

# LYMPHATIC ANOMALIES PANEL WITH GENOME WIDE CNV ANALYSIS DG-5.0.0 (57 GENES)

| Gene    | Twist X2 covered 10x | Twist X2 covered 20x | srWGS covered 10x | srWGS covered 15x | srWGS covered 20x | Associated Phenotype description and OMIM disease ID                                                                                                                                                                                                   |
|---------|----------------------|----------------------|-------------------|-------------------|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ABCC9   | 96%                  | 96%                  | 100%              | 100%              | 99.7%             | Cardiomyopathy, dilated, 10, 608569;Hypertrichotic osteochondrodysplasia (Cantu syndrome), 239850;?Atrial fibrillation, familial, 12, 614050;Intellectual disability and myopathy syndrome, 619719                                                     |
| ADAMTS3 | 100%                 | 100%                 | 100%              | 100%              | 99.9%             | Hennekam lymphangiectasia-lymphedema syndrome 3, 618154                                                                                                                                                                                                |
| ALG8    | 79.8%                | 77.9%                | 100%              | 100%              | 99.6%             | Congenital disorder of glycosylation, type 1h, 608104;Polycystic liver disease 3 with or without kidney cysts, 617874                                                                                                                                  |
| ANGPT2  | 100%                 | 100%                 | 100%              | 100%              | 99.8%             | Lymphatic malformation 10, 619369                                                                                                                                                                                                                      |
| ARAF    | 100%                 | 99.9%                | 98.3%             | 86.5%             | 66.6%             |                                                                                                                                                                                                                                                        |
| BRAF    | 100%                 | 100%                 | 100%              | 99.7%             | 98.3%             | Melanoma, malignant, somatic, 155600;LEOPARD syndrome 3, 613707;Cardiofaciocutaneous syndrome, 115150;Adenocarcinoma of lung, somatic, 211980;Noonan syndrome 7, 613706;Colorectal cancer, somatic, 114500;Non-small cell lung cancer, somatic, 211980 |

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| CBL    | 100%  | 100% | 100% | 100%  | 99.5% | Noonan syndrome-like disorder with or without juvenile myelomonocytic leukemia, 613563;?Juvenile myelomonocytic leukemia, 607785 |
| CCBE1  | 100%  | 100% | 100% | 100%  | 99.7% | Hennekam lymphangiectasia-lymphedema syndrome 1, 235510                                                                          |
| CD55   | 98.5% | 95%  | 100% | 100%  | 99.6% | [Blood group Cromer], 613793;Complement hyperactivation, angiopathic thrombosis, and protein-losing enteropathy, 226300          |
| CDC42  | 100%  | 100% | 100% | 100%  | 99.8% | Takenouchi-Kosaki syndrome, 616737                                                                                               |
| CELSR1 | 100%  | 100% | 100% | 99.9% | 98.9% | Lymphatic malformation 9, 619319                                                                                                 |
| DGAT1  | 100%  | 100% | 100% | 100%  | 99.6% | Diarrhea 7, protein-losing enteropathy type, 615863                                                                              |
| EPHB4  | 98.6% | 96%  | 100% | 99.9% | 99%   | Capillary malformation-arteriovenous malformation 2, 618196;Lymphatic malformation 7, 617300                                     |
| ERF    | 100%  | 100% | 100% | 100%  | 98.8% | Craniosynostosis 4, 600775;Chitayat syndrome, 617180                                                                             |
| ERG    | 100%  | 100% | 100% | 100%  | 99.4% | Lymphatic malformation 14, 620602                                                                                                |
| FAT4   | 100%  | 100% | 100% | 100%  | 99.6% | Van Maldergem syndrome 2, 615546;Hennekam lymphangiectasia-lymphedema syndrome 2, 616006                                         |

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| FLT4  | 99.7% | 98%   | 100% | 99.9% | 99.6% | Hemangioma, capillary infantile, somatic, 602089;Lymphatic malformation 1, 153100;Congenital heart defects, multiple types, 7, 618780                                                                                                                                                     |
| FOXC2 | 100%  | 100%  | 100% | 99.8% | 97.7% | Lymphedema-distichias syndrome, 153400;Lymphedema-distichiasis syndrome with renal disease and diabetes mellitus, 153400                                                                                                                                                                  |
| GATA2 | 85.7% | 85.7% | 100% | 100%  | 99.2% | {Leukemia, acute myeloid, susceptibility to}, 601626;Emberger syndrome, 614038;Immunodeficiency 21, 614172;{Myelodysplastic syndrome, susceptibility to}, 614286                                                                                                                          |
| GJA1  | 100%  | 100%  | 100% | 99.9% | 99.1% | Erythrokeratoderma variabilis et progressiva 3, 617525;Craniometaphyseal dysplasia, autosomal recessive, 218400;Oculodigital dysplasia, 164200;Palmoplantar keratoderma with congenital alopecia, 104100;Syndactyly, type III, 186100;Oculodigital dysplasia, autosomal recessive, 257850 |
| GJC2  | 100%  | 99.2% | 100% | 99.3% | 97.1% | Lymphatic malformation 3, 613480;?Spastic paraplegia 44, autosomal recessive, 613206;Leukodystrophy, hypomyelinating, 2, 608804                                                                                                                                                           |

