Supplementary (Appendix, online only material, etc.)

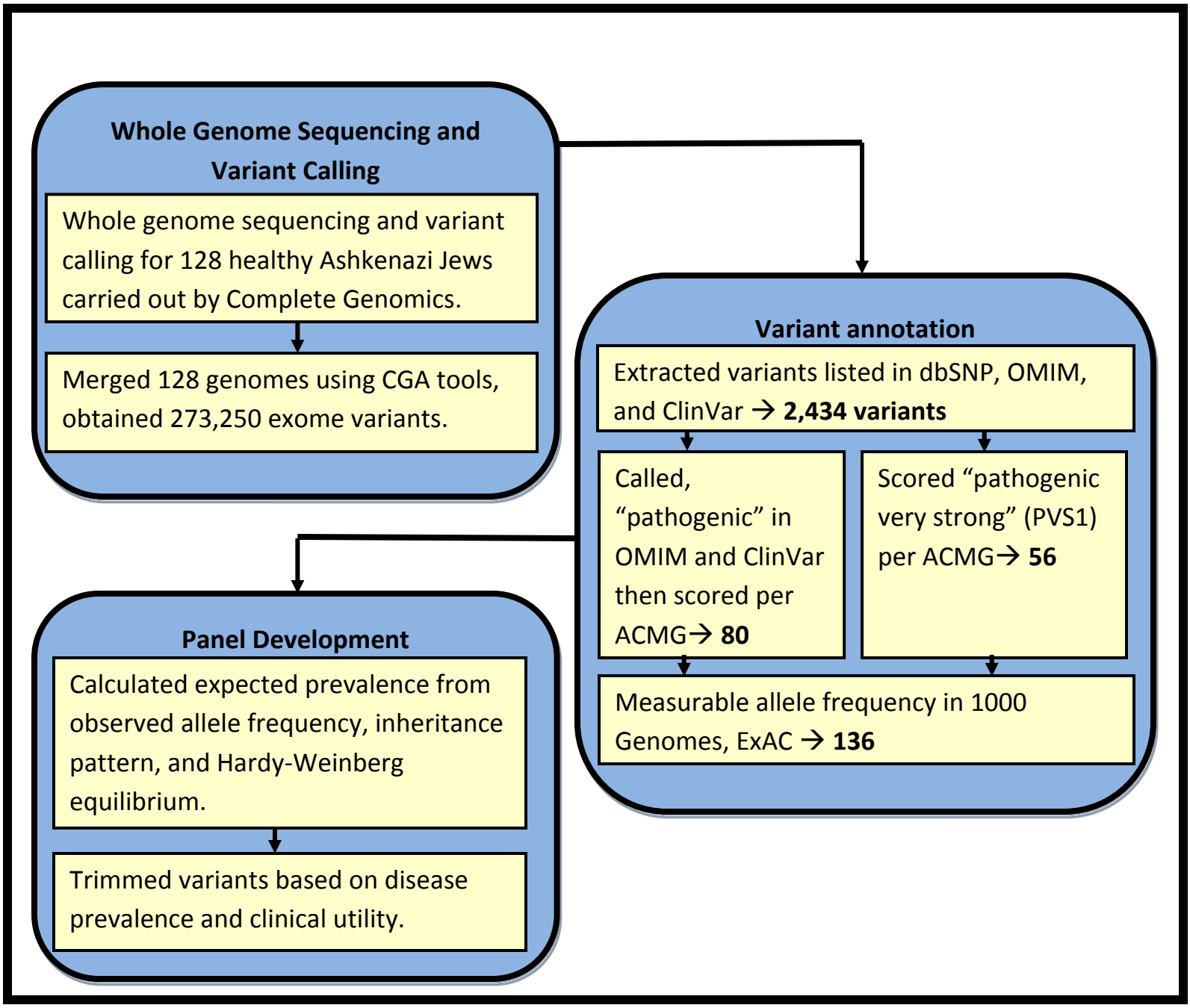


**Figure 1S. Workflow for filtering genetic variants.**

| Chr | Pos | Ref | Alt | Variation | dbSNPID | Gene Symbol | Phenotype | ACMG score | TAGC Frequency | 1000 Genomes Frequency | ExAC Frequency |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 16382003 | G | A | p.W610X | rs121909136 | CLCNKB | Bartter syndrome, type3 | PVS1/PS3 | 0.0156 | | 0.000165 |
| 1 | 40558135 | . | T | c.169dupA | rs386833634 | PPT1 | Neuronal ceroid lipofuscinosis, infantile | PVS1 | 0.012097 | | 0.00004183 |
| 1 | 40756542 | . | T | c.1085dupT | rs137854889 | ZMPSTE24 | Mandibuloacral dysplasia | PVS1 | 0.008368 | | 0.000384 |
| 1 | 43803600 | T | A | c.79+2T>A | rs146249964 | MPL | Amegakaryocytic thrombocytopaenia, congenital | PVS1 | 0.015625 | | 0.000316 |
| 1 | 53676584 | AG | . | c.1239_1240delGA | rs397509431 | CPT2 | Carnitine palmitoyltransferase 2 deficiency | PVS1 | 0.003906 | | 0.000107 |
| 1 | 68904737 | . | T | c.886dupA | | RPE65 | Leber congenital amaurosis | PVS1 | 0.003968 | | 0.00004127 |
| 1 | 68910347 | . | A | c.361dupT | rs121918844 | RPE65 | Leber congenital amaurosis | PVS1 | 0.011811 | | |
| 1 | 70881670 | C | T | p.T67I | rs28941785 | CTH | Cystathioninuria | PS3/PS4/PM2 | 0.0117 | 0.003 | 0.006485 |
| 1 | 94473807 | C | T | p.G1961E | rs1800553 | ABCA4 | Stargardt disease 1 | PS4/PM3 | 0.0205 | 0.002 | 0.005054 |
| 1 | 97915614 | C | T | c.1905+1G>A | rs3918290 | DPYD | Dihydropyrimidine dehydrogenase deficiency | PVS1 | 0.007813 | 0.003 | 0.005229 |
| 1 | 115236057 | G | A | p.Q45X | rs17602729 | AMPD1 | Myoadenylate deaminase deficiency, myopathy due to | PVS1/PS3 | 0.0653 | 0.054 | 0.08714 |
| 1 | 120286529 | G | A | p.V490M | rs121907987 | PHGDH | Phosphoglycerate dehydrogenase deficiency | PS3/PM3 | 0.0039 | 0 | 0.00009905 |
| 1 | 152285077 | ACTG | . | c.2282_2285delCAGT | | FLG | Ichthyosis vulgaris | PVS1 | 0.003906 | 0.005 | 0.01347 |
| 1 | 152285861 | G | A | p.R501X | rs61816761 | FLG | Ichthyosis vulgaris | PVS1/PS4/PM3 | 0.004 | 0.005 | 0.00876 |
| 1 | 155205634 | T | C | p.N409S | rs76763715 | GBA | Gaucher disease, type 1 | PS1/PS3 | 0.0041 | 0.001 | 0.00221 |
| 1 | 169437881 | C | T | c.1223+1G>A | | SLC19A2 | Megaloblastic anaemia, thiamine responsive | PVS1 | 0.003906 | | 0.00002477 |
| 1 | 173800770 | T | C | c.492+2T>C | rs142433332 | DARS2 | Leukoencephalopathy, brain & spine involvement, lactate elevation | PVS1 | 0.003906 | | 0.000307 |
| 2 | 44539792 | T | C | p.M467T | rs121912691 | SLC3A1 | Cystinuria | PS3/PM3/PP1 | 0.0117 | | 0.002713 |
| 2 | 48027806 | . | A | c.2690dupA | | MSH6 | Lynch syndrome | PVS1 | 0.007874 | | |
| 2 | 48030640 | C | . | c.3261delC | rs267608078 | MSH6 | Lynch syndrome | PVS1 | 0.007937 | | 0.000175 |
| 2 | 178879181 | G | A | p.R307X | rs76308115 | PDE11A | Adrenocortical hyperplasia | PVS1/PS3 | 0.0039 | 0.002 | 0.003037 |
| 2 | 178936994 | A | . | c.171delT | | PDE11A | Adrenocortical hyperplasia | PVS1 | 0.007813 | 0.009 | 0.006463 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 3 | 14200382 | G | T | p.P334H | rs74737358 | XPC | Xeroderma pigmentosum, group C | PS3 | 0.0039 | 0.004 | 0.00286 |
| 3 | 38592093 | C | T | p.A1924T | rs137854603 | SCN5A | Brugada syndrome 1 | PS3 | 0.0039 | | 0.00004144 |
| 3 | 45814094 | G | A | p.T199M | rs17279437 | SLC6A20 | Hyperglycinuria | PS3/PM3/PP1 | 0.1289 | 0.047 | 0.07515 |
| 3 | 47044241 | . | G | c.5413dupG | | NBEAL2 | Grey platelet syndrome | PVS1 | 0.009756 | | 0.00002391 |
| 3 | 48622501 | . | C | c.3942dupG | | COL7A1 | Epidermolysis bullosa dystrophica | PVS1 | 0.003906 | | .000008513 |
| 3 | 133666103 | G | . | c.1292delC | | SLCO2A1 | Hypertrophic osteoarthropathy, primary | PVS1 | 0.003906 | | .000008293 |
| 3 | 133670082 | . | A | c.830dupT | | SLCO2A1 | Hypertrophic osteoarthropathy, primary | PVS1 | 0.003953 | | 0.00001651 |
| 3 | 148863334 | G | A | c.1163+1G>A | rs201227603 | HPS3 | Hermasky-Pudlak syndrome 3 | PVS1/PS3/PS4 | 0.0039 | | 0.00009061 |
| 3 | 150690352 | A | C | p.N48K | rs111033258 | CLRN1 | Usher syndrome, type 3A | PS3/PM3/PP1 | 0.0039 | | 0.0002059 |
| 3 | 165547663 | . | A | c.1158dupT | | BCHE | Hypocholinesterasaemia (same as Serum cholinesterase deficiency) | PVS1 | 0.007874 | | 0.00001667 |
| 3 | 165547794 | . | T | c.1027dupA | | BCHE | Hypocholinesterasaemia | PVS1 | 0.003906 | | 0.0001263 |
| 3 | 165548387 | A | CT | c.435delTinsAG | rs398124632 | BCHE | Hypocholinesterasaemia | PVS1 | 0.007813 | | 0.0005863 |
| 3 | 165548420 | . | T | c.401dupA | | BCHE | Hypocholinesterasaemia | PVS1 | 0.003906 | | 0.00007434 |
| 4 | 100543913 | G | T | p.G865X | rs146064714 | MTTP | Abetalipoproteinemia | PVS1/PM3/PP1 | 0.0039 | | 0.00006589 |
| 4 | 187158051 | . | T | c.451dupT | rs560588447 | KLKB1 | Prekallikrein deficiency | PVS1 | 0.004132 | | 0.001318 |
| 4 | 187208978 | G | A | c.1716+1G>A | rs373297713 | F11 | Factor XI deficiency | PVS1 | 0.003968 | | 0.00002471 |
| 5 | 218471 | A | G | p.M1V | rs1061517 | SDHA | Leigh syndrome due to mitochondrial comples II deficiency | PVS1/PS3 | 0.0054 | | 0.0000165 |
| 5 | 1293767 | G | A | p.H412Y | rs34094720 | TERT | Bone marrow failure, telomere-related, 1 | PS3/PM3 | 0.0156 | 0.001 | 0.006342 |
| 5 | 13841161 | . | T | c.5563dupA | | DNAH5 | Primary ciliary dyskinesia | PVS1 | 0.008065 | | 0.00003256 |
| 5 | 37148319 | . | T | c.8263dupA | | C5orf42 | Joubert syndrome | PVS1 | 0.003937 | | .000008263 |
| 5 | 60240799 | C | A | p.E13X | rs121434324 | ERCC8 | Cockayne syndrome A | PVS1/PS3 | 0.0078 | | 0.00003295 |
| 5 | 126754828 | C | . | c.1325delC | | MEGF10 | EMARDD | PVS1 | 0.003937 | | .000008258 |
| 6 | 109802729 | . | T | c.501dupA | | ZBTB24 | Immunodeficiency, centromeric instability & facial anomalies syndrome | PVS1 | 0.003968 | | 0.00001648 |
| 6 | 161006077 | C | T | c.4289+1G>A | rs41272114 | LPA | Lp(a) deficiency | PVS1/benign phenotype | 0.035156 | 0.023 | 0.03706 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 7 | 117232266 | . | A | c.2052dupA | rs121908786 | CFTR | Cystic fibrosis | PVS1 | 0.004065 | | 0.00001672 |
| 7 | 117282620 | G | A | p.W1282X | rs77010898 | CFTR | Cystic Fibrosis | PVS1/PS4/PS3 | 0.0078 | | 0.000381 |
| 8 | 19805708 | G | A | p.D36N | rs1801177 | LPL | Combined hyperlipidemia, familial | PS4/PS3/PP1 | 0.0078 | 0.014 | 0.01492 |
| 8 | 19813529 | A | G | p.N318S | rs268 | LPL | Combined hyperlipidemia, familial | PS4/PS3 | 0.0039 | 0.008 | 0.01336 |
| 8 | 55541376 | . | T | c.4941dupT | | RP1 | Retinitis pigmentosa, autosomal recessive | PVS1 | 0.003906 | | 0.000008265 |
| 8 | 133894854 | C | T | p.R296X | rs121912648 | TG | Thyroid dyshormonogenesis 3 | PVS1 | 0.0039 | | 0.000363 |
| 9 | 104189856 | C | G | p.A150P | rs1800546 | ALDOB | Fructose intolerance | PS4/PS3/PP1 | 0.0078 | 0.003 | 0.002702 |
| 9 | 108382330 | . | A | c.1167dupA | rs398123555 | FKTN | Walker-Warburg syndrome | PVS1 | 0.016 | | 0.000283 |
| 9 | 111662096 | A | G | c.2204+6T>C | rs111033171 | IKBKAP | Familial dysautonomia | PS4/PS3/PP1 | 0.0195 | | 0.000653 |
| 9 | 136302063 | C | T | p.P475S | rs11575933 | ADAMTS13 | Thrombotic thrombocytopenic purpura, familial | PS4/PS3/PP1 | 0.0079 | 0.009 | 0.007333 |
| 9 | 137642654 | G | A | p.G530S | rs61735045 | COL5A1 | Ehlers-Danlos syndrome, type II | PS4/PS3/PP1 | 0.0469 | 0.026 | 0.03574 |
| 10 | 13325695 | G | A | p.R175W | rs104894178 | PHYH | Refsum disease | PS4/PS3 | 0.0039 | | 0.000148 |
| 10 | 43613908 | A | T | p.Y791F | rs77724903 | RET | Thyroid carcinoma, familial medullary | PS4/PM1 | 0.0273 | | 0.001803 |
| 10 | 56077174 | G | A | p.R245X | rs111033260 | PCDH15 | Usher syndrome, type 1F | PVS1 | 0.0081 | | 0.000223 |
| 10 | 99371292 | G | T | p.G287V | rs138207257 | HOGA1 | Hyperoxaluria, primary, type 3 | PM3/PP1 | 0.0039 | | 0.00009886 |
| 10 | 100186987 | G | . | c.972delC | rs281865082 | HPS1 | Hermansky-Pudlak syndrome | PVS1 | 0.003968 | | 0.002165 |
| 11 | 6415434 | G | T | p.R497L | rs120074117 | SMPD1 | Niemann-Pick disease, type A | PS4/PS3/PP1 | 0.0039 | | 0.000116 |
| 11 | 17418602 | C | T | c.3989-9G>A | rs151344623 | ABCC8 | Hyperinsulinemic hypoglycemia, familial, 1 | PS4/PS3/PP1 | 0.0039 | | 0.000181 |
| 11 | 22242646 | . | A | c.191dupA | rs137854521 | ANO5 | Muscular dystrophy, limb girdle 2L | PVS1 | 0.003968 | | 0.001027 |
| 11 | 30255192 | GT | . | c.236_237delTG | rs5030646 | FSHB | Follicle-stimulating hormone deficiency | PVS1 | 0.007813 | | 0.000116 |
| 11 | 61723364 | G | A | p.R81H | rs121918284 | BEST1 | Vitelliform macular dystrophy, adult onset | PS4/PS3 | 0.0039 | 0 | 0.000123 |
