Supplementary table 5- Compound Heterozygote Variants (>2 significant variants within the gene) that are ‘Disease-associated polymorphisms with supporting functional evidence’, ‘Disease causing mutation’, ‘Probable/possible pathological mutation’ (HGMD) or CADD >20, MAF <0.01.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | **Phenotype** | | | | | | | |
|  | |  | | | **VEO**  **IBD** | **EOIBD** | **PIBD** | | | | | |
|  |  | | | | | | | | | | | | | | | | | | **CD** | **CD** | **CD** | | | **UC** | | |
| **Defect type** | | **Gene** | **Chromosome** | **Location** | **Base change** | **Amino Acid change** | **Isoform** | **Variant Type** | **Zygosity** | **Inheritance** | **Frequency (gnomAD)** | **CADD** | **HGMD** | | **ClinVar** | | | **M** | | **F** | **M** | **M** | **M** | **F** | **F** | **F** |
| T + B cell defects | | DCLRE1C | 10 | Exon 6 | G457A | G153R | NM\_001033857 | NS | Het | AR | 0.0106 | 33.0 | DM? | | C | | |  | |  | • |  |  | • |  |  |
| DCLRE1C | 10 | Exon 7 | C512G | P171R | NM\_001033857 | NS | Het | AR | 0.0937 | 25.0 | DFP | | B/LB | | |  | |  | • |  |  | • |  |  |
| Phagocytic defects | | NCF2 | 1 | Exon 13 | C1167A | H389Q | NM\_001127651 | NS | Het | AR | 0.0333 | 23.0 | DFP | | B/LB | | |  | |  |  | • |  |  | • |  |
| NCF2 | 1 | Exon 14 | A1256T | N419I | NM\_001127651 | NS | Het | AR | 0.0044 | 28.4 | DM? | | B/LB | | |  | |  |  | • |  |  |  |  |
| NCF2 | 1 | Exon 14 | G1184A | R395Q | NM\_001127651 | NS | Het | AR | 0.0012 | 23.4 | DM? | | U | | |  | |  |  |  |  |  | • |  |
| Immunoregulation | | TRIM22 | 11 | Exon 8 | G950A | R321K | NM\_006074 | NS | Het | AR | 0.0255 | 25.0 | DM | |  | | | • | | • |  |  | • |  |  | • |
| TRIM22 | 11 | Exon 8 | C1324T | R442C | NM\_006074 | NS | Het | AR | 0.0069 | 23.8 | DM | |  | | |  | |  |  |  | • |  |  | • |
| TRIM22 | 11 | Exon 4 | C731T | S244L | NM\_006074 | NS | Het | AR | 0.0402 | 25.7 | DM | |  | | | • | |  |  |  |  |  |  |  |
| TRIM22 | 11 | Exon 8 | C1450T | P484S | NM\_006074 | NS | Het | AR | 0.0006 | 27.6 | - | |  | | |  | | • |  |  |  |  |  |  |

NS- nonsynonymous, Het- heterozygote, AR- autosomal recessive, 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

● Heterozygous variant