|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Gene** | **Chromosome** | **Location** | **Base change** | **Amino Acid change** | **Isoform** | **Variant Type** | **Zygosity** | **Inheritance** | **Frequency (gnomAD)** | **CADD** | **CLINVAR** | **HGMD** | **Phenotype** | | | | | | | | | | | | | | | | | | | | |
| **VEOIBD** | | **EOIBD** | | | | | | **PIBD** | | | | | | | | | | | | |
| **CD** | | **CD** | | | | | | **CD** | | | | | | | | | | | | **UC** |
| **M** | **M** | **F** | **F** | **M** | **F** | **F** | **F** | | **F** | **M** | **F** | **M** | **F\*** | **M** | **M** | **M\*** | **M** | **F** | **M** | **M** |
| NOD2 | 16 | Exon 4 | C2104T | R702W | NM\_022162 | NS | Hom Het | AR | 0.0236 | 24.1 | C | DFP | • | • | •• | •• |  | • | • | •• | | •• |  | • | • | • | • |  | • |  |  |  |  |
| NOD2 | 16 | Exon 9 | G2863A | V955I | NM\_022162 | NS | Het | AR | 0.0527 | 1.3 | B | DM? |  | • |  |  |  | • | • |  | |  |  |  |  |  |  |  |  | • | • | • | • |
| NOD2 | 16 | Exon 4 | C2264T | A755V | NM\_022162 | NS | Het | AR | 0.003 | 24.4 | LB | DM? | • |  |  |  |  |  |  |  | |  | • | • |  |  |  |  |  |  |  |  |  |
| NOD2 | 16 | Exon 4 | A1055G | H352R | NM\_022162 | NS | Het | AR | 0.0039 | 15.9 | B | DM? |  |  |  |  |  |  |  |  | |  |  |  |  |  | • |  |  |  |  |  |  |
| NOD2 | 16 | Exon 5 | G2470A | D824N | NM\_022162 | NS | Het | AR | 0.00009689 | 15.7 | - | DM? |  |  |  |  | • |  |  |  | |  |  |  |  |  |  |  |  |  |  |  |  |
| NOD2 | 16 | Exon 6 | A2555G | N852S | NM\_022162 | NS | Het | AR | 0.0005 | 23.6 | C | DM? |  |  |  |  |  |  |  |  | |  |  |  | • |  |  |  |  |  |  |  |  |
| NOD2 | 16 | Exon 8 | G2722C | G908R | NM\_022162 | NS | Het | AR | 0.0076 | 31.0 | C | DM? |  |  |  |  | • |  |  |  | |  | • |  |  |  |  | • |  |  |  |  | • |
| NOD2 | 16 | Exon 11 | 3017dupC | A1007fs | NM\_022162 | FSI | Het | AR | 0.0167 | 26.8 | LB | DFP |  |  |  |  |  |  |  |  | |  |  |  |  | • |  |  | • |  |  | • |  |
| NOD2 | 16 | Exon 4 | C2230T | R744W | NM\_022162 | NS | Het | AR | 0.00006455 | 26.8 | - | - |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  |  | • |  |  |
| NOD2 | 16 | Exon 4 | G2123A. | R708H | NM\_022162 | NS | Het | AR | 0.0058 | 22.8 | B/LB | - |  |  |  |  |  |  |  |  | |  |  |  |  |  |  | • |  |  |  |  |  |
| NOD2 | 16 | Exon 10 | A2888G | E963G | NM\_022162 | NS | Het | AR | Novel | 27.3 | U | - |  |  |  |  |  |  |  |  | |  |  |  |  |  |  |  |  | • |  |  |  |

Supplementary Table 4- Variants in NOD2 identified that are ‘Disease-associated polymorphisms with supporting functional evidence’, ‘Disease causing mutation’, ‘Probable/possible pathological mutation’ (HGMD) or CADD >20, MAF <0.01, that are homozygous or compound heterozygote.

NS- nonsynonymous, FSI- Frameshift insertion, Het- heterozygote, , AR- autosomal recessive, SG- stopgain, UC- ulcerative colitis, CD- Crohn’s disease

CLINVAR- B- benign, LB- likely benign, C- conflicting evidence, U- uncertain significance

HGMD- DFP- Disease-associated polymorphism with supporting functional evidence, DM- Disease causing mutation, DM?- probable/possible pathological mutation

M- male, F- female

● Heterozygous variant

●● Homozygous variant

\*Patients are siblings