| 11 | 71146886 | C | G | c.964-1G>C | rs138659167 | DHCR7 | Smith-Lemli-Opitz syndrome | PVS1 | 0.007813 | 0.005 | 0.004196 |
| 11 | 89017973 | C | T | p.P406L | rs104894313 | TYR | Albinism, oculocutaneous, type IB | PS4/PP1 | 0.0079 | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 11 | 111957665 | G | A | p.G12S | rs34677591 | SDHD | Carcinoid tumors /Cowden disease 3 | PS4/PS3/PP1 | 0.0117 | 0.006 | 0.007268 |
| 11 | 111958677 | A | G | p.H50R | rs11214077 | SDHD | Carcinoid tumors /Cowden disease 3 | PS4/PS3 | 0.0039 | 0.009 | 0.006515 |
| 12 | 2659186 | G | A | p.G490R | rs121912775 | CACNA1C | Timothy syndrome | PS4/PS3/PP1 | 0.0117 | | 0.000809 |
| 12 | 6143978 | C | T | p.R854Q | rs41276738 | VWF | Von Willebrand disease, type 2N | PS4/PS3/PP1 | 0.0039 | 0.001 | 0.003081 |
| 12 | 6458350 | A | G | p.W516R | rs5742912 | SCNN1A | Bronchiectasis with or without elevated sweat chloride 2 | PS4/PS3 | 0.0195 | 0.012 | 0.01824 |
| 12 | 10271087 | A | C | p.Y159X | rs16910526 | CLEC7A | Candidiasis, familial, 4 | PVS1 | 0.082 | 0.034 | 0.06307 |
| 12 | 40734202 | G | A | p.G2019S | rs34637584 | LRRK2 | Parkinson disease 8, autosomal dominant | PS4/PS3/PP1 | 0.004 | 0 | 0.000387 |
| 12 | 110034320 | G | A | p.V377I | rs28934897 | MVK | Hyper IgD syndrome | PS4/PS3 | 0.0039 | | 0.00141 |
| 13 | 20763471 | C | T | p.V84M | rs104894409 | GJB2 | Deafness, autosomal recessive 1A | PS4/PM3 | 0.0039 | | 0.00000824 |
| 13 | 20763554 | A | . | c.167delT | rs80338942 | GJB2 | Deafness, autosomal recessive 1A | PVS1 | 0.011719 | | 0.000684 |
| 13 | 20763612 | C | T | p.V37I | rs72474224 | GJB2 | Deafness, autosomal recessive 1A | PS4/PM3 | 0.0156 | 0.012 | 0.006587 |
| 13 | 20763620 | A | G | p.M34T | rs35887622 | GJB2 | Deafness, autosomal recessive 1A | PS4/PM3 | 0.0117 | 0.01 | 0.008504 |
| 13 | 20763686 | C | . | c.35delG | rs80338939 | GJB2 | Deafness, autosomal recessive 1A | PVS1 | 0.003906 | 0.002396 | 0.00604 |
| 13 | 32351535 | A | C | p.T222P | rs121918303 | RXFP2 | Cryptorchidism | PS4/PS3 | 0.0234 | 0.002 | 0.004881 |
| 13 | 32913559 | . | A | c.5073dupA | rs80359480 | BRCA2 | Breast/ovarian cancer predisposition | PVS1 | 0.004032 | | .000008472 |
| 13 | 100914987 | G | . | c.722delG | | PCCA | Propionic acidaemia | PVS1 | 0.003968 | | 0.00003329 |
| 13 | 100925452 | . | T | c.923dupT | rs573607437 | PCCA | Propionic acidaemia | PVS1 | 0.004132 | | 0.00002518 |
| 14 | 24724663 | C | T | p.V518M | rs35312232 | TGM1 | Ichthyosis, congenital, autosomal recessive 1 | PS4/PS3/PM3 | 0.0039 | 0.007 | 0.0104 |
| 14 | 24731434 | G | T | p.S42Y | rs41295338 | TGM1 | Ichthyosis, congenital, autosomal recessive 1 | PS4/PS3/PM3 | 0.0117 | 0.003 | 0.000008297 |
| 15 | 28228553 | C | T | p.A481T | rs74653330 | OCA2 | Albinism oculocutaneous, type II | PS4/PS3/PM3 | 0.0079 | 0.015 | 0.007751 |
| 15 | 28230247 | C | T | p.V443I | rs121918166 | OCA2 | Albinism oculocutaneous, type II | PS4/PS3/PM3 | 0.0039 | 0.002 | 0.002846 |
| 15 | 44914106 | . | A | c.2471dupT | | SPG11 | Spastic paraplegia, autosomal recessive | PVS1 | 0.007937 | | 0.000008327 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 15 | 72105913 | G | A | p.R311Q | rs28937873 | NR2E3 | Enhanced S-cone syndrome | PS3/PM3 | 0.0078 | 0.002 | 0.000342 |
| 15 | 72638575 | C | G | c.1421+1G>C | rs147324677 | HEXA | Tay-Sachs disease | PVS1 | 0.003906 | | 0.00008823 |
| 15 | 72638920 | . | GATA | c.1274_1277dupTATC | rs387906309 | HEXA | Tay-Sachs disease | PVS1 | 0.011719 | | |
| 16 | 3293310 | A | G | p.V726A | rs28940579 | MEFV | Familial Mediterranean fever | PS4/PM3/PP1 | 0.0352 | 0 | 0.001845 |
| 16 | 3293403 | T | C | p.K695R | rs104895094 | MEFV | Familial Mediterranean fever | PS4/PM3/PP1 | 0.0078 | 0.003 | 0.005502 |
| 16 | 3304626 | C | G | p.E148Q | rs3743930 | MEFV | Familial Mediterranean fever | PS4/PM3/PP1 | 0.0474 | 0.082 | 0.09001 |
| 16 | 23360165 | C | G | p.S82C | rs35731153 | SCNN1B | Bronchiectasis with or without elevated sweat chloride 1 | PS4/PM3 | 0.0117 | 0 | 0.004789 |
| 16 | 31105945 | C | A | p.D36Y | rs61742245 | VKROC1 | Warfarin resistance | PS4/PP5 | 0.0433 | 0.000399 | 0.002159 |
| 17 | 3384898 | . | A | c.244dupA | | ASPA | Canavan disease | PVS1 | 0.004098 | | 0.000009076 |
| 17 | 3397702 | C | A | p.Y231X | rs12948217 | ASPA | Canavan disease | PVS1 | 0.007874 | | 0.00005775 |
| 17 | 3402294 | A | C | p.E285A | rs28940279 | ASPA | Canavan disease | PS4/PS3/PM3 | 0.0158 | | 0.000356 |
| 17 | 4802160 | . | C | c.1353dupG | | CHRNE | Congenital myasthenic syndrome | PVS1 | 0.003937 | | 0.000236 |
| 17 | 7606088 | C | T | p.R398W | rs281865548 | WRAP53 | Dyskeratosis congenita, autosomal recessive, 3 | PS3/PM3 | 0.0117 | | 0.000223 |
| 17 | 15134364 | G | A | p.T118M | rs104894619 | PMP22 | Charcot-Marie-Tooth disease, type 1A | PS4/PS3/PM3 | 0.0039 | 0.002 | 0.004682 |
| 17 | 41055964 | C | T | p.R83C | rs1801175 | G6PC | Glycogen storage disease Ia | PS4/PS3/PM3 | 0.0039 | | 0.000528 |
| 17 | 58227435 | C | T | p.R14W | rs104894559 | CA4 | Retinitis pigmentosa 17 | PS4/PS3/PM3 | 0.0041 | | 0.000439 |
| 17 | 72745313 | C | G | p.L110V | rs35910969 | SLC9A3R1 | Nephrolithiasis/osteoporosis, hypophosphatemic, 2 | PS4/PS3 | 0.0337 | 0.012 | 0.01657 |
| 17 | 73836587 | C | A | c.753+1G>T | rs201908137 | UNC13D | Haemophagocytic lymphohistiocytosis, familial | PVS1 | 0.003906 | | 0.00004123 |
| 18 | 28647999 | . | TC | c.2686_2687dupGA | rs200056085 | DSC2 | Arrhythmogenic right ventricular dysplasia/cardiomyopathy | PVS1 | 0.003937 | 0.004 | 0.008334 |
| 18 | 43459142 | . | A | c.5704dupT | | EPG5 | Vici syndrome | PVS1 | 0.003968 | | 0.00001663 |
| 18 | 55238820 | A | G | c.333-48T>C | rs2272783 | FECH | Protoporphyria, erythropoietic | PVS1/PS4/PS3/PP2 | 0.0547 | 0.156 | 0.1073 |
| 18 | 58039060 | C | T | p.A175T | rs121913563 | MC4R | Obesity, autosomal dominant | PS4/PM3/PP1 | 0.0117 | | 0.000486 |
| 19 | 5831840 | C | T | p.E247K | rs17855739 | FUT6 | Fucosyltransferase 6 deficiency | PS4/PS3 | 0.0781 | 0.127 | 0.08334 |
| 19 | 7125518 | C | T | p.V1000M | rs1799816 | INSR | Diabetes mellitus, noninsulin-dependent | PS4/PP2 | 0.0078 | 0.004 | 0.008997 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 19 | 33353427 | C | T | p.A182T | rs79389353 | SLC7A9 | Cystinuria | PS4/PS3 | 0.0117 | 0.002 | 0.002745 |
| 19 | 34856230 | A | C | p.H59P | rs137853586 | GPI | Hemolytic anemia, nonspherocytic, due to glucose phosphate isomerase deficiency | PM1/PM3 | 0.004 | | 0.00002615 |
| 19 | 39991297 | G | . | c.395delG | | DLL3 | Spondylocostal dysostosis | PVS1 | 0.003906 | | 0.00004118 |
| 19 | 45411941 | T | C | p.C130R | rs429358 | APOE | Hyperlipoprotenemia, type III, autosomal dominant | PS3/PM3 | 0.0898 | 0.149 | 0.1843 |
| 19 | 48806291 | A | . | c.939delT | | CCDC114 | Primary ciliary dyskinesia | PVS1 | 0.003906 | | 0.00002472 |
| 20 | 25060096 | C | T | p.G160D | rs74315433 | VSX1 | Corneal dystrophy, hereditary polymorphous posterior | PS4/PS3/PP1 | 0.0079 | 0.005 | 0.002108 |
| 20 | 33539652 | C | . | c.4delG | | GSS | Glutathione synthetase deficiency | PVS1 | 0.007813 | | 0.000208 |
| 21 | 35821680 | C | T | p.D85N | rs1805128 | KCNE1 | Jervell and Lange-Nielsen syndrome 2 | PS4/PP1 | 0.0273 | 0.005 | 0.009158 |
| 21 | 44479080 | T | G | c.1224-2A>C | rs375846341 | CBS | Homocystinuria | PVS1 | 0.007813 | | 0.000154 |
| 21 | 44483184 | A | G | p.I278T | rs5742905 | CBS | Homocysitnuria, pyridoxine-responsive | PS4/PM3/PP1 | 0.0317 | 0.0002 | |
| 22 | 18905859 | G | A | p.T358M | rs2870984 | PRODH | Hyperprolinemia, type I | PS4/PS3 | 0.0078 | | 0.005658 |
| 22 | 18905934 | A | G | p.L333P | rs2904551 | PRODH | Hyperprolinemia, type I | PS4/PS3/PP1 | 0.0079 | 0.003 | 0.005755 |
| 22 | 18905964 | C | T | p.R323H | rs2904552 | PRODH | Hyperprolinemia, type I | PS4/PS3 | 0.084 | 0.05 | 0.07940 |
| 22 | 18909902 | A | T | p.L181M | rs137852934 | PRODH | Hyperprolinemia, type I | PS4/PS3 | 0.0079 | | 0.004186 |
| 22 | 24919586 | G | A | NM_016327.2:c.917-1G>A | rs143493067 | UPB1 | Beta-ureidopropionase deficiency | PVS1 | 0.003906 | | 0.001919 |
| 22 | 50518820 | G | A | p.P92S | rs121908345 | MLC1 | Megalencephalic leukoencephalopathy with subcortical cysts | PS4/PM3/PP1 | 0.0039 | | 0.000207 |
| 22 | 50965067 | T | C | p.E289G | rs121913036 | TYMP | Mitochondrial DNA depletion syndrome 1 (MNGIE type) | PS1/PM3 | 0.0042 | | 0.000149 |
| X | 50658966 | G | A | p.A180T | rs104894767 | BMP15 | Premature ovarian failure 4 | PS4/PM3 | 0.0049 | 0.001 | 0.01051 |
| X | 84563194 | C | T | p.R329Q | rs75398746 | POF1B | Premature ovarian failure 2B | PS4/PS3/PP1 | 0.0243 | 0.004 | 0.002724 |
| X | 107939580 | G | A | p.R1677Q | rs104886308 | COL4A5 | Alport syndrome | PS4/PS3/PP1 | 0.0049 | | 0.00002284 |

