

ОБРАЗЕЦ АНОМАЛИИ НЕ ОБНАРУЖЕНЫ

PATIENT INFORMATION		REFERRAL INFORMATION	
NAME Sample 1		CLINIC NAME New Testing Clinic	
ID NUMBER 389274		CLINIC ID 446	
DATE OF BIRTH (DD/MM/YYYY) 25/03/1985	GESTATIONAL AGE Week: 13 Day: 0	REFERRING CLINICIAN Dr. New Doctor	
IVF STATUS No	NUMBER OF FETUSES One	CLINIC FAX	
SAMPLE INFORMATION			
ORDER NUMBER V977146	LAB NUMBER 678	DATE OF COLLECTION (DD/MM/YYYY) 05/06/2018	DATE RECEIVED (DD/MM/YYYY) 05/06/2018
VERAgene PRENATAL SCREENING TEST RESULTS			
VERY LOW RISK NIPT Results	CONDITION	REMARK	
	Trisomy 21	The results show very low risk for trisomy 21	
	Trisomy 18	The results show very low risk for trisomy 18	
	Trisomy 13	The results show very low risk for trisomy 13	
	Trisomy X	The results show very low risk for trisomy X	
	Monosomy X	The results show very low risk for monosomy X	
	XXY Constitution	The results show very low risk for XXY constitution	
FETAL FRACTION	XXY Constitution	The results show very low risk for XXY constitution	
8.9%	XXYY Constitution	The results show very low risk for XXYY constitution	
	Microdeletions: (DiGeorge,1p36 deletion syndrome,Smith-Magenis, Wolf Hirschhorn)	The results show very low risk for microdeletions (DiGeorge (22q11), 1p36 deletion syndrome, Smith-Magenis (17p11.2), Wolf Hirschhorn (4p16.3))	
	Panel of 50 single gene diseases	The results show very low risk for the panel of 50 monogenic diseases	
	Presence/Absence of Y chromosome	The results show the presence of Y chromosome	
INTERPRETATION			
The results show very low risk for all tested conditions screened. The fetal fraction is 8.9%, which is sufficient for analysis. The results should be communicated by the referring clinician with appropriate counselling.			

TEST METHOD

VERAgene is a Laboratory Developed Test (LDT) from NIPD Genetics Public Company Ltd for prenatal screening that analyses cell-free DNA (cfDNA) from maternal plasma and sample from biological father. Multiplexed parallel analysis of specific regions of interest was applied for the copy number determination of chromosomes 13, 18, 21, aneuploidies of X, Y, select microdeletions including, DiGeorge (22q11 deletion), 1p36 deletion syndrome, Smith-Magenis (17p11.2 deletion), Wolf Hirschhorn (4p16.3 deletion), Y detection and mutation detection for 50 single gene diseases (Table 1).


TEST DESCRIPTION

Test performance is valid only for full chromosomal aneuploidies for chromosomes 21, 18, and 13 aneuploidies of X, Y, select microdeletions, Y detection and a number of pathogenic and likely pathogenic mutations associated with monogenic diseases listed in Table 1. It does not exclude other chromosomal disorders, birth defects or other complications. VERAgene is available for singleton and twin pregnancies only, including in-vitro fertilization (IVF) pregnancies of at least 10 weeks of gestation. Sex chromosome aneuploidies are not reportable for twin gestations. The VERAgene test cannot be performed on pregnancies achieved with egg/sperm donation or surrogacy or vanished twin pregnancies. Patients with malignancy or history of malignancy, patients with bone marrow or organ transplant are not eligible for the test. Furthermore, samples from both biological parents are required for the test to be performed. In a small number of cases the amount of fetal DNA present in maternal blood (fetal fraction), is not sufficient for analysis and a redraw maybe requested.

