Supplementary Table 1: Genetics-1. *NOD2* Genotypes in enrolled patients

Patient N	*NOD2* Genotype
1	p.[(Arg334Trp)]; [(=)]
2	p.[(Arg334Gln)]; [(=)]
3	p.[(Arg334Trp)]; [(=)]
4	p.[(Arg334Trp)]; [(=)]
5	p.[(Arg334Trp);(Arg346Trp]; [(=)]
6	p.[(Arg334Trp);(Arg346Trp]; [(=)]
7	p.[(Gln809Lys); [(=)]
8	p.[(Glu383Asp)];[(Asp390Val)]; [(=)]
9	p.[(Gln809Lys); [(=)]
10	p.[(Arg334Gln)]; [(=)]
11	p.[(Arg334Trp)]; [(=)]
12	p.[(Arg334Trp)]; [(=)]
13	Documented to have a mutation, details unavailable

Supplementary Table 2: Genetics-2. Classification of *NOD2* Variants. [1]Genome Build: GRCh37/hg19. [2]RefSeq: NM_022162.3. [2]Classification of pathogenicity of gene variants performed based on standards and guidelines proposed in the consensus recommendations of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. [3]The specific nucleotide exchange (G>T or G>C) that provoked the NODS2 variant detected in patient 8 at the amino acid level could not be retrieved.
Abbreviations: Chr, chromosome; 1000 GP, 1000 Genomes Project Phase 3; NHLBI-ESP, National Heart, Lung and Blood Institute-Exome Sequencing Project; gnomAD, Genome Aggregation Database; SIFT, Sorting Intolerant from Tolerant; CADD, Combined Annotation Dependent Depletion; ACMG / AMP, American College of Medical Genetics and Genomics / Association for Molecular Pathology; VUS, variant of uncertain significance; n.r., not registered.

Structural Features of Variants						
Chromosome position[1]	Chr 16: 50744822	Chr 16: 50744823	Chr 16: 50744858	Chr 16: 50744971	Chr 16: 50744991	Chr 16: 50746247
Reference allele	C	G	C	G	A	C
Variant allele	T	A	T	T/C[3]	T	A
Gene[2]	*NOD2*	*NOD2*	*NOD2*	*NOD2*	*NOD2*	*NOD2*
Exon	Exon 4	Exon 4	Exon 4	Exon 4	Exon 4	Exon 4
cDNA alteration	c.1000C>T	c.1001G>A	c.1036C>T	c.1149G>T/C	c.1169A>T	c.2425C>A
Predicted amino acid alteration	p.(Arg334Trp)	p.(Arg334Gln)	p.(Arg346Trp)	p.(Glu383Asp)	p.(Asp390Val)	p.(Gln809Lys)
Population Genetics (MAF)						
NHLBI-ESP (ESP6500SI-V2 version)	0%	0%	0%	0%	0%	0%
gnomAD (v2.1.1)	0%	0%	0.0016%	0%	0.0038%	0%
Bioinformatics						
Polyphen-2 (Hum Var)	Probably Damaging (1)	Probably Damaging (0.998)	Possibly Damaging (0.87)	Probably Damaging (0.994)	Possibly Damaging (0.895)	Probably Damaging (0.968)
SIFT (Score)	Deleterious (0)	Deleterious (0)	Deleterious (0.02)	Deleterious (0)	Deleterious (0)	Deleterious (0)
CADD PHRED	23.4	23.6	18.71	23.7	23.1	25.3
Phenotype-Genotype Databases						
ClinVar database	Pathogenic	Pathogenic	VUS	n.r.	n.r.	n.r.
INFEVERS database	Pathogenic	Pathogenic	n.r.	n.r.	Likely Pathogenic	Likely Pathogenic
ACMG / AMP Classification[2]	Pathogenic	Pathogenic	VUS	Likely Pathogenic	Likely Pathogenic	Likely Pathogenic