**Table 1S: Variants identified in 128 Ashkenazi Jewish genomes and their allele frequencies in the source population, the 1000 Genomes population and the ExAC population. ACMG scores are as follows - *PVS1:* Truncating variant in a gene where LOF is a known mechanism of disease, *PS1:* Same amino acid change as an established pathogenic variant, *PS3:* Well-established functional studies**

**show a deleterious effect, *PS4:* Prevalence in affecteds statistically increased over controls, *PM1*: Located in a mutational hot spot and/or known functional domain, *PM2*: Absent in 1000G and ESP, *PM3*: For recessive disorders, detected in *trans* with a pathogenic variant, *PP1*: Co-segregation with disease in multiple affected family members, *PP2*: Missense in gene with low rate of benign missense variants and pathogenic missenses common .**

| Gene Symbol | Phenotype | dbSNP ID | Variation | Sensitivity AJ | Sensitivity Gen. Pop. | No. variants per disease | Inheritance | Repr. Risk | Pers Risk | Dx | Prevalence of phenotype (1 in X) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| HBA1 | Alpha thalassemia | | del 3.7Kb | | | 1 | Recessive | X | | X | 1156 |
| MTTP | Abetalipoproteinemia | rs146064714 | p.G865X* | | | 1 | Recessive | X | | X | 65746 |
| ACADS | Acyl CoA dehydrogenase deficiency | rs61732144 | c.319C>T | 1.9%[57] | | 1 | Recessive | X | | X | 900 |
| PDE11A | Adrenocortical hyperplasia | rs76308115 | p.R307X | | | 2 | Dominant | | X | | 64 |
| PDE11A | Adrenocortical hyperplasia | | c.171delT | | | | Dominant | | | | |
| OCA2 | Albinism oculocutaneous, type II | rs74653330 | p.A481T | | | 2 | Recessive | X | | X | 16023 |
| OCA2 | Albinism oculocutaneous, type II | rs121918166 | p.V443I* | | | | Recessive | | | | |
| TYR | Albinism, oculocutaneous, type IB | rs104894313 | p.P406L | | | 1 | Recessive | | | | |
| COL4A5 | Alport syndrome | rs104886308 | p.R1677Q* | | | 1 | X-linked | X | | X | 188 |
| MPL | Amegakaryocytic thrombocytopenia | rs146249964 | c.79+2T>A | | | 1 | Recessive | X | | X | 4096 |
| DSC2 | Arrhythmogenic right ventricular dysplasia/cardiomyopathy | rs200056085 | c.2686_2687dupGA* | | | 1 | Dominant | X | X | X | 127 |
| CLCNKB | Bartter syndrome type [3] | rs121909136 | p.W610X | | | 1 | Recessive | X | | X | 4110 |
| UPB1 | Beta-ureidopropionase deficiency | rs143493067 | c.917-1G>A* | | | 1 | Recessive | X | | X | 65544 |
| BLM | Bloom syndrome | rs113993962 | c.2207_2212 delATCTGA insTAGAT | 98% [1] | | 1 | Recessive | X | X | | 40000 |
| TERT | Bone marrow failure, telomere-related, 1 | rs34094720 | p.H412Y | | | 1 | Dominant | X | X | | 33 |
| BRCA1 | Breast/ovarian cancer predisposition | rs80357906 | c.5266dupC | 5% [2] | | 4 | Dominant | | X | | 56 |
| BRCA1 | Breast/ovarian cancer predisposition | rs80357713 | c.68_69delAG | 0.4 | | | | | | | |
| BRCA2 | Breast/ovarian cancer predisposition | rs80359550 | c.6174 delT | 0.55 | | | | | | | 33 |
| BRCA2 | Breast/ovarian cancer | rs80359480 | c.5073dupA* | | | | | | X | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | predisposition | | | | | | | | | | |
| SCNN1B | Bronchiectasis with or without elevated sweat chloride 1 | rs35731153 | p.S82C | | | 1 | | X | | X | 7162 |
| SCNN1A | Bronchiectasis with or without elevated sweat chloride 2 | rs5742912 | p.W516R | | | 1 | Recessive | X | | X | 2630 |
| SCN5A | Brugada syndrome 1 | rs137854603 | p.A1924T* | | | 1 | Dominant | | X | | 128 |
| ASPA | Canavan disease | rs12948217 | p.Y231X | 99% [3] | 0.03 | 4 | Recessive | X | | X | 4006 |
| ASPA | Canavan disease | rs28940279 | p.E285A | | | | | | | | |
| ASPA | Canavan disease | rs28940574 | p.A305E | | 30-60% | | | | | | |
| ASPA | Canavan disease | | c.244dupA* | | | | | X | | X | |
| CLEC7A | Candidiasis, familial, 4 | rs16910526 | p.Y159X | | | 1 | Recessive | X | | X | 149 |
| SDHD | Carcinoid tumors /Cowden disease 3 | rs34677591 | p.G12S | | | 2 | Dominant | | X | X | 43 |
| SDHD | Carcinoid tumors /Cowden disease 3 | rs11214077 | p.H50R* | | | | | | | | |
| CPT2 | Carnitine palmitoyltransferase 2 deficiency | rs397509431 | c.1239_1240delGA* | | | 1 | Recessive | X | | X | 65544 |
| CCM2 | Cerebral cavernous malformations | | c.30+5delinsTT | | | 1 | Dominant | | X | | Unknown |
| PMP22 | Charcot-Marie-Tooth disease, type 1A | rs104894619 | p.T118M* | | | 1 | Recessive | X | | X | 65746 |
| ERCC8 | Cockayne syndrome A | rs121434324 | p.E13X | | | 1 | Recessive | X | | X | 16436 |
| APC | Colon cancer predisposition | rs1801155 | p.I1307K | | | 1 | Dominant | | X | | 11 |
| LPL | Combined hyperlipidemia, familial | rs1801177 | p.D36N | | | 2 | Recessive | X | | X | 16436 |
| LPL | Combined hyperlipidemia, familial | rs268 | p.N318S | | | | | X | | X | |
| CYP21A2 | Congenital adrenal hyperplasia | rs6471 | p.V281L | 63% [4] | | 10 | Recessive | X | | X | 9 |
| CYP21A2 | Congenital adrenal hyperplasia | rs9378251 | p.P30L | | | | | | | | |
| CYP21A2 | Congenital adrenal hyperplasia | | IVS2−13C>G (IVS−2) | | | | | | | | |
| CYP21A2 | Congenital adrenal | rs6475 | p.I172N | | | | | | | | |

