table 3. FRG control with random phenotypes.

Gene	FRG P-value (N=443)
CECR1	0.62
MEFV	0.70
NOD2	0.79
MVK	0.27
TNFRSF1A	0.84
NLRP3	0.14
PSTPIP1	0.68

BD patients and IBS 1000 genome controls were randomly assigned as affected or unaffected. Phenotype groups were compared using FRG analysis for epistasis of the studied genes with HLA-B51.

Supplementary Figure 2. QQ-Plots of FRG P-values. **A.** QQ-Plot constructed with FRG P-values from Table 2. **B.** QQ-Plot constructed with FRG P-values from Supplementary Table 3.

A.



B.