Validation studies are carried out for all conditions by NIPD Genetics Public Company Ltd. The test is not intended and not validated for mosaicism, triploidy, partial trisomy or translocations. This test has been validated on full region deletions and maybe unable to detect deletion of smaller regions. The test will not identify all deletions associated

with each microdeletion syndrome. Furthermore, the test is mutations which are associated with the monogenic diseases risk result reduces but does not eliminate the possibility of the result for twin pregnancies indicates high risk for the presence detection of Y indicates the presence of at least one Y chromosome. Although this test is highly accurate, there is still a small possibility for false positive or false negative results. This may be caused by technical and/or biological limitations, including but not limited to confined placental mosaicism (CPM) or other types of mosaicism, maternal constitutional or somatic chromosomal abnormalities, residual cfDNA from a vanished twin or other rare molecular events. The VERAgene test is not diagnostic but a screening test and results should be considered in the context of other clinical criteria. Clinical correlation with ultrasound findings, and other clinical data and tests is recommended. If definitive diagnosis is desired, amniocentesis is necessary. The referral clinician is responsible for counselling before and after the test including the provision of advice regarding the need for additional invasive genetic testing.

not intended and not validated for a number of listed in Table1 but are not tested. Therefore, a very low fetus to be affected or carry the mutation. A very high risk of at least one affected fetus. In twin pregnancies,

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 ASCP Approved by:

DATE OF REPORT (DD/MM/YYYY): **06/06/2018**

TABLE 1

Condition	Gene	Mutations	Det Freq	Area	References
3 Methylcrotonyl CoA Carboxylase Deficiency 1	MCCC1	c.1310T>C (p.Leu437Pro); c.1155A>C (p.Arg385Ser)	28% >35%	European ppn General ppn	Baumgartner, M. R. et al. (2001); Fonseca, H. et al.(2016); Grünert, S. C. et al. (2012)
3 Methylcrotonyl CoA Carboxylase Deficiency 2	MCCC2	c.295G>C (p.Glu99Gln); c.464G>A (p.Arg155Gln); c.499T>C (p.Cys167Arg); c.569A>G (p.His190Arg); c.803G>C (p.Arg268Thr); c.838G>T (p.Asp280Tyr); c.929C>G (p.Pro310Arg); c.1309A>G (p.Ile437Val)	>35%	General ppn	Baumgartner, M. R. et al. (2001); Fonseca, H. et al.(2016); Grünert, S. C. et al. (2012)
Abetalipoproteinemia	MTTP	c.2593G>T (p.Gly865Ter)	95%	Ashkenazi Jewish	Benayoun, L. et al. (2007)
Arthrogryposis Mental Retardation Seizures	SLC35A3	c.514C>T (p.Gln172Ter)	>50%	Ashkenazi Jewish	Edvardson, S. et al. (2013)
Autosomal recessive polycystic kidney disease	PKHD1	c.10658T>C (p.Ile3553Thr); c.10444C>T (p.Arg3482Cys); c.10412T>G (p.Val3471Gly); c.10219C>T (p.Gln3407Ter); c.10174C>T (p.Gln3392Ter); c.9689delA (p.Asp3230Valfs); c.9530T>C (p.Ile3177Thr); c.9053C>T (p.Ser3018Phe); c.8870T>C (p.Ile2957Thr); c.8581A>G (p.Ser2861Gly); c.8011C>T (p.Arg2671Ter); c.6992T>A (p.Ile2331Lys); c.5895dupA (p.Leu1966Thrfs); c.5513A>G (p.Tyr1838Cys); c.5236+1G>A; c.4991C>T (p.Ser1664Phe); c.4870C>T (p.Arg1624Trp); c.3761_3762delCCinsG (p.Ala1254Glyfs); c.3407A>G (p.Tyr1136Cys); c.3367G>A (p.Gly1123Ser); c.2854G>A (p.Gly952Arg); c.2414C>T (p.Pro805Leu); c.2341C>T (p.Arg781Ter); c.2279G>A (p.Arg760His); c.1486C>T (p.Arg496Ter); c.1068dup (p.Asn357IlefsX57); c.664A>G (p.Ile222Val); c.383delC (p.Thr128IlefsX25); c.370C>T (p.Arg124Ter); c.107C>T (p.Thr36Met)	90% 69% 70%	Ashkenazi Jewish General ppn Caucasian	Sweeney, W. E. & Avner, E. D. (1993); Shi, L. et al.(2017).
Bardet Biedl syndrome 12	BBS12	c.335_337delTAG (p.Val113del); c.865G>C (p.Ala289Pro); c.1063C>T (p.Arg355Ter); c.1483_1484delGA (p.Glu495Argfs)	>50%	European ppn	Stoetzel, C. et al. (2007); Burstedt, M. et al. (2013); Burstedt, M. S. et al. (2001); Muller, J. et al. (2010)
Canavan disease	ASPA	c.433-2A>G; c.693C>A (p.Tyr231Ter); c.854A>C (p.Glu285Ala); c.914C>A (p.Ala305Glu)	97-98% 60%	Ashkenazi Jewish EU	Feigenbaum, A. et al. (2004); Kaul, R. et al. (1994); Matalon, R. & Matalon, K. M. (Elsevier, 2015)
Choreacanthocytosis	VPS13A	c.6059delC (p.Pro2020fs)	66.67%	Ashkenazi Jewish (founder)	Rampoldi, L. et al. (2001); Dobson-Stone, C. et al. (2002); Siegl, C. et al. (2013); Lossos, A. et al. (2005)