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| | hyperplasia | | | | | | | | | | |
| CYP21A2 | Congenital adrenal hyperplasia | rs111647200 | p.I236N | Haplotype | | | | | | | |
| CYP21A2 | Congenital adrenal hyperplasia | rs12530380 | p.V237E | | | | | | | | |
| CYP21A2 | Congenital adrenal hyperplasia | rs6476 | p.M239K | | | | | | | | |
| CYP21A2 | Congenital adrenal hyperplasia | rs7755898 | p.Q318X | | | | | | | | |
| CYP21A2 | Congenital adrenal hyperplasia | rs7769409 | p.R356W | | | | | | | | |
| CYP21A2 | Congenital adrenal hyperplasia | rs387906510 | 8−bp−deletion in exon 3 | | | | | | | | |
| CHRNE | Congenital myasthenic syndrome | | c.1353dupG* | | | | Recessive | X | | X | 64516 |
| VSX1 | Corneal dystrophy, hereditary polymorphous posterior | rs74315433 | p.G160D | | | 1 | Dominant | | X | X | 28 |
| RXFP2 | Cryptorchidism | rs121918303 | p.T222P | | | 1 | Recessive | X | | X | 2000 |
| CFTR | Cystic Fibrosis | rs77010898 | p.W1282X | 97% [5,6] | 75% [7] | 10 | Recessive | X | | X | 2704 |
| CFTR | Cystic fibrosis | rs113993960 | p.508delF | | | | | | | | |
| CFTR | Cystic fibrosis | rs113993959 | p.G542X | | | | | | | | |
| CFTR | Cystic fibrosis | rs80034486 | p.N1303K | | | | | | | | |
| CFTR | Cystic fibrosis | rs75039782 | c.3717+ 12191C>T | | | | | | | | |
| CFTR | Cystic fibrosis | rs78802634 | p.W1089X | | | | | | | | |
| CFTR | Cystic fibrosis | rs75541969 | p.D1152H | | | | | | | | |
| CFTR | Cystic fibrosis | rs121908791 | c.273+1G>A | | | | | | | | |
| CFTR | Cystic Fibrosis | rs121909019 | p.R1066H | | | | | | | | |
| CFTR | Cystic fibrosis | rs121908786 | c.2052dupA* | | | | | | | | |
| SLC3A1 | Cystinuria | rs121912691 | p.M467T | | | 2 | Recessive | X | | X | 10000 |
| SLC7A9 | Cystinuria | rs79389353 | p.A182T | | | | | | | | |
| GJB2 | Deafness, autosomal recessive 1A | rs80338942 | c.167delT | 70-100% [8,9] | | 6 | Recessive | X | | X | 4110 |
| GJB2 | Deafness, autosomal recessive 1A | rs80338939 | c.35delG* | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| GJB2 | Deafness, autosomal recessive 1A | rs72474224 | p.V37I | | | | | | | | |
| GJB2 | Deafness, autosomal recessive 1A | rs35887622 | p.M34T | | | | | | | | |
| GJB2 | Deafness, autosomal recessive 1A | rs104894409 | p.V84M* | | | | | | | | |
| LOXHD1 | Deafness, autosomal recessive 1A | rs75949023 | p.R1572X | 55%[58] | | | | | | | 33057 |
| INSR | Diabetes mellitus, noninsulin-dependent | rs1799816 | p.V1000M | | | 1 | Dominant | X | | X | 64 |
| DLD | Dihydrolipoamide dehydrogenase deficiency | rs121964990 | p.G229C | 95% [10] | | 2 | Recessive | X | | X | 10000 |
| DLD | Dihydrolipoamide dehydrogenase deficiency | | p.Y35X | | | | | | | | |
| DPYD | Dihydropyrimidine dehydrogenase deficiency | rs3918290 | c.1905+1G>A | | | 1 | Recessive | X | | X | 16382 |
| WRAP53 | Dyskeratosis congenita, autosomal recessive, 3 | rs281865548 | p.R398W | | | 1 | Recessive | X | | X | 7162 |
| MEGF10 | Early-onset myopathy, areflexia, respiratory distress, and dysphagia | | c.1325delC* | | | 1 | Recessive | X | | X | 64516 |
| COL5A1 | Ehlers-Danlos syndrome, type II | rs61735045 | p.G530S | | | 1 | Recessive | X | | X | 455 |
| NR2E3 | Enhanced S-cone syndrome | rs28937873 | p.R311Q | | | 1 | Dominant | X | | X | 64 |
| COL7A1 | Epidermolysis bullosa dystrophica | | c.3942dupG* | | | 1 | Recessive | X | | X | 65544 |
| F11 | Factor XI deficiency (PTA) | rs121965064 | p.F283L | 54%[59,60] | | 3 | Recessive | X | | X | 576 |
| F11 | Factor XI deficiency (PTA) | rs121965063 | p.E117X | | | | | | | | |
| F11 | Factor XI deficiency (PTA) | rs373297713 | IVS14+1G>A (c.1716+1G>A)*[11] | | | | | | | | |
| IKBKAP | Familial dysautonomia | rs111033171 | c.2204+6T>C | >99% [12,13] | | 2 | Recessive | X | | X | 2630 |
| IKBKAP | Familial dysautonomia | rs137853022 | p.R696P | | | | | | | | |
| LDLR | Familial hypercholesterolemia | rs121908027 | p.G197del | 8.1%[61] | | 1 | Dominant | X | | X | 10 |
| ABCC8 | Familial hyperinsulinism | rs151344623 | c.3989-9G>A* | 90% [14] | | 2 | Recessive | X | | X | 10000 |
| ABCC8 | Familial hyperinsulinism | rs151344624 | p.F1387del | | | | | X | | X | |
| MEFV | Familial Mediterranean | rs28940579 | p.V726A | 38-45%, | | 6 | Recessive | X | | X | 100 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | Fever | | | [15–17] | | | | | | | |
| MEFV | Familial Mediterranean Fever | rs28940578 | p.M694I | | | | | | | | |
| MEFV | Familial Mediterranean Fever | rs61752717 | p.M694V | | | | | | | | |
| MEFV | Familial Mediterranean Fever | rs28940580 | p.M680I | | | | | | | | |
| MEFV | Familial Mediterranean Fever | rs104895094 | p.K695R | | | | | | | | |
| MEFV | Familial Mediterranean Fever | rs3743930 | p.E148Q | | | | | | | | |
| FANCC | Fanconi anemia, complementation group C | rs104886456 | c.456+4A>T | 99% [18] | | 1 | Recessive | X | X | X | 31684 |
| FSHB | Follicle-stimulating hormone deficiency | rs5030646 | c.236_237delTG | | | 1 | Recessive | X | | X | 16382 |
| FMR1 | Fragile X syndrome | | CGG repeat | 99% [19] | | 1 | X-linked | X | | X | 250 |
| ALDOB | Fructose intolerance | rs1800546 | p.A149P | | | 1 | Recessive | X | | X | 16436 |
| FUT6 | Fucosyltransferase 6 deficiency | rs17855739 | p.E247K | | | 1 | Recessive | X | | X | 164 |
| GALT | Galactosemia | | del 5kb [20,21] | | | 3 | Recessive | X | | X | 57600 |
| GALT | Galactosemia | rs75391579 | Q188R | | 65% Euro [22] | | | | | | |
| GALT | Galactosemia | rs111033773 | K285N | | 8%, 25-40% Euro | | | | | | |
| GBA | Gaucher disease, type 1 | rs76763715 | p.N409S* | 98% [23,24] | 50-60% | 4 | Recessive | X | X | X | 900 |
| GBA | Gaucher disease, type 1 | rs421016 | p.L444P | | | | | | | | |
| GBA | Gaucher disease, type 1 | rs104886460 | c.115+1G>A | | | | | | | | |
| GBA | Gaucher disease, type 1 | rs387906315 | c.84dupG | | | | | | | | |
| GSS | Glutathione synthetase deficiency | | c.4delG | | | 1 | Recessive | X | | X | 16382 |
| G6PC | Glycogen storage disease Ia | rs1801175 | p.R83C* | 93-100% [25,26] | 0.3 | 1 | Recessive | X | | X | 65746 |
| NBEAL2 | Grey platelet syndrome | | c.5413dupG | | | 1 | Recessive | X | | X | 10505 |
| UNC13D | Haemophagocytic lymphohistiocytosis, familial | rs201908137 | c.753+1G>T* | | | 1 | Recessive | X | | X | 65544 |
| HFE | Hemochromatosis | rs1799945 | p.H63D | 20.3% [62] | | 1 | Recessive | X | | X | 25 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| GPI | Hemolytic anemia, nonspherocytic, due to glucose phosphate isomerase deficiency | rs137853586 | p.H59P* | | | 1 | Recessive | X | | X | 100000 |
| HPS1 | Hermansky-Pudlak syndrome 1 | rs281865082 | c.972delC* | | | 1 | Recessive | X | | X | 63512 |
| HPS3 | Hermasky-Pudlak syndrome 3 | rs201227603 | c.1163+1G>A* | | | 1 | Recessive | | | | 65746 |
| CBS | Homocystinuria | rs375846341 | c.1224-2A>C | | | 1 | Recessive | X | | X | 16382 |
| CBS | Homocystinuria, pyridoxine-responsive | rs5742905 | p.I278T | | | 1 | | X | | X | 995 |
| MVK | Hyper IgD syndrome | rs28934897 | p.V377I* | | | 1 | Recessive | X | | | 65746 |
| SLC6A20 | Hyperglycinuria | rs17279437 | p.T199M | | | 1 | Dominant | X | X | | 5 |
| APOE | Hyperlipoprotenemia, type III | rs429358 | p.C130R | | | 1 | Dominant | X | | X | 6 |
| HOGA1 | Hyperoxaluria, primary, type 3 | rs138207257 | p.G287V* | | | 2 | Recessive | X | | X | 65746 |
| HOGA1 | Hyperoxaluria, primary, type 3 | rs397509360 | c.944_946delAGG | | | | | | | | unknown |
| PRODH | Hyperprolinemia, type I | rs2904552 | p.R323H | | | 4 | Recessive | X | | X | 142 |
| PRODH | Hyperprolinemia, type I | rs2870984 | p.T358M | | | | | | | | |
| PRODH | Hyperprolinemia, type I | rs2904551 | p.L333P | | | | | | | | |
| PRODH | Hyperprolinemia, type I | rs137852934 | p.L181M | | | | | | | | |
