Whole Exome Sequencing
Gene package Very early onset inflammatory bowel disease / congenital diarrhea, version 3.1, 31-1-2020

Technical information
DNA was enriched using Agilent SureSelect DNA + SureSelect OneSeq 300kb CNV Backbone + Human All Exon V7 capture and paired-end sequenced on the Illumina platform (outsourced). The aim is to obtain 10 Giga base pairs per exome with a mapped fraction of 0.99. The average coverage of the exome is ~50x. Duplicate and non-unique reads are excluded. Data are demultiplexed with bcl2fastq Conversion Software from Illumina. Reads are mapped to the genome using the BWA-MEM algorithm (reference: http://bio-bwa.sourceforge.net/). Variant detection is performed by the Genome Analysis Toolkit HaplotypeCaller (reference: http://www.broadinstitute.org/gatk/). The detected variants are filtered and annotated with Cartagenia software and classified with Alamut Visual. It is not excluded that pathogenic mutations are being missed using this technology. At this moment, there is not enough information about the sensitivity of this technique with respect to the detection of deletions and duplications of more than 5 nucleotides and of somatic mosaic mutations (all types of sequence changes).

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HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x	% covered >30x
ACTG2	Visceral myopathy, 155310	102545	95	100	100	100
ADAM17	?Inflammatory skin and bowel disease, neonatal, 1, 614328	603639	67	100	99	94
AIRE	Autoimmune polyendocrinopathy syndrome , type I, with or without reversible metaphyseal dysplasia, 240300	607358	100	100	100	100
ALPI	No OMIM phenotype	171740	200	100	100	100
ANKZF1	No OMIM phenotype	617541	80	100	100	99
ARPC1B	Platelet abnormalities with eosinophilia and immune-mediated inflammatory disease, 617718	604223	107	100	100	100
ARX	Epileptic encephalopathy, early infantile, 1, 308350 Hydranencephaly with abnormal genitalia, 300215 Lissencephaly 2, 300215 Mental retardation 29 and others, 300419 Partington syndrome, 309510 Proud syndrome, 300004	300382	46	89	79	68
BACH2	Immunodeficiency 60, 618394	605394	118	100	100	100
CARD8	No OMIM phenotype	609051	67	100	100	95
CARMIL2	Immunodeficiency 58, 618131	610859	125	100	96	94

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CD19	Immunodeficiency, common variable, 3, 613493	107265	107	100	100	99
CD40	Immunodeficiency with hyper-IgM, type 3, 606843	109535	104	100	100	100
CD40LG	Immunodeficiency, with hyper-IgM, 308230	300386	67	100	100	97
CD55	[Blood group Cromer], 613793 Complement hyperactivation, angiopathic thrombosis, and protein-losing enteropathy, 226300	125240	55	91	85	79
CLMP	Congenital short bowel syndrome, 615237	611693	73	100	100	100
COG6	Congenital disorder of glycosylation, type III, 614576 Shaheen syndrome, 615328	606977	65	100	99	90
CR2	Immunodeficiency, common variable, 7, 614699 {Systemic lupus erythematosus, susceptibility to, 9}, 610927	120650	63	100	100	97
CTLA4	Autoimmune lymphoproliferative syndrome, type V, 616100 {Celiac disease, susceptibility to, 3}, 609755 {Diabetes mellitus, insulin-dependent, 12}, 601388 {Hashimoto thyroiditis}, 140300 {Systemic lupus erythematosus, susceptibility to}, 152700	123890	90	100	100	100
CYBA	Chronic granulomatous disease, autosomal, due to deficiency of CYBA, 233690	608508	106	94	81	66
CYBB	Chronic granulomatous disease, 306400 Immunodeficiency 34, mycobacteriosis, 300645	300481	49	100	98	91
CYBC1	No OMIM phenotype	No id	No coverage data			
DGAT1	?Diarrhea 7, protein-losing enteropathy type, 615863	604900	116	96	91	85
DOCK2	Immunodeficiency 40, 616433	603122	82	100	100	97
DOCK8	Hyper-IgE recurrent infection syndrome, 243700	611432	74	100	99	94
DUOX2	Thyroid dyshormonogenesis 6, 607200	606759	113	98	97	96
EGFR	Adenocarcinoma of lung, response to tyrosine kinase inhibitor in, 211980 ?Inflammatory skin and bowel disease, neonatal, 2, 616069 Nonsmall cell lung cancer, response to tyrosine kinase inhibitor in, 211980 {Nonsmall cell lung cancer, susceptibility to}, 211980	131550	87	100	100	98
EPCAM	Colorectal cancer, hereditary nonpolyposis, type 8, 613244 Diarrhea 5, with tufting enteropathy, congenital, 613217	185535	58	100	100	93
FOXP3	Immunodysregulation, polyendocrinopathy, and enteropathy, 304790	300292	69	100	99	88
GUCY2C	Diarrhea 6, 614616 Meconium ileus, 614665	601330	80	100	100	97
HPS1	Hermansky-Pudlak syndrome 1, 203300	604982	103	100	100	97
HPS4	Hermansky-Pudlak syndrome 4, 614073	606682	103	100	100	98
HPS6	Hermansky-Pudlak syndrome 6, 614075	607522	130	100	100	93

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ICOS	Immunodeficiency, common variable, 1, 607594	604558	57	100	100	95
IKBKG	Ectodermal dysplasia and immunodeficiency 1, 300291 Ectodermal, dysplasia, anhidrotic, lymphedema and immunodeficiency, 300301 Immunodeficiency 33, 300636 Immunodeficiency, isolated, 300584 Incontinentia pigmenti, 308300 Invasive pneumococcal disease, recurrent isolated, 2, 300640	300248	24	38	33	31
IL10	{Graft-versus-host disease, protection against}, 614395 {HIV-1, susceptibility to}, 609423 {Rheumatoid arthritis, progression of}, 180300	124092	120	100	100	99
IL10RA	Inflammatory bowel disease 28, early onset, 613148	146933	125	100	100	99
IL10RB	{Hepatitis B virus, susceptibility to}, 610424 Inflammatory bowel disease 25, early onset, 612567	123889	69	100	100	97
IL21	?Immunodeficiency, common variable, 11, 615767	605384	69	100	99	89
IL21R	[IgE, elevated level of], 147050 Immunodeficiency 56, 615207	605383	113	100	100	100
IL2RA	{Diabetes, mellitus, insulin-dependent, susceptibility to, 10}, 601942 Immunodeficiency 41 with lymphoproliferation and autoimmunity, 606367	147730	96	100	100	100
IL2RB	Immunodeficiency 63 with lymphoproliferation and autoimmunity, 618495	146710	84	100	100	99
ITCH	Autoimmune disease, multisystem, with facial dysmorphism, 613385	606409	61	96	95	90
ITGB2	Leukocyte adhesion deficiency, 116920	600065	140	100	100	100
LCT	Lactase deficiency, congenital, 223000	603202	114	100	100	100
LRBA	Immunodeficiency, common variable, 8, with autoimmunity, 614700	606453	65	100	99	94
MALT1	Immunodeficiency 12, 615468	604860	68	97	93	89
MEFV	Familial Mediterranean fever, AD, 134610 Familial Mediterranean fever, AR, 249100	608107	105	100	100	100
MPI	Congenital disorder of glycosylation, type Ib, 602579	154550	154	100	100	99
MVK	Hyper-IgD syndrome, 260920 Mevalonic aciduria, 610377 Porokeratosis 3, multiple types, 175900	251170	100	100	100	100
MYO5B	Microvillus inclusion disease, 251850	606540	103	100	100	98
NCF1	Chronic granulomatous disease due to deficiency of NCF-1, 233700	608512	108	68	65	61
NCF2	Chronic granulomatous disease due to deficiency of NCF-2, 233710	608515	94	100	100	98
NCF4	?Granulomatous disease, chronic, cytochrome b-positive, type III, 613960	601488	121	100	100	100
NEUROG3	Diarrhea 4, malabsorptive, congenital, 610370	604882	161	100	100	100

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NFKBIA	Ectodermal dysplasia and immunodeficiency 2, 612132	164008	131	100	100	100
NLRC4	Autoinflammation with infantile enterocolitis, 616050 ?Familial cold autoinflammatory syndrome 4, 616115	606831	83	100	100	97
NOD2	Blau syndrome, 186580 {Inflammatory bowel disease 1, Crohn disease}, 266600 {Psoriatic arthritis, susceptibility to}, 607507 {Yao syndrome}, 617321	605956	113	100	100	99
OTULIN	Autoinflammation, panniculitis, and dermatosis syndrome, 617099	615712	70	97	91	82
PCSK1	Obesity with impaired prohormone processing, 600955 {Obesity, susceptibility to, BMIQ12}, 612362	162150	68	100	100	97
PLCG2	Autoinflammation, antibody deficiency, and immune dysregulation syndrome, 614878 Familial cold autoinflammatory syndrome 3, 614468	600220	107	100	100	99
PLVAP	Diarrhea 10, protein-losing enteropathy type, 618183	607647	142	100	100	100
PNLIP	?Pancreatic lipase deficiency, 614338	246600	60	100	100	95
POLA1	Pigmentary disorder, reticulate, with systemic manifestations, 301220 Van Esch-O'Driscoll syndrome, 301030	312040	44	99	92	77
RAC2	Neutrophil immunodeficiency syndrome, 608203	602049	99	100	100	100
RFX6	Mitchell-Riley syndrome, 615710	612659	91	100	99	95
RIPK1	Immunodeficiency 57, 618108	603453	54	100	97	91
SAR1B	Chylomicron retention disease, 246700	607690	79	100	100	97
SH2D1A	Lymphoproliferative syndrome, 1, 308240	300490	56	100	98	83
SI	Sucrase-isomaltase deficiency, congenital, 222900	609845	60	100	99	92
SKIV2L	Trichohepatoenteric syndrome 2, 614602	600478	124	100	100	100
SLC10A2	Bile acid malabsorption, primary, 613291	601295	78	100	100	96
SLC26A3	Diarrhea 1, secretory chloride, congenital, 214700	126650	72	100	100	95
SLC2A2	{Diabetes mellitus, noninsulin-dependent}, 125853 Fanconi-Bickel syndrome, 227810	138160	63	100	100	96
SLC37A4	Glycogen storage disease Ib, 232220 Glycogen storage disease Ic, 232240	602671	96	100	100	95
SLC39A4	Acrodermatitis enteropathica, 201100	607059	125	100	100	100
SLC5A1	Glucose/galactose malabsorption, 606824	182380	104	100	100	96
SLC7A7	Lysinuric protein intolerance, 222700	603593	79	100	100	97
SLC9A3	Diarrhea 8, secretory sodium, congenital, 616868	182307	133	100	100	98
SPINT2	Diarrhea 3, secretory sodium, congenital, syndromic, 270420	605124	94	100	100	100

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STAT1	Immunodeficiency 31A, mycobacteriosis, 614892 Immunodeficiency 31B, mycobacterial and viral infections, 613796 Immunodeficiency 31C, 614162	600555	64	100	99	94
STAT3	Autoimmune disease, multisystem, infantile-onset, 1, 615952 Hyper-IgE recurrent infection syndrome, 147060	102582	90	100	100	99
STAT5B	Growth hormone insensitivity with immunodeficiency, 245590 Leukemia, acute promyelocytic, somatic, 102578	604260	107	100	100	97
STX3	No OMIM phenotype	600876	75	100	100	96
STXBP2	Hemophagocytic lymphohistiocytosis, familial, 5, 613101	601717	121	100	100	100
TCN2	Transcobalamin II deficiency, 275350	613441	118	100	100	100
TGFB1	Camurati-Engelmann disease, 131300 {Cystic fibrosis lung disease, modifier of}, 219700 Inflammatory bowel disease, immunodeficiency, and encephalopathy, 618213	190180	111	100	99	95
TMPRSS15	Enterokinase deficiency, 226200	606635	68	100	98	91
TNFAIP3	Autoinflammatory syndrome, familial, Behcet-like, 616744	191163	106	100	99	96
TNFRSF13B	Immunodeficiency, common variable, 2, 240500 Immunoglobulin A deficiency 2, 609529	604907	106	100	100	100
TNFRSF13C	Immunodeficiency, common variable, 4, 613494	606269	78	100	91	73
TOM1	No OMIM phenotype	604700	115	100	100	100
TRIM22	No OMIM phenotype	606559	86	100	100	98
TTC37	Trichohepatoenteric syndrome 1, 222470	614589	58	100	99	93
TTC7A	Gastrointestinal defects and immunodeficiency syndrome, 243150	609332	110	100	100	99
TYMP	Mitochondrial DNA depletion syndrome 1 (MNGIE type), 603041	131222	102	100	100	100
WAS	Neutropenia, severe congenital, 300299 Thrombocytopenia, 313900 Thrombocytopenia, intermittent, 313900 Wiskott-Aldrich syndrome, 301000	300392	66	97	84	76
WIPF1	?Wiskott-Aldrich syndrome 2, 614493	602357	73	100	100	96
WNT2B	Diarrhea 9, 618168	601968	86	100	95	86
XIAP	Lymphoproliferative syndrome, 2, 300635	300079	47	100	95	80
ZAP70	Autoimmune disease, multisystem, infantile-onset, 2, 617006 Immunodeficiency 48, 269840	176947	151	100	100	100

- Gene symbols according HGCN
- OMIM release used: 8-9-2019
- "No OMIM phenotypes" indicates a gene without a current OMIM association

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- OMIM phenotypes between "[ ]", indicate "nondiseases," mainly genetic variations that lead to apparently abnormal laboratory test values
- OMIM phenotypes between "{}", indicate risk factors
- OMIM phenotypes with a question mark, "?", before the disease name indicates an unconfirmed or possibly spurious mapping
- The statistics above are based on a set of 100 samples
- Median depth is the median of the mean sequence depth over the protein coding exons (±10bp flanking introns) of the longest transcript
- % Covered 10x , 20x and 30 x describes the percentage of a gene's coding sequence (±10bp flanking introns) that is covered at least 10x, 20x or 30x