Crigler Najjar syndrome, Type I	UGT1A1	c.513_515delCTT (p.Phe171del); c.524T>A (p.Leu175Gln); c.840C>A (p.Cys280Ter); c.923G>A (p.Gly308Glu); c.991C>T (p.Gln331Ter); c.992A>G (p.Gln331Arg); c.1021C>T (p.Arg341Ter); c.1070A>G (p.Gln357Arg); c.1124C>T (p.Ser375Phe); c.1198A>G (p.Asn400Asp)	>99% >70%	Tunisia (founder) Sardinia	Francoual, J. et al. (2002)
Factor V Leiden thrombophilia	F5	c.1601G>A (p.Arg534Gln)	100% 100% 100% 100% 100%	General ppn European ppn US (caucasian) US (Afr-Am) US (Hispanic)	Kujovich, J. L. (2011)
Factor XI deficiency	F11	c.400C>T (p.Gln134Ter); c.403G>T (p.Glu135Ter); c.408C>A (p.Cys136Ter); c.901T>C (p.Phe301Leu)	>95%	Ashkenazi Jewish	Peretz, H. et al. (2013); Asakai, R., et al. (1991); Shpilberg, O. et al. (1995)
Familial dysautonomia	IKBKAP	c.2741C>T (p.Pro914Leu); c.2204+6T>C; c.2087G>C (p.Arg696Pro)	>99.5%	Ashkenazi Jewish	Chaverra, M. et al. (2017); Shohat, M. & Weisz Hubshman, M. (2003); Peters, N. et al. (Springer Berlin Heidelberg, 2009)
Familial Mediterranean fever	MEFV	c.1437C>G (p.Phe479Leu); c.2177T>C (p.Val726Ala); c.2082G>A (p.Met694Ile); c.2080A>G (p.Met694Val); c.2076_2078delAAT (p.Ile692del); c.2040G>C (p.Met680Ile); c.2040G>A (p.Met680Ile); c.1958G>A (p.Arg653His)	>70% >85% >75% 64%	Mediterranean Middle Eastern Cypriot Turkish	Fujikura, K. (2015); Shohat, M. (2000); Neocleous, V. et al. (2015); Ben-Chetrit, E. & Touitou, I. (2009); Mikula, M. et al. (2008)