| SLCO2A1 | Hypertrophic osteoarthropathy, primary | | c.830dupT* | | | 2 | Recessive | X | | X | 63995 |
| SLCO2A1 | Hypertrophic osteoarthropathy, primary | | c.1292delC* | | | | | | | | |
| BCHE | Hypocholinesterasaemia | | c.1158dupT | | | | | X | X | | 16129 |
| BCHE | Hypocholinesterasaemia | | c.1027dupA* | | | 4 | Recessive | X | X | | |
| BCHE | Hypocholinesterasaemia | | c.401dupA* | | | | | X | X | | |
| BCHE | Hypocholinesterasaemia | rs398124632 | c.435delTinsAG | | | | | X | X | | |
| FLG | Ichthyosis vulgaris | | c.2282_2285delCAGT* | | | 2 | Recessive | X | | X | 65544 |
| FLG | Ichthyosis vulgaris | rs61816761 | p.R501X* | | | | | | | | |
| TGM1 | Ichthyosis, congenital, autosomal recessive 1 | rs41295338 | p.S42Y | | | 2 | Recessive | X | | X | 7162 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| TGM1 | Ichthyosis, congenital, autosomal recessive 1 | rs35312232 | p.V518M* | | | | | | | | 65746 |
| ZBTB24 | Immunodeficiency, centromeric instability & facial anomalies syndrome | | c.501dupA* | | | 1 | Recessive | X | | X | 63512 |
| C5orf42 | Joubert syndrome | | c.8263dupA | | | 2 | Recessive | X | | X | 33856 |
| TMEM216 | Joubert Syndrome | rs201108965 | p.R73L | 95% [27] | | | | | | | |
| LCA5 | Leber congenital amaurosis | rs121918165 | c.835C>T | 1%[63] | | | | X | | X | 10000 |
| RPE65 | Leber congenital amaurosis 2 | | c.886dupA* | | | 2 | Recessive | X | | X | 7168 |
| RPE65 | Leber congenital amaurosis 2 | rs121918844 | c.361dupT | | | | | | | | |
| NDUFS4 | Leigh Syndrome | rs587776949 | c.462delA | | | | Recessive | X | | X | 100000 |
| DARS2 | Leukoencephalopathy, brain & spine involvement, lactate elevation | rs142433332 | c.492+2T>C* | | | 1 | Recessive | X | | X | 65544 |
| KCNE1 | Long QT syndrome 5 | rs1805128 | p.D85N | | | 1 | Dominant | X | X | X | 19 |
| MSH2 | Lynch syndrome | rs63750875 | p.A636P | 30% [28] | | 5 | Dominant | | X | | 118 |
| MSH6 | Lynch syndrome | rs267608078 | c.3261delC | | | | | | | | |
| MSH6 | Lynch syndrome | | c.2690dupA | | | | | | | | |
| MSH6 | Lynch syndrome | rs267608121 | c.3984_3987dupGTCA | | | | | | | | |
| MSH6 | Lynch syndrome | rs267608120 | c.3959_3962delCAAG | | | | | | | | |
| ZMPSTE24 | Mandibuloacral dysplasia | rs137854889 | c.1085dupT | | | 1 | Recessive | X | | X | 14281 |
| BCKDHB | Maple syrup urine disease | rs79761867 | p.R183P | >95% [29] | | 2 | Recessive | X | | X | 26244 |
| BCKDHB | Maple syrup urine disease | rs150084361 | p.G278S | | | | | | | | |
| MLC1 | Megalencephalic leukoencephalopathy with subcortical cysts | rs121908345 | p.P92S | | | 1 | Recessive | X | | X | 65746 |
| SLC19A2 | Megaloblastic anaemia, thiamine responsive | | c.1223+1G>A* | | | | Recessive | X | | X | 65544 |
| TYMP | Mitochondrial DNA depletion syndrome 1 (MNGIE type) | rs121913036 | p.E289G* | | | | Recessive | X | | X | 56689 |
| MCOLN1 | Mucolipidosis IV | rs104886461 | c.406-2A>G | 95% [30] | | 2 | Recessive | X | | X | 59536 |
| MCOLN1 | Mucolipidosis IV | | g.511_6943del | | | | | | | | |
| ANO5 | Muscular dystrophy, limb girdle 2L | rs137854521 | c.191dupA* | | | 1 | Recessive | X | | X | 63512 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| AMPD1 | Myoadenylate deaminase deficiency, myopathy due to | rs17602729 | p.Q45X | | | 1 | Recessive | X | | X | 235 |
| NEB | Nemaline myopathy | [31] | p.R2478_D2512del | 60%[64] | | 1 | Recessive | X | | X | 88804 |
| SLC9A3R1 | Nephrolithiasis/osteoporosis, hypophosphatemic, 2 | rs35910969 | p.L110V | | | 1 | Dominant | X | | X | 15 |
| PPT1 | Neuronal ceroid lipofuscinosis, infantile | rs386833634 | c.169dupA | | | 1 | Recessive | X | | X | 6833 |
| SMPD1 | Niemann-Pick disease, type A | rs120074118 | p.R610del | 99% [24,32,33] | | 4 | Recessive | X | | X | 32400 |
| SMPD1 | Niemann-Pick disease, type A | rs387906289 | c.996delC | | | | | | | | |
| SMPD1 | Niemann-Pick disease, type A | rs120074124 | p.L304P | | | | | | | | |
| SMPD1 | Niemann-Pick disease, type A/B | rs120074117 | p.R496L* | | | | | | | | |
| MC4R | Obesity | rs121913563 | p.A175T | | | 1 | Dominant | | X | | 43 |
| SDHA | Paraganglioma 5 | rs1061517 | p.M1L | | | 1 | Dominant | | X | | 93 |
| LRRK2 | Parkinson disease 8 | rs34637584 | p.G2019S* | | | 1 | Dominant | | X | | 8 |
| PHGDH | Phosphoglycerate dehydrogenase deficiency | rs121907987 | p.V490M* | | | 1 | Recessive | X | | X | 65746 |
| KLKB1 | Prekallikrein deficiency | rs560588447 | c.451dupT* | | | 1 | Recessive | X | | X | 58571 |
| POF1B | Premature ovarian failure 2B | rs75398746 | p.R329Q | | | 1 | X-linked | X | | X | 50 |
| BMP15 | Premature ovarian failure 4 | rs104894767 | p.A180T* | | | 1 | X-linked | X | | X | 250 |
| CCDC114 | Primary ciliary dyskinesia | | c.939delT | | | 2 | Recessive | X | | X | 65544 |
| DNAH5 | Primary ciliary dyskinesia | | c.5563dupA | | | | | X | | X | 15374 |
| PCCA | Propionic acidaemia | | c.722delG* | | | 2 | Recessive | X | | X | 63512 |
| PCCA | Propionic acidaemia | | c.923dupT* | | | | | | | | 58571 |
| FECH | Protoporphyria, erythropoietic | rs2272783 | c.333-48T>C | | | 1 | Recessive | X | | X | 334 |
| PHYH | Refsum disease | rs104894178 | p.R175W* | | | 1 | Recessive | X | | | 65746 |
| RP1 | Retinitis pigmentosa 1 | | c.4941dupT | | | 1 | Recessive | X | | X | 65544 |
| CA4 | Retinitis pigmentosa 17 | rs104894559 | p.R14W* | | | 1 | Dominant | X | X | | 122 |
| FAM161A | Retinitis pigmentosa 28 | rs397704718 | c.1355_1356delCA | | | 2 | Recessive | X | | X | unknown |
| FAM161A | Retinitis pigmentosa 28 | rs267606793 | p.R596X | | | | | X | | X | |
| DHDDS | Retinitis pigmentosa 59 | rs147394623 | c.124A>G | 0.86%*65* | | 1 | Recessive | X | | X | 55696 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| MAK[35] | Retinitis pigmentosa 62 | | 353-bp Alu ins Ex9 | | | 1 | Recessive | X | | X | 3018 |
| DHCR7 | Smith-Lemli-Opitz syndrome | rs138659167 | c.964-1G>C | | | | | | | | 5184 |
| DHCR7 | Smith-Lemli-Opitz syndrome | | p.M1V | >75%[36] | | 2 | Recessive | X | | X | |
| SPG11 | Spastic paraplegia | | c.2471dupT | | | 1 | Recessive | X | | X | 15874 |
| SMN1 | Spinal muscular atrophy37 | | Exon 7, copy number | >94%[37] | | 1 | Recessive | X | | X | 6724 |
| DLL3 | Spondylocostal dysostosis | | c.395delG* | | | 1 | Recessive | X | | X | 65544 |
| ABCA4 | Stargardt disease 1 | rs1800553 | p.G1961E | | | 1 | Recessive | X | | X | 2380 |
| HEXA | Tay-Sachs disease | rs387906309 | c.1277_1281 insTATC | 95% [24,38,39] | | 3 | Recessive | X | | X | 3600 |
| HEXA | Tay-Sachs disease | rs147324677 | c.1421+1G>C* | | | | | | | | |
| HEXA | Tay-Sachs disease | rs121907954 | p.G269S | 4%[66] | | | | | | | |
| ADAMTS13 | Thrombotic thrombocytopenic purpura, familial | rs11575933 | p.P475S | | | 1 | Recessive | X | | X | 16023 |
| RET | Thyroid carcinoma, familial medullary | rs77724903 | p.Y791F | | | 1 | Dominant | | X | | 19 |
| TG | Thyroid dyshormonogenesis 3 | rs121912648 | p.R296X* | | | 1 | Recessive | X | | X | 65746 |
| CACNA1C | Timothy syndrome | rs121912775 | p.G490R | | | 1 | Dominant | X | X | | 43 |
| PCDH15 | Usher syndrome, type 1F | rs111033260 | p.R245X | 75% [41] | | 1 | Recessive | X | | X | 15241 |
| CLRN1 | Usher syndrome, type 3A | rs111033258 | p.N48K* | 95-98% [42] | | 1 | Recessive | X | | X | 65746 |
| EPG5 | Vici syndrome | | c.5704dupT* | | | 1 | Recessive | X | | X | 100000 |
| BEST1 | Vitelliform macular dystrophy, adult onset | rs121918284 | p.R81H* | | | 1 | Dominant | | X | | 129 |
| VWF | Von Willebrand disease, type 2N | rs41276738 | p.R854Q* | | | 1 | Dominant | X | X | X | 128 |
| FKTN | Walker-Warburg syndrome | rs398123555 | c.1167_1168insA | 95% [43] | | 1 | Recessive | X | | X | 3906 |
| XPC | Xeroderma pigmentosum, group C | rs74737358 | p.P334H* | | | 1 | Recessive | X | | X | 65746 |