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| GLA   | 91.4% | 91.4% | 98.6% | 90.2% | 70.6% | Fabry disease, cardiac variant, 301500;Fabry disease, 301500                                                                                                                                                                                                                                                                             |
| HRAS  | 100%  | 100%  | 100%  | 100%  | 99.6% | Bladder cancer, somatic, 109800;Thyroid carcinoma, follicular, somatic, 188470;Congenital myopathy with excess of muscle spindles, 218040;Nevus sebaceous or woolly hair nevus, somatic, 162900;Schimmelpennin g-Feuerstein-Mims syndrome, somatic mosaic, 163200;Spitz nevus or nevus spilus, somatic, 137550;Costello syndrome, 218040 |
| KIF11 | 100%  | 100%  | 100%  | 100%  | 99.5% | Microcephaly with or without chorioretinopathy, lymphedema, or impaired intellectual development, 152950                                                                                                                                                                                                                                 |

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| KRAS   | 100%  | 100%  | 100% | 100% | 99.7% | Gastric cancer, somatic, 613659;Oculoectoderm al syndrome, somatic, 600268;Breast cancer, somatic, 114480;Noonan syndrome 3, 609942;RAS-associated autoimmune leukoproliferative disorder, 614470;Arteriovenous malformation of the brain, somatic, 108010;Lung cancer, somatic, 211980;Pancreatic carcinoma, somatic, 260350;Leukemia, acute myeloid, somatic, 601626;Schimmelpennin g-Feuerstein-Mims syndrome, somatic mosaic, 163200;Cardiofaciocuta neous syndrome 2, 615278;Bladder cancer, somatic, 109800 |
| LZTR1  | 100%  | 100%  | 100% | 100% | 99.4% | Noonan syndrome 2, 605275;Noonan syndrome 10, 616564;{Schwannomat osis-2, susceptibility to}, 615670                                                                                                                                                                                                                                                                                                                                                                                                              |
| MAP2K1 | 95.8% | 95.8% | 100% | 100% | 99.7% | Cardiofaciocutaneous syndrome 3, 615279;Melorheostosis , isolated, somatic mosaic, 155950                                                                                                                                                                                                                                                                                                                                                                                                                         |
| MAP2K2 | 92.4% | 92.4% | 100% | 100% | 99.1% | Cardiofaciocutaneous syndrome 4, 615280                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| MAPK1  | 100%  | 100%  | 100% | 100% | 99.7% | Noonan syndrome 13, 619087                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| MDFIC  | 100%  | 100%  | 100% | 100% | 99.9% | Lymphatic malformation 12, 620014                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |

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| MPI    | 100%  | 100%  | 100% | 100%  | 99.6% | Congenital disorder of glycosylation, type Ib, 602579                                                                                                                                                                                                                                                                                                                                             |
| MRAS   | 100%  | 100%  | 100% | 100%  | 99.6% | Noonan syndrome 11, 618499                                                                                                                                                                                                                                                                                                                                                                        |
| NF1    | 99.4% | 99.4% | 100% | 100%  | 99.8% | Watson syndrome, 193520;Leukemia, juvenile myelomonocytic, 607785;Neurofibromatosis, familial spinal, 162210;Neurofibromatosis, type 1, 162200;Neurofibromatosis-Noonan syndrome, 601321                                                                                                                                                                                                          |
| NRAS   | 89.6% | 89.4% | 100% | 100%  | 99.2% | Noonan syndrome 6, 613224;?RAS-associated autoimmune lymphoproliferative syndrome type IV, somatic, 614470;Melanocytic nevus syndrome, congenital, somatic, 137550;Epidermal nevus, somatic, 162900;Schimmelpenninng-Feuerstein-Mims syndrome, somatic mosaic, 163200;Thyroid carcinoma, follicular, somatic, 188470;Neurocutaneous melanosis, somatic, 249400;Colorectal cancer, somatic, 114500 |
| PIEZO1 | 100%  | 100%  | 100% | 99.9% | 99.1% | [ER blood group system], 620207;Lymphatic malformation 6, 616843;Dehydrated hereditary stomatocytosis with or without pseudohyperkalemia and/or perinatal edema, 194380                                                                                                                                                                                                                           |