Fanconi anemia (FANCG-related)	FANCG	c.1480+1G>C; c.925-2A>G; c.307+1G>C	>80% >65% >80%	French-Canadian Korean/Japanese Portuguese-Brazilian	Auerbach, A. D. et al. (2003); Mehta, P. A. & Tolar, J. (2002); Fanconi Anemia: Guidelines for Diagnosis and Management, Fourth Edition (2014)
Glycine encephalopathy (GLDCrelated)	GLDC	c.2284G>A (p.Gly762Arg); c.1691G>T (p.Ser564Ile)	78% 10%	Finland General ppn	Van Hove, J., Coughlin, C. & Scharer, G. (2002)
Glycogen storage disease, Type 3	AGL	c.16C>T (p.Gln6Ter); c.18_19delGA (p.Gln6Hisfs); c.1222C>T (p.Arg408Ter); c.1384delG (p.Val462Terfs); c.2039G>A (p.Trp680Ter); c.2590C>T (p.Arg864Ter); c.2681+1G>A; c.3439A>G (p.Arg1147Gly); c.3682C>T (p.Arg1228Ter); c.3965delT (p.Val1322Alafs); c.3980G>A (p.Trp1327Ter); c.4260-12A>G; c.4342G>C (p.Gly1448Arg); c.4456delT (p.Ser1486Profs)	>99% >99%	Sephardic Jewish - Moroccan Faroese	Kishnani, P. S. et al. (2010); Santer, R. et al. (2001); Goldstein, J. L. et al. (2010); Parvari, R. et al. (1997)
Glycogen storage disease, Type 7	PFKM	c.329G>T (p.Arg110Leu); c.450+1G>A; c.496C>T (p.Arg166Ter)	>95%	Ashkenazi Jewish	Sherman, J. B. et al. (1994)
GRACILE Syndrome	BCS1L	c.103G>C (p.Gly35Arg); c.133C>T (p.Arg45Cys); c.148A>G (p.Thr50Ala); c.166C>T (p.Arg56Ter); c.232A>G (p.Ser78Gly); c.296C>T (p.Pro99Leu); c.464G>C (p.Arg155Pro); c.547C>T (p.Arg183Cys); c.548G>A (p.Arg183His); c.550C>T (p.Arg184Cys)	>95%	Finland	de Lonlay, P. et al. (2001); Visapää, I. et al. (2002)
Inclusion body myopathy, Type 2	GNE	c.2228T>C (p.Met743Thr); c.1714G>C (p.Val572Leu)	>95% 48.3% 50%	Iranian Jewish Japanese Korean	Haghighi, A. et al. (2015); Cho, A. et al. (2014); Park, Y.-E. et al. (2012)
Isovaleric acidemia	IVD	c.941C>T (p.Ala314Val)	>50%	General ppn	Vockley, J. & Ensenauer, R. (2006); Mohsen, A.-W. A. et al. (1998); Moorhith, S., et al. (2014); Ensenauer, R. et al. (2004)
Joubert syndrome, Type 2	TMEM216	c.218G>A (p.Arg73His); c.218G>T (p.Arg73Leu)	>99%	Ashkenazi Jewish	Edvardson, S. et al. (2010)
Junctional epidermolysis bullosa, Herlitz type	LAMC2	c.283C>T (p.Arg95Ter)	>30%	Italian	Posteraro, P. et al. (2004); Castori, M. et al. (2007)

Leber congenital amaurosis (LCA5related)	LCA5	c.1476dupA (p.Pro493Thrfs); c.1151delC (p.Pro384Glnfs); c.835C>T (p.Gln279Ter)	unknown >80%	General ppn Pakistani	Weleber, R. G. et al. (2004); Mackay, D. S. et al. (2013); Corton, M. et al. (2014)
Leydig cell hypoplasia [Luteinizing Hormone Resistance]	LHCGR	c.1505T>C (p.Leu502Pro); c.1847C>A (p.Ser616Tyr); c.1777G>C (p.Ala593Pro); c.1660C>T (p.Arg554Ter); c.1635C>A (p.Cys545Ter); c.1627T>C (p.Cys543Arg); c.1060G>A (p.Glu354Lys); c.1027T>A (p.Cys343Ser); c.430G>T (p.Val144Phe); c.391T>C (p.Cys131Arg)	>90%	Brazilian	Latronico, A. C. et al. (1996); Laue, L. et al. (1995)
Limb girdle muscular dystrophy, Type 2E	SGCB	c.452C>G (p.Thr151Arg); c.341C>T (p.Ser114Phe); c.323T>G (p.Leu108Arg); c.299T>A (p.Met100Lys); c.272G>C (p.Arg91Pro); c.272G>T (p.Arg91Leu)	>99% >55% 25% 12.5%	US Amish Brazilian EU General ppn	Duclos, F. et al. (1998); Semplicini, C. et al. (2015); Vainzof, M. et al. (1999); Bönnemann, C. G. et al. (1996)
Lipoamide Dehydrogenase Deficiency [Maple syrup urine disease, Type 3]	DLD	c.214A>G (p.Lys72Glu); c.685G>T (p.Gly229Cys); c.1081A>G (p.Met361Val); c.1123G>A (p.Glu375Lys); c.1178T>C (p.Ile393Thr); c.1463C>T (p.Pro488Leu); c.1483A>G (p.Arg495Gly)	>85%	Ashkenazi Jewish	Scott, S. A. et al. (2010); Quinonez, S. C. & Thoene, J. G. (2014); Shaag, A. et al. (1999)
Lipoprotein lipase deficiency	LPL	c.644G>A (p.Gly215Glu)	23%	General ppn	Monsalve, M. V et al. (1990); Gilbert, B. et al. (2001)
Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency	HADHA	c.1528G>C (p.Glu510Gln); c.1132C>T (p.Gln378Ter)	>80%	EU	IJlst, L. et al. (1996); Nedoszytko, B. et al. (2017); IJlst, L. et al. (1994)
Maple syrup urine disease, Type 1B	BCKDHB	c.548G>C (p.Arg183Pro); c.832G>A (p.Gly278Ser); c.853C>T (p.Arg285Ter); c.970C>T (p.Arg324Ter); c.1114G>T (p.Glu372Ter)	>95%	Ashkenazi Jewish	Baskovich, B. et al. (2016); Edelmann, L. et al. (2001); Scott, S. A. et al. (2010)
Methylmalonic acidemia (MMAArelated)	MMAA	c.64C>T (p.Arg22Ter); c.161G>A (p.Trp54Ter); c.266T>C (p.Leu89Pro); c.283C>T (p.Gln95Ter); c.358C>T (p.Gln120Ter); c.397C>T (p.Gln133Ter); c.433C>T (p.Arg145Ter); c.503delC (p.Thr168Metfs); c.562G>C (p.Gly188Arg); c.650T>A (p.Leu217Ter); c.653G>A (p.Gly218Glu); c.733+1G>A; c.988C>T (p.Arg330Ter); c.1076G>A (p.Arg359Gln)	>80%	General ppn	Manoli, I., Sloan, J. L. & Venditti, C. P. (2005); Lerner-Ellis, J. P. et al. (2004)