**Table 2S. List of mutations found that would be useful on a screening panel. Shaded mutations were detected in the sequenced TAGC samples. Unshaded mutations were not detected during sequencing but were added to the panel because they were previously known in the literature. Sensitivity AJ = sensitivity for picking up this disease in the AJ population. Sensitivity Gen. Pop. = sensitivity for picking up this disease in the general**

**population. No. variants per disease = Number of variants (mutations) listed for this disease. Repr. Risk = An X indicates that this variant would be tested to determine reproductive (carrier) risk. Pers. Risk = An X indicates that this variant would be tested to determine a person's personal risk of developing a disease. Dx = Diagnostic. Calculated prevalence = Prevalence for which this variant's frequency would predict, based on the Hardy-Weinberg equilibrium. Single prevalence derived from references in supplemental materials without additional of calculated prevalences. * = variant was only present in one allele in our test population, but was found in other populations.**

| Disease | ACMG recs | ACOG recs | Quest | LabCorp | Mount Sinai | Counsyl | Arup Lab | Center for Human Genetics (MA) | Emory | Mayo | University Hospitals Case Medical Center |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Bloom | X | X* | X | X | X | X | X | X | X | X | X |
| Canavan | X | X | X | X | X | X | X | X | X | X | X |
| Cystic Fibrosis | X | X | X | X | X | X | | | X | | |
| Dihydrolipoamide dehydrogenase def | | | | X | X | | | | X | | |
| Factor XI deficiency | | | | | | | | X | | | |
| Familial Dysautonomia | X | X | X | X | X | X | X | X | X | X | X |
| Familial hyperinsulinism | | | | X | X | X | | | X | | |
| Fanconi Anemia Group C | X | X* | X | X | X | X | X | X | X | X | X |
| Fragile X | | | | | | X | | | | | |
| Gaucher | X | X* | X | X | X | X | X | X | X | X | X |
| Glycogen Storage Disease Type 1a | | | X | X | X | X | | X | X | | |
| Joubert Syndrome 2 | | | | X | X | X | | | X | | |
| Maple Syrup Urine Disease | | | X | X | X | X | | X | X | | |
| Mucolipidosis IV | X | X* | X | X | X | X | X | X | X | X | X |
| Nemaline Myopathy | | | | | X | X | | | X | | |
| Niemann-Pick Type A | X | X* | X | X | X | X | X | X | X | X | X |
| Niemann-Pick Type B | | | X | | | | | | | X | |
| Spinal Muscular Atrophy | | | | X | | X | | | | | |
| Tay Sachs | X | X | X | X | X | X | X | X | X | X | X |
| Usher syndrome type 1F | | | | X | X | X | | | X | | |
| Usher syndrome type III | | | | X | X | X | | | X | | |
| Walker-Warburg syndrome | | | | X | X | | | | | | |
| Reference | 45 | 46 | 47 | 48 | 49 | 50 | 51 | 52 | 53 | 54 | 55 |

**Table 3S. Ashkenazi screening panels and recommendations referenced in our paper. An asterisk indicates that this test is optional.**

**Supplemental References**


1. Ellis, N. A. *et al.* The Ashkenazic Jewish Bloom syndrome mutation blmAsh is present in non-Jewish Americans of Spanish ancestry. *Am. J. Hum. Genet.* **63,** 1685–1693 (1998).
2. Petrucelli, N., Daly, M. & Feldman, G. *GeneReviews: BRCA1 and BRCA2 Hereditary Breast and Ovarian Cancer*.
3. Kaul, R. *et al.* Canavan disease: mutations among Jewish and non-Jewish patients. *Am. J. Hum. Genet.* **55,** 34–41 (1994).
4. Wilson, R. C. *et al.* Ethnic-specific distribution of mutations in 716 patients with congenital adrenal hyperplasia owing to 21-hydroxylase deficiency. *Mol. Genet. Metab.* **90,** 414–421 (2007).
5. Abeliovich, D. *et al.* Screening for five mutations detects 97% of cystic fibrosis (CF) chromosomes and predicts a carrier frequency of 1:29 in the Jewish Ashkenazi population. *Am. J. Hum. Genet.* **51,** 951–956 (1992).
6. Quint, A., Lerer, I., Sagi, M. & Abeliovich, D. Mutation spectrum in Jewish cystic fibrosis patients in Israel: implication to carrier screening. *Am. J. Med. Genet. A.* **136,** 246–248 (2005).
7. Palomaki, G. E., Haddow, J. E., Bradley, L. A. & FitzSimmons, S. C. Updated assessment of cystic fibrosis mutation frequencies in non-Hispanic Caucasians. *Genet. Med. Off. J. Am. Coll. Med. Genet.* **4,** 90–94 (2002).
8. Morell, R. J. *et al.* Mutations in the connexin 26 gene (GJB2) among Ashkenazi Jews with nonsyndromic recessive deafness. *N. Engl. J. Med.* **339,** 1500–1505 (1998).
9. Lerer, I. *et al.* Contribution of connexin 26 mutations to nonsyndromic deafness in Ashkenazi patients and the variable phenotypic effect of the mutation 167delT. *Am. J. Med. Genet.* **95,** 53–56 (2000).
10. Shaag, A. *et al.* Molecular basis of lipoamide dehydrogenase deficiency in Ashkenazi Jews. *Am. J. Med. Genet.* **82,** 177–182 (1999).

11. Peretz, H. *et al.* Type I mutation in the F11 gene is a third ancestral mutation which causes factor XI deficiency in Ashkenazi Jews. *J. Thromb. Haemost. JTH* **11,** 724–730 (2013).

12. Anderson, S. L. *et al.* Familial dysautonomia is caused by mutations of the IKAP gene. *Am. J. Hum. Genet.* **68,** 753–758 (2001).

13. Slaugenhaupt, S. A. *et al.* Tissue-specific expression of a splicing mutation in the IKBKAP gene causes familial dysautonomia. *Am. J. Hum. Genet.* **68,** 598–605 (2001).

14. Nestorowicz, A. *et al.* Mutations in the sulonylurea receptor gene are associated with familial hyperinsulinism in Ashkenazi Jews. *Hum. Mol. Genet.* **5,** 1813–1822 (1996).

15. Aksentijevich, I. *et al.* Mutation and haplotype studies of familial Mediterranean fever reveal new ancestral relationships and evidence for a high carrier frequency with reduced penetrance in the Ashkenazi Jewish population. *Am. J. Hum. Genet.* **64,** 949–962 (1999).

16. Stoffman, N. *et al.* Higher than expected carrier rates for familial Mediterranean fever in various Jewish ethnic groups. *Eur. J. Hum. Genet. EJHG* **8,** 307–310 (2000).

17. Touitou, I. The spectrum of Familial Mediterranean Fever (FMF) mutations. *Eur. J. Hum. Genet. EJHG* **9,** 473–483 (2001).

18. Auerbach, A. D. Fanconi anemia: genetic testing in Ashkenazi Jews. *Genet. Test.* **1,** 27–33 (1997).

19. Hantash, F. M. *et al.* FMR1 premutation carrier frequency in patients undergoing routine population-based carrier screening: insights into the prevalence of fragile X syndrome, fragile X-associated tremor/ataxia syndrome, and fragile X-associated primary ovarian insufficiency in the United States. *Genet. Med. Off. J. Am. Coll. Med. Genet.* **13,** 39–45 (2011).

20. Elsas, L. J., 2nd & Lai, K. The molecular biology of galactosemia. *Genet. Med. Off. J. Am. Coll. Med. Genet.* **1,** 40–48 (1998).

21. Goldstein, N. *et al.* The GALT rush: high carrier frequency of an unusual deletion mutation of the GALT gene in the Ashkenazi population. *Mol. Genet. Metab.* **102,** 157–160 (2011).

22. Tyfield, L. *et al.* Classical galactosemia and mutations at the galactose-1-phosphate uridyl transferase (GALT) gene. *Hum. Mutat.* **13,** 417–430 (1999).

23. Beutler, E., Gelbart, T., Kuhl, W., Sorge, J. & West, C. Identification of the second common Jewish Gaucher disease mutation makes possible population-based screening for the heterozygous state. *Proc. Natl. Acad. Sci. U. S. A.* **88,** 10544–10547 (1991).