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| PIK3CA | 100%  | 100%  | 100% | 100% | 99.6% | Hemifacial myohyperplasia, somatic, 606773;CLOVE syndrome, somatic, 612918;Hepatocellular carcinoma, somatic, 114550;Breast cancer, somatic, 114480;Cerebral cavernous malformations 4, somatic, 619538;Ovarian cancer, somatic, 167000;Colorectal cancer, somatic, 114500;Macroductyly, somatic, 155500;CLAPO syndrome, somatic, 613089;Keratosis, seborrheic, somatic, 182000;Gastric cancer, somatic, 613659;Non-small cell lung cancer, somatic, 211980;Nevus, epidermal, somatic mosaic, 162900;Megalencephaly-capillary malformation-polymicrogyria syndrome, somatic, 602501;Cowden syndrome 5, 615108 |
| PLVAP  | 94.1% | 94.1% | 100% | 100% | 98.3% | Diarrhea 10, protein-losing enteropathy type, 618183                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| PMM2   | 94.6% | 94.6% | 100% | 100% | 99.8% | Congenital disorder of glycosylation, type Ia, 212065                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| PPP1CB | 88.1% | 87.6% | 100% | 100% | 99.8% | Noonan syndrome-like disorder with loose anagen hair 2, 617506                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

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| PTPN11 | 90.5% | 89.2% | 100% | 100%  | 99.6% | Noonan syndrome 1, 163950;LEOPARD syndrome 1, 151100;Metachondromatosis, 156250;Leukemia, juvenile myelomonocytic, somatic, 607785 |
| PTPN14 | 100%  | 100%  | 100% | 100%  | 99.7% | Choanal atresia and lymphedema, 613611                                                                                             |
| RAC1   | 78.8% | 78.8% | 100% | 100%  | 99.3% | Intellectual developmental disorder, autosomal dominant 48, 617751                                                                 |
| RAF1   | 98.5% | 95.2% | 100% | 100%  | 99.8% | Cardiomyopathy, dilated, 1NN, 615916;Noonan syndrome 5, 611553;LEOPARD syndrome 2, 611554                                          |
| RASA1  | 100%  | 100%  | 100% | 100%  | 99.8% | Capillary malformation-arteriovenous malformation 1, 608354;Basal cell carcinoma, somatic, 605462                                  |
| RIT1   | 100%  | 100%  | 100% | 100%  | 99.9% | Noonan syndrome 8, 615355                                                                                                          |
| RRAS   | 93.2% | 93.2% | 100% | 99.8% | 98.2% |                                                                                                                                    |
| RRAS2  | 95.5% | 95.5% | 100% | 100%  | 99.8% | Ovarian carcinoma;Noonan syndrome 12, 618624                                                                                       |
| RREB1  | 100%  | 100%  | 100% | 100%  | 98.8% |                                                                                                                                    |
| SHOC2  | 100%  | 100%  | 100% | 100%  | 99.3% | Noonan syndrome-like with loose anagen hair 1, 607721                                                                              |
| SOS1   | 98.8% | 98.8% | 100% | 100%  | 99.8% | Noonan syndrome 4, 610733;Fibromatosis, gingival, 1, 135300                                                                        |
| SOS2   | 95%   | 95%   | 100% | 100%  | 99.3% | Noonan syndrome 9, 616559                                                                                                          |

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| SOX18  | 100%  | 99.7% | 100% | 99.9% | 97.7% | Hypotrichosis-lymphedema-telangiectasia syndrome, 607823;Hypotrichosis-lymphedema-telangiectasia-renal defect syndrome, 137940 |
| SPRED1 | 97.6% | 97.6% | 100% | 100%  | 99.9% | Legius syndrome, 611431                                                                                                        |
| SPRED2 | 100%  | 100%  | 100% | 100%  | 99.4% | Noonan syndrome 14, 619745                                                                                                     |
| THSD1  | 100%  | 100%  | 100% | 100%  | 99.7% | ?Aneurysm, intracranial berry, 12, 618734;Lymphatic malformation 13, 620244                                                    |
| TIE1   | 100%  | 100%  | 100% | 100%  | 99.4% | Lymphatic malformation 11, 619401                                                                                              |
| VEGFC  | 100%  | 100%  | 100% | 100%  | 99.7% | Lymphatic malformation 4, 615907                                                                                               |

Gene symbols used follow HGCN guidelines: Gray KA, Yates B, Seal RL, Wright MW, Bruford EA. Nucleic Acids Res. 2015 Jan 43(Database issue):D1079-85.

TWIST X2 covered 10x describes the percentage of a gene's coding sequence that is covered at least 10x when analyzed by WES using TWIST X2 chemistry mapped against GRCh38.  
TWIST X2 covered 20x describes the percentage of a gene's coding sequence that is covered at least 20x when analyzed by WES using TWIST X2 chemistry mapped against GRCh38.  
srWGS covered 10x describes the percentage of a gene's coding sequence that is covered at least 10x when analyzed by WGS mapped against GRCh38.  
srWGS covered 15x describes the percentage of a gene's coding sequence that is covered at least 15x when analyzed by WGS mapped against GRCh38.  
srWGS covered 20x describes the percentage of a gene's coding sequence that is covered at least 20x when analyzed by WGS mapped against GRCh38.  
non-protein coding genes are covered, but as coverage statistics are based on protein coding regions, statistics could not be generated.  
OMIM release used for OMIM disease identifiers and descriptions : November 25th, 2024.  
This list is accurate for panel version DG 4.4.0  
Ad 1. Blank field signifies a gene without a current OMIM association Ad 2. OMIM phenotype descriptions between {} signify risk factors