Multiple sulfatase deficiency	SUMF1	c.463T>C (p.Ser155Pro)	95%	Ashkenazi Jewish	Shi, L. et al. (2017)
Navajo neurohepatopathy [MPV17related hepatocerebral mitochondrial DNA depletion syndrome]	MPV17	c.149G>A (p.Arg50Gln)	>99%	Navajo ppn	El-Hattab, A. W., Scaglia, F., Craigen, W. J. & Wong, L.-J. C. (2012)
Neuronal ceroid lipofuscinosis (MFSD8-related)	MFSD8	c.881C>A (p.Thr294Lys); c.754+2T>A; c.894T>G (p.Tyr298Ter); c.929G>A (p.Gly310Asp)	55% 70%	General ppn Turkish	Kousi, M., Lehesjoki, A.-E. & Mole, S. E. (2012)
Nijmegen breakage syndrome	NBN	c.657_661delACAAA (p.Lys219Asnfs)	100% 70%	Slavic N American	Varon, R., Demuth, I. & Chrzanowska, K. H. (1999)
Ornithine translocase deficiency [HyperornithinemiaHyperammonemia-Homocitrullinuria (HHH) Syndrome]	SLC25A15	c.95C>G (p.Thr32Arg); c.535C>T (p.Arg179Ter); c.562_564delTTC (p.Phe188del)	95% >50%	French-Canadian Japanese	Debray, F.-G. et al. (2008); Miyamoto, T. et al. (2001); Salvi, S. et al. (2001); Salvi, S. et al. (2001); Sokoro, A. A. H. et al. (2010); Camacho, J. & Rioseco-Camacho, N. (2012)
Peroxisome biogenesis disorders Zellweger syndrome spectrum (PEX1-related)	PEX1	c.2916delA (p.Gly973Alafs); c.2528G>A (p.Gly843Asp); c.2097dupT (p.Ile700Tyrfs)	>70% >70%	General ppn Caucasian	Walter, C. et al. (2001); Maxwell, M. A. et al. (1999); Walter, C. et al. (2001); Maxwell, M. A. et al. (2002); Weller, S., Gould, S. J. & Valle, D. P. (2003); Steinberg, S. et al. (2004)
Peroxisome biogenesis disorders Zellweger syndrome spectrum (PEX2-related)	PEX2	c.355C>T (p.Arg119Ter)	95%	Ashkenazi Jewish	Shi, L. et al. (2017)