24. Scott, S. A. *et al.* Experience with carrier screening and prenatal diagnosis for 16 Ashkenazi Jewish genetic diseases. *Hum. Mutat.* **31,** 1240–1250 (2010).

25. Parvari, R. *et al.* Glycogen storage disease type 1a in Israel: biochemical, clinical, and mutational studies. *Am. J. Med. Genet.* **72,** 286–290 (1997).

26. Lei, K. J. *et al.* Genetic basis of glycogen storage disease type 1a: prevalent mutations at the glucose-6-phosphatase locus. *Am. J. Hum. Genet.* **57,** 766–771 (1995).

27. Edvardson, S. *et al.* Joubert syndrome 2 (JBTS2) in Ashkenazi Jews is associated with a TMEM216 mutation. *Am. J. Hum. Genet.* **86,** 93–97 (2010).

28. Guillem, J. G. *et al.* A636P testing in Ashkenazi Jews. *Fam. Cancer* **3,** 223–227 (2004).

29. Edelmann, L. *et al.* Maple syrup urine disease: identification and carrier-frequency determination of a novel founder mutation in the Ashkenazi Jewish population. *Am. J. Hum. Genet.* **69,** 863–868 (2001).

30. Bassi, M. T. *et al.* Cloning of the gene encoding a novel integral membrane protein, mucolipidin- and identification of the two major founder mutations causing mucolipidosis type IV. *Am. J. Hum. Genet.* **67,** 1110–1120 (2000).

31. Anderson, S. L. *et al.* Nemaline myopathy in the Ashkenazi Jewish population is caused by a deletion in the nebulin gene. *Hum. Genet.* **115,** 185–190 (2004).

32. Levran, O., Desnick, R. J. & Schuchman, E. H. Identification and expression of a common missense mutation (L302P) in the acid sphingomyelinase gene of Ashkenazi Jewish type A Niemann-Pick disease patients. *Blood* **80,** 2081–2087 (1992).

33. Levran, O., Desnick, R. J. & Schuchman, E. H. Type A Niemann-Pick disease: a frameshift mutation in the acid sphingomyelinase gene (fsP330) occurs in Ashkenazi Jewish patients. *Hum. Mutat.* **2,** 317–319 (1993).

34. Schuchman, E. H. & Miranda, S. R. Niemann-Pick disease: mutation update, genotype/phenotype correlations, and prospects for genetic testing. *Genet. Test.* **1,** 13–19 (1997).

35. Stone, E. M. *et al.* Autosomal recessive retinitis pigmentosa caused by mutations in the MAK gene. *Invest. Ophthalmol. Vis. Sci.* **52,** 9665–9673 (2011).

36. Witsch-Baumgartner, M. *et al.* Identification of 14 novel mutations in DHCR7 causing the Smith-Lemli-Opitz syndrome and delineation of the DHCR7 mutational spectra in Spain and Italy. *Hum. Mutat.* **25,** 412 (2005).

37. Luo, M. *et al.* An Ashkenazi Jewish SMN1 haplotype specific to duplication alleles improves pan-ethnic carrier screening for spinal muscular atrophy. *Genet. Med. Off. J. Am. Coll. Med. Genet.* **16,** 149–156 (2014).

38. Triggs-Raine, B. L. & Gravel, R. A. Diagnostic heteroduplexes: simple detection of carriers of a 4-bp insertion mutation in Tay-Sachs disease. *Am. J. Hum. Genet.* **46,** 183–184 (1990).

39. Triggs-Raine, B. L., Akerman, B. R., Clarke, J. T. & Gravel, R. A. Sequence of DNA flanking the exons of the HEXA gene, and identification of mutations in Tay-Sachs disease. *Am. J. Hum. Genet.* **49,** 1041–1054 (1991).

40. Elpeleg, O. N. *et al.* Mutation analysis of the FAH gene in Israeli patients with tyrosinemia type I. *Hum. Mutat.* **19,** 80–81 (2002).

41. Ben-Yosef, T. *et al.* A mutation of PCDH15 among Ashkenazi Jews with the type 1 Usher syndrome. *N. Engl. J. Med.* **348,** 1664–1670 (2003).

42. Ness, S. L. *et al.* Genetic homogeneity and phenotypic variability among Ashkenazi Jews with Usher syndrome type III. *J. Med. Genet.* **40,** 767–772 (2003).

43. Chang, W. *et al.* Founder Fukutin mutation causes Walker-Warburg syndrome in four Ashkenazi Jewish families. *Prenat. Diagn.* **29,** 560–569 (2009).

44. Fedick, A., Jalas, C. & Treff, N. R. A deleterious mutation in the PEX2 gene causes Zellweger syndrome in individuals of Ashkenazi Jewish descent. *Clin. Genet.* **85,** 343–346 (2014).

45. Gross, S. J., Pletcher, B. A., Monaghan, K. G. & Professional Practice and Guidelines Committee. Carrier screening in individuals of Ashkenazi Jewish descent. *Genet. Med. Off. J. Am. Coll. Med. Genet.* **10,** 54–56 (2008).

46. ACOG Committee on Genetics. ACOG Committee Opinion No. 442: Preconception and prenatal carrier screening for genetic diseases in individuals of Eastern European Jewish descent. *Obstet. Gynecol.* **114,** 950–953 (2009).

47. Ashkenazi Jewish Panel. at <http://www.questdiagnostics.com/testcenter/testguide.action?dc=TH_AshJPnl>

48. Ashkenazi Jewish Carrier Testing - Integrated Genetics. at <https://www.labcorp.com/wps/portal/integratedgenetics?WCM_GLOBAL_CONTEXT=/wps/wcm/connect/IntGeneticsLib/integratedgenetics/home/our+services/reproductive+testing/aj-carrier-test>

49. Jewish Genetic Screening Brochure. at <https://icahn.mssm.edu/static_files/MSSM/Files/Research/Labs/Genetic%20Testing%20Laboratory/Jewish-Genetic-Screening-Brochure.pdf>

50. Program for Jewish Genetic Health | Yeshiva University, New York. at <http://www.yu.edu/jll/geneticheath/core-efforts/awareness-education/program-resources/genetic-basics/#List%20of%20Diseases>

51. Brochure AJ Patients. at <http://www.aruplab.com/files/resources/genetics/Brochure_patient_aj.pdf>

52. DNA Tests (Descriptions and CPT Codes) | Center for Human Genetics, Inc. at <http://chginc.org/dna-diagnostics/dna-tests-descriptions-and-cpt-codes/>

53. Emory Ashkenazi Screening Panel. at <http://genetics.emory.edu/egl/documents/AJ1012.pdf>

54. AJPWO - Clinical: Ashkenazi Jewish Mutation Analysis Panel Without Cystic Fibrosis (CF). at <http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/88887>

55. Ashkenazi Jewish Disease Targeted Sequence Analysis Panel | Center for Human Genetics | University Hospitals Case Medical Center | Cleveland, OH. at <http://www.uhhospitals.org/case/services/genetics/laboratory/tests-offered/ashkenazi-jewish-disease-carrier-screening-panel>

1. Ellis, N. A. *et al.* The Ashkenazic Jewish Bloom syndrome mutation blmAsh is present in non-Jewish Americans of Spanish ancestry. *Am. J. Hum. Genet.* **63,** 1685–1693 (1998).
2. Petrucelli, N., Daly, M. & Feldman, G. *GeneReviews: BRCA1 and BRCA2 Hereditary Breast and Ovarian Cancer*.
3. Kaul, R. *et al.* Canavan disease: mutations among Jewish and non-Jewish patients. *Am. J. Hum. Genet.* **55,** 34–41 (1994).
4. Wilson, R. C. *et al.* Ethnic-specific distribution of mutations in 716 patients with congenital adrenal hyperplasia owing to 21-hydroxylase deficiency. *Mol. Genet. Metab.* **90,** 414–421 (2007).

5. Abeliovich, D. *et al.* Screening for five mutations detects 97% of cystic fibrosis (CF) chromosomes and predicts a carrier frequency of 1:29 in the Jewish Ashkenazi population. *Am. J. Hum. Genet.* **51,** 951–956 (1992).
6. Quint, A., Lerer, I., Sagi, M. & Abeliovich, D. Mutation spectrum in Jewish cystic fibrosis patients in Israel: implication to carrier screening. *Am. J. Med. Genet. A.* **136,** 246–248 (2005).
7. Palomaki, G. E., Haddow, J. E., Bradley, L. A. & FitzSimmons, S. C. Updated assessment of cystic fibrosis mutation frequencies in non-Hispanic Caucasians. *Genet. Med. Off. J. Am. Coll. Med. Genet.* **4,** 90–94 (2002).
8. Morell, R. J. *et al.* Mutations in the connexin 26 gene (GJB2) among Ashkenazi Jews with nonsyndromic recessive deafness. *N. Engl. J. Med.* **339,** 1500–1505 (1998).
9. Lerer, I. *et al.* Contribution of connexin 26 mutations to nonsyndromic deafness in Ashkenazi patients and the variable phenotypic effect of the mutation 167delT. *Am. J. Med. Genet.* **95,** 53–56 (2000).
10. Shaag, A. *et al.* Molecular basis of lipoamide dehydrogenase deficiency in Ashkenazi Jews. *Am. J. Med. Genet.* **82,** 177–182 (1999).
11. Peretz, H. *et al.* Type I mutation in the F11 gene is a third ancestral mutation which causes factor XI deficiency in Ashkenazi Jews. *J. Thromb. Haemost. JTH* **11,** 724–730 (2013).
12. Anderson, S. L. *et al.* Familial dysautonomia is caused by mutations of the IKAP gene. *Am. J. Hum. Genet.* **68,** 753–758 (2001).
13. Slaugenhaupt, S. A. *et al.* Tissue-specific expression of a splicing mutation in the IKBKAP gene causes familial dysautonomia. *Am. J. Hum. Genet.* **68,** 598–605 (2001).
14. Nestorowicz, A. *et al.* Mutations in the sulonylurea receptor gene are associated with familial hyperinsulinism in Ashkenazi Jews. *Hum. Mol. Genet.* **5,** 1813–1822 (1996).

15. Aksentijevich, I. *et al.* Mutation and haplotype studies of familial Mediterranean fever reveal new ancestral relationships and evidence for a high carrier frequency with reduced penetrance in the Ashkenazi Jewish population. *Am. J. Hum. Genet.* **64,** 949–962 (1999).

16. Stoffman, N. *et al.* Higher than expected carrier rates for familial Mediterranean fever in various Jewish ethnic groups. *Eur. J. Hum. Genet. EJHG* **8,** 307–310 (2000).

17. Touitou, I. The spectrum of Familial Mediterranean Fever (FMF) mutations. *Eur. J. Hum. Genet. EJHG* **9,** 473–483 (2001).

18. Auerbach, A. D. Fanconi anemia: genetic testing in Ashkenazi Jews. *Genet. Test.* **1,** 27–33 (1997).

19. Hantash, F. M. *et al.* FMR1 premutation carrier frequency in patients undergoing routine population-based carrier screening: insights into the prevalence of fragile X syndrome, fragile X-associated tremor/ataxia syndrome, and fragile X-associated primary ovarian insufficiency in the United States. *Genet. Med. Off. J. Am. Coll. Med. Genet.* **13,** 39–45 (2011).

20. Elsas, L. J., 2nd & Lai, K. The molecular biology of galactosemia. *Genet. Med. Off. J. Am. Coll. Med. Genet.* **1,** 40–48 (1998).

21. Goldstein, N. *et al.* The GALT rush: high carrier frequency of an unusual deletion mutation of the GALT gene in the Ashkenazi population. *Mol. Genet. Metab.* **102,** 157–160 (2011).

22. Tyfield, L. *et al.* Classical galactosemia and mutations at the galactose-1-phosphate uridyl transferase (GALT) gene. *Hum. Mutat.* **13,** 417–430 (1999).

23. Beutler, E., Gelbart, T., Kuhl, W., Sorge, J. & West, C. Identification of the second common Jewish Gaucher disease mutation makes possible population-based screening for the heterozygous state. *Proc. Natl. Acad. Sci. U. S. A.* **88,** 10544–10547 (1991).

24. Scott, S. A. *et al.* Experience with carrier screening and prenatal diagnosis for 16 Ashkenazi Jewish genetic diseases. *Hum. Mutat.* **31,** 1240–1250 (2010).

25. Parvari, R. *et al.* Glycogen storage disease type 1a in Israel: biochemical, clinical, and mutational studies. *Am. J. Med. Genet.* **72,** 286–290 (1997).

26. Lei, K. J. *et al.* Genetic basis of glycogen storage disease type 1a: prevalent mutations at the glucose-6-phosphatase locus. *Am. J. Hum. Genet.* **57,** 766–771 (1995).

27. Edvardson, S. *et al.* Joubert syndrome 2 (JBTS2) in Ashkenazi Jews is associated with a TMEM216 mutation. *Am. J. Hum. Genet.* **86,** 93–97 (2010).

28. Guillem, J. G. *et al.* A636P testing in Ashkenazi Jews. *Fam. Cancer* **3,** 223–227 (2004).

29. Edelmann, L. *et al.* Maple syrup urine disease: identification and carrier-frequency determination of a novel founder mutation in the Ashkenazi Jewish population. *Am. J. Hum. Genet.* **69,** 863–868 (2001).

30. Bassi, M. T. *et al.* Cloning of the gene encoding a novel integral membrane protein, mucolipidin- and identification of the two major founder mutations causing mucolipidosis type IV. *Am. J. Hum. Genet.* **67,** 1110–1120 (2000).

31. Anderson, S. L. *et al.* Nemaline myopathy in the Ashkenazi Jewish population is caused by a deletion in the nebulin gene. *Hum. Genet.* **115,** 185–190 (2004).

32. Levran, O., Desnick, R. J. & Schuchman, E. H. Identification and expression of a common missense mutation (L302P) in the acid sphingomyelinase gene of Ashkenazi Jewish type A Niemann-Pick disease patients. *Blood* **80,** 2081–2087 (1992).

33. Levran, O., Desnick, R. J. & Schuchman, E. H. Type A Niemann-Pick disease: a frameshift mutation in the acid sphingomyelinase gene (fsP330) occurs in Ashkenazi Jewish patients. *Hum. Mutat.* **2,** 317–319 (1993).

34. Schuchman, E. H. & Miranda, S. R. Niemann-Pick disease: mutation update, genotype/phenotype correlations, and prospects for genetic testing. *Genet. Test.* **1,** 13–19 (1997).

35. Stone, E. M. *et al.* Autosomal recessive retinitis pigmentosa caused by mutations in the MAK gene. *Invest. Ophthalmol. Vis. Sci.* **52,** 9665–9673 (2011).

36. Witsch-Baumgartner, M. *et al.* Identification of 14 novel mutations in DHCR7 causing the Smith-Lemli-Opitz syndrome and delineation of the DHCR7 mutational spectra in Spain and Italy. *Hum. Mutat.* **25,** 412 (2005).

37. Luo, M. *et al.* An Ashkenazi Jewish SMN1 haplotype specific to duplication alleles improves pan-ethnic carrier screening for spinal muscular atrophy. *Genet. Med. Off. J. Am. Coll. Med. Genet.* **16,** 149–156 (2014).

38. Triggs-Raine, B. L. & Gravel, R. A. Diagnostic heteroduplexes: simple detection of carriers of a 4-bp insertion mutation in Tay-Sachs disease. *Am. J. Hum. Genet.* **46,** 183–184 (1990).

39. Triggs-Raine, B. L., Akerman, B. R., Clarke, J. T. & Gravel, R. A. Sequence of DNA flanking the exons of the HEXA gene, and identification of mutations in Tay-Sachs disease. *Am. J. Hum. Genet.* **49,** 1041–1054 (1991).

40. Elpeleg, O. N. *et al.* Mutation analysis of the FAH gene in Israeli patients with tyrosinemia type I. *Hum. Mutat.* **19,** 80–81 (2002).

41. Ben-Yosef, T. *et al.* A mutation of PCDH15 among Ashkenazi Jews with the type 1 Usher syndrome. *N. Engl. J. Med.* **348,** 1664–1670 (2003).

42. Ness, S. L. *et al.* Genetic homogeneity and phenotypic variability among Ashkenazi Jews with Usher syndrome type III. *J. Med. Genet.* **40,** 767–772 (2003).

43. Chang, W. *et al.* Founder Fukutin mutation causes Walker-Warburg syndrome in four Ashkenazi Jewish families. *Prenat. Diagn.* **29,** 560–569 (2009).

44. Fedick, A., Jalas, C. & Treff, N. R. A deleterious mutation in the PEX2 gene causes Zellweger syndrome in individuals of Ashkenazi Jewish descent. *Clin. Genet.* **85,** 343–346 (2014).

45. Gross, S. J., Pletcher, B. A., Monaghan, K. G. & Professional Practice and Guidelines Committee. Carrier screening in individuals of Ashkenazi Jewish descent. *Genet. Med. Off. J. Am. Coll. Med. Genet.* **10,** 54–56 (2008).

46. ACOG Committee on Genetics. ACOG Committee Opinion No. 442: Preconception and prenatal carrier screening for genetic diseases in individuals of Eastern European Jewish descent. *Obstet. Gynecol.* **114,** 950–953 (2009).

47. Ashkenazi Jewish Panel. at <http://www.questdiagnostics.com/testcenter/testguide.action?dc=TH_AshJPnl>

48. Ashkenazi Jewish Carrier Testing - Integrated Genetics. at <https://www.labcorp.com/wps/portal/integratedgenetics?WCM_GLOBAL_CONTEXT=/wps/wcm/connect/IntGeneticsLib/integratedgenetics/home/our+services/reproductive+testing/aj-carrier-test>

49. Jewish Genetic Screening Brochure. at <https://icahn.mssm.edu/static_files/MSSM/Files/Research/Labs/Genetic%20Testing%20Laboratory/Jewish-Genetic-Screening-Brochure.pdf>

50. Program for Jewish Genetic Health | Yeshiva University, New York. at <http://www.yu.edu/jll/geneticheath/core-efforts/awareness-education/program-resources/genetic-basics/#List%20of%20Diseases>

51. Brochure AJ Patients. at <http://www.aruplab.com/files/resources/genetics/Brochure_patient_aj.pdf>

52. DNA Tests (Descriptions and CPT Codes) | Center for Human Genetics, Inc. at <http://chginc.org/dna-diagnostics/dna-tests-descriptions-and-cpt-codes/>

53. Emory Ashkenazi Screening Panel. at <http://genetics.emory.edu/egl/documents/AJ1012.pdf>

54. AJPWO - Clinical: Ashkenazi Jewish Mutation Analysis Panel Without Cystic Fibrosis (CF). at <http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/88887>

55. Ashkenazi Jewish Disease Targeted Sequence Analysis Panel | Center for Human Genetics | University Hospitals Case Medical Center | Cleveland, OH. <http://www.uhhospitals.org/case/services/genetics/laboratory/tests-offered/ashkenazi-jewish-disease-carrier-screening-panel>

56. Shalmon, L., Kirschmann, C., & Zaizov, R. Alpha-thalassemia genes in Israel: deletional and nondeletional mutations in patients of various origins. *Hum. Hered.* **46,** 15-9, (1996).

57. Tein I., *et al.* Short-chain acyl-CoA dehydrogenase gene mutation (c.319C>T) presents with clinical heterogeneity and is candidate founder mutation in individuals of Ashkenazi Jewish origin. *Mol. Genet. Metab*. **93**, 179-89, (2008).

58. Edvardson, S., *et al.* A deleterious mutation in the LOXHD1 gene causes autosomal recessive hearing loss in Ashkenazi Jews. *Am. J. Med. Genet* .A. **155A**, 1170-2 (2011.)

59. Asakai, R., *et al.* Factor XI deficiency in Ashkenazi Jews in Israel. *N. Engl. J. Med*. **325**, 153-8, (1991).

60. Shpilberg, O., *et al.* One of the two common mutations causing factor XI deficiency in Ashkenazi Jews (type II) is also prevalent in Iraqi Jews, who represent the ancient gene pool of Jews. *Blood*. **85**, 429-32, (1995).

61. Meiner, V., *et al.* A common Lithuanian mutation causing familial hypercholesterolemia in Ashkenazi Jews. *Am. J. Hum. Genet*.**49**, 443-9 (1991).

62. Reish, O., *et al.* Frequencies of C282Y and H63D alleles in the HFE gene among various Jewish ethnic groups in Israel: a change of concept required. *Genet. Med*. **12**, 122-5, (2010).

63. Banin, E., *et al.*. Molecular anthropology meets genetic medicine to treat blindness in the North African Jewish population: human gene therapy initiated in Israel. *Hum. Gene. Ther*. **21**, 1749-57, (2010).

64. Anderson, S., *et al.* Nemaline myopathy in the Ashkenazi Jewish population is caused by a deletion in the nebulin gene. *Hum Genet*.**115**, 185-90, (2004).

65. Zelinger, L., *et al.* A missense mutation in DHDDS, encoding dehydrodolichyl diphosphate synthase, is associated with autosomal-recessive retinitis pigmentosa in Ashkenazi Jews. *Am. J. Hum. Genet*. **88**, 207-15,(2011).

66. Triggs-Raine, B.L., *et al.* Screening for carriers of Tay-Sachs disease among Ashkenazi Jews. A comparison of DNA-based and enzyme-based tests. *N. Engl. J. Med*. **323,** 6-12, (1990).