Phenylketonurea	PAH	c.1315+1G>A; c.1301C>A (p. Ala434Asp); c.1243G>A (p. Asp415Asn); c.1241A>G (p. Tyr414Cys); c.1238G>C (p. Arg413Pro); c.1223G>A (p. Arg408Gln); c.1222C>T (p. Arg408Trp); c.1220C>T (p. Pro407Leu); c.1208C>T (p. Ala403Val); c.1200-1G>A; c.1169A>G (p. Glu390Gly); c.1162G>A (p. Val388Met); c.1157A>G (p. Tyr386Cys); c.1139C>T (p. Thr380Met); c.1129delT (p. Tyr377Thrfs); c.1068C>G (p. Tyr356Ter); c.1068C>A (p. Tyr356Ter); c.1066-3C>T; c.1066-11G>A; c.1055delG (p. Gly352Valfs); c.1045T>C (p. Ser349Pro); c.1042C>G (p. Leu348Val); c.932T>C (p. Leu311Pro); c.926C>T (p. Ala309Val); c.912+1G>A; c.898G>T (p. Ala300Ser); c.896T>G (p. Phe299Cys); c.856G>A (p. Glu286Lys); c.842+5G>A; c.842+2T>A; c.842+1G>A; c.842C>T (p. Pro281Leu); c.838G>A (p. Glu280Lys); c.829T>G (p. Tyr277Asp); c.818C>T (p. Ser273Phe); c.814G>T (p. Gly272Ter); c.782G>A (p. Arg261Gln); c.781C>T (p. Arg261Ter); c.770G>T (p. Gly257Val); c.764T>C (p. Leu255Ser); c.755G>A (p. Arg252Gln); c.754C>T (p. Arg252Trp); c.745C>T (p. Leu249Phe); c.728G>A (p. Arg243Gln); c.727C>T (p. Arg243Ter); c.722G>A (p. Arg241His); c.721C>T (p. Arg241Cys); c.688G>A (p. Val230Ile); c.611A>G (p. Tyr204Cys); c.581T>C (p. Leu194Pro); c.561G>A (p. Trp187Ter); c.473G>A (p. Arg158Gln); c.442-1G>A; c.442-2A>C; c.331C>T (p. Arg111Ter); c.311C>A (p. Ala104Asp); c.284_286delTCA (p. Ile95del); c.204A>T (p. Arg68Ser); c.194T>C (p. Ile65Thr); c.143T>C (p. Leu48Ser); c.136G>A (p. Gly46Ser); c.116_118delTCT (p. Phe39del); c.117C>G (p. Phe39Leu)	>75% >70%	General ppn EU	van Wegberg, A. M. J. et al. (2017); Braun-Falco, M. et al. (Springer Berlin Heidelberg, 2009)
Pontocerebellar hypoplasia, Type 2E	VPS53	c.2084A>G (p. Gln695Arg); c.1556+5G>A	99%	Moroccan Jewish	Ben-Zeev, B. et al. (2003); Feinstein, M. et al. (2014)
Pycnodysostosis	CTSK	c.990A>G (p. Ter330Trp); c.926T>C (p. Leu309Pro)	87.5%	Danish	Haagerup, A. et al. (2000)
Pyruvate dehydrogenase deficiency (PDHB-related)	PDHB	c.1030C>T (p. Pro344Ser); c.395A>G (p. Tyr132Cys)	20%	General ppn	Brown, R. et al. (2004); Okajima, K. et al. (2008)
Retinal Dystrophy (RLBP1-related) [Bothnia retinal dystrophy]	RLBP1	c.700C>T (p. Arg234Trp)	>99%	Sweden (founder)	Burststedt, M. et al. (2013); Burststedt, M. S. et al. (2001); Burststedt, M. S. et al. (1999)
Retinitis pigmentosa (DHDDS-related)	DHDDS	c.124A>G (p. Lys42Glu)	95%	Ashkenazi Jewish	Shi, L. et al. (2017); Zelinger, L. et al. (2011)
Sanfilippo syndrome, Type D [Mucopolysaccharidosis IIID]	GNS	c.1226dupG (p. Ser410Ilefs); c.1169delA (p. Gln390Argfs); c.1168C>T (p. Gln390Ter); c.1138_1139insGTCCT (p. Asp380Glyfs); c.1063C>T (p. Arg355Ter)	>80%	General ppn	Jansen, A. C. M. et al. (2007); Mok, A., Cao, H. & Hegele, R. A. (2003)
Sickle-cell disease	HBB	c.80A>G (p. Glu27Gly); c.247A>G (p. Lys83Glu); c.82G>T (p. Ala28Ser); c.4G>T (p. Val2Leu); c.70G>T (p. Val24Phe); c.103G>T (p. Val35Phe); c.263C>T (p. Thr88Ile); c.19G>A (p. Glu7Lys); c.220G>A (p. Asp74Asn); c.364G>C (p. Glu122Gln); c.79G>A (p. Glu27Lys); c.184A>G (p. Lys62Glu); c.364G>A (p. Glu122Lys); c.184A>C (p. Lys62Gln); c.20A>T (p. Glu7Val)	100%	Severe pathogenic alleles	Rees, D. C., Williams, T. N. & Gladwin, M. T. (2010); Stuart, M. J. & Nagel, R. L. (2004); Leung, A. K. C. et al. (Springer Berlin Heidelberg, 2009)

Sjögren-Larsson syndrome	ALDH3A2	c.943C>T (p.Pro315Ser); c.1297_1298delGA (p.Glu433Argfs)	>95% 69%	Swedish Dutch	Jagell, S., Henrik, K. & Holmgren, G. (2008); Willemsen, M. A. A. P. et al. (1999)
Tay-Sachs disease	HEXA	c.745C>T (p.Arg249Trp); c.739C>T (p.Arg247Trp); c.1330+1G>A; c.1307_1308delTA (p.Ile436Serfs); c.1302C>G (p.Phe434Leu); c.1274_1277dupTATC (p.Tyr427Ilefs); c.1260G>C (p.Trp420Cys); c.1178G>C (p.Arg393Pro); c.1177C>T (p.Arg393Ter); c.1176G>A (p.Trp392Ter); c.1073+1G>A; c.987G>A (p.Trp329Ter); c.805G>A (p.Gly269Ser)	81% 32%	Ashkenazi Jewish non-Jewish	Scott, S. A. et al. (2010); Kaback, M. et al. (1993)
Usher syndrome, Type 1F	PCDH15	c.733C>T (p.Arg245Ter); c.7C>T (p.Arg3Ter)	64%	Ashkenazi Jewish	Ben-Yosef, T. et al. (2003); Brownstein, Z. et al. (2004)
Beta thalassemia	HBB	c.316-3C>G; c.316-3C>A; c.316-106C>G; c.316-146T>G; c.93-21G>A; c.92+6T>C; c.75T>A (p.Gly25=); c.-29G>A; c.-50A>C; c.-78A>G; c.-50-29A>G; c.-80T>A; c.-81A>G; c.-136C>G; c.-137C>A; c.-137C>G; c.-50-88C>T_c.-138C>T; c.-138C>A; c.316-197C>T; c.92+5G>T; c.92+5G>A; c.383_385delAGG (p.Gln128_Ala129delinsPro); c.316-2A>G; c.316-2A>C; c.315+1G>A; c.287dupA (p.Leu97Alafs); c.271G>T (p.Glu91Ter); c.257T>C (p.Phe86Ser); c.251delG (p.Gly84Alafs); c.230delC (p.Ala77Valfs); c.217_221delAGTG AinsT; c.216_217insA (p.Ser73Lysfs); c.216dupT (p.Ser73Terfs); c.203_204delITG (p.Val68Alafs); c.193delG (p.Gly65Alafs); c.184A>T (p.Lys62Ter); c.143_144insA (p.Asp48Glu fs); c.135delC (p.Phe46Leufs); c.130G>T (p.Glu44Ter); c.126_129delCTTT (p.Phe42fs); c.114_120delGACCCAG (p.Trp38Terfs); c.118C>T (p.Gln40Ter); c.116_117delCC (p.Gln40Glu fs); c.114G>A (p.Trp38Ter); c.113G>A (p.Trp38Ter); c.112delT (p.Trp38Glyfs); c.108C>A (p.Tyr36Ter); c.108delC (p.Pro37Leufs); c.93-22_95del25 no_chnage; c.93-1G>C; c.93-1G>A; c.92+5G>C; c.92+2T>A; c.92+2T>C; c.92+1G>T; c.92+1G>A; c.92+1G>C; c.92G>C (p.Arg31Thr); c.85dupC (p.Leu29Profs); c.52A>T (p.Lys18Ter); c.51delC (p.Lys18Argfs); c.47G>A (p.Trp16Ter); c.45dupG (p.Trp16Valfs); c.36delT (p.Thr13Leufs); c.27dupG; c.25_26delAA; c.20delA; c.17_18delCT (p.Pro6Argfs); c.4delG (p.Val2Cysfs); c.2T>G (p.Met1Arg); c.2T>C (p.Met1Thr); c.93_94insCGG (p.Arg31_Leu32insArg); c.93G>T (p.Arg31Ser); c.415G>C (p.Ala139Pro); c.127_129delTTT (p.Phe43del); c.182T>A (p.Val61Glu); c.176C>G (p.Pro59Arg); c.70_72delGTT (p.Val24del); c.169G>C (p.Gly57Arg);	91-95% 91-95% 91-95% 91-95% 75-80%	Mediterranean Middle-Eastern Thai Chinese African-American	Origa, R. (2000)
		c.34G>A (p.Val12Ile); c.128T>C (p.Phe43Ser); c.298G>A (p.Asp100Asn); c.295G>A (p.Val99Met); c.277C>T (p.His93Tyr); c.59A>G (p.Asn20Ser); c.86T>A (p.Leu29Gln); c.127T>G (p.Phe43Val); c.199A>G (p.Lys67Glu)			

Cystic fibrosis	CFTR	<p>c.1000C>T (p.Arg334Trp); c.489+1G>T; c.165-1G>A; c.170G>A (p.Trp57Ter); c.171G>A (p.Trp57Ter); c.175dupA (p.Arg59Lysfs); c.178G>T (p.Glu60Ter); c.200C>T (p.Pro67Leu); c.223C>T (p.Arg75Ter); c.233dupT (p.Trp79Leufs); c.254G>A(p.Gly85Glu); c.262_263delTT (p.Leu88Ilefs); c.263T>G (p.Leu88Ter); c.271G>A (p.Gly91Arg); c.273+1G>A; c.273+3A>C; c.274-1G>A; c.274G>A (p.Glu92Lys); c.274G>T (p.Glu92Ter); c.292C>T (p.Gln98Ter); c.293A>G (p.Gln98Arg); c.310delA (p.Arg104Glu fs); c.313delA (p.Ile105Serfs); c.325_327delTATinsG (p.Tyr109Glyfs); c.328G>C (p.Asp110His); c.349C>T (p.Arg117Cys); c.350G>A (p.Arg117His); c.366T>A (p.Tyr122Ter); c.409delC (p.Leu137Serfs); c.424delA (p.Ile142Phefs); c.429delT (p.Phe143Leufs); c.442delA(p.Ile148Leufs); c.550delC (p.Leu184Phefs); c.579+1G>T; c.1364C>A (p.Ala455Glu); c.1397C>A (p.Ser466Ter); c.1397C>G (p.Ser466Ter); c.1400T>C (p.Leu467Pro); c.1418delG (p.Gly473Glu fs); c.1438G>T (p.Gly480Cys); c.1466C>A (p.Ser489Ter); c.1475C>T (p.Ser492Phe); c.1477_1478delCA (p.Gln493Valfs); c.1477C>T (p.Gln493Ter); c.1519_1521delATC (p.Ile507del); c.1518C>G (p.Ile506Met); c.1521_1523delCTT (p.deltaF508); c.1520_1522delTCT (p.deltaF508); c.1545_1546delTA (p.Tyr515Terfs); c.1558G>T (p.Val520Phe); c.1572C>A (p.Cys524Ter); c.1573C>T (p.Gln525Ter); c.1584+1G>A; c.1585-8G>A; c.1585-1G>A; c.1601C>A (p.Ala534Glu); c.1624G>T (p.Gly542Ter); c.1645A>C (p.Ser549Arg); c.1646G>A (p.Ser549Asn); c.1646G>T (p.Ser549Ile); c.1647T>G (p.Ser549Arg); c.1648G>T(p.Gly550Ter); c.1650delA (p.Gly551Valfs); c.1651G>A (p.Gly551Ser); c.1652G>A (p.Gly551Asp); c.1654C>T (p.Gln552Ter); c.1657C>T (p.Arg553Ter); c.1658G>A (p.Arg553Gln); c.1675G>A (p.Ala559Thr); c.1679G>A (p.Arg560Lys); c.1679G>C (p.Arg560Thr);c.1679+1G>A; c.1679+1G>C; c.1766+1G>A; c.1973_1985del13insAGAAA (p.Arg658Lysfs); c.1986_1989delAACT (p.Thr663Argfs); c.2012delT (p.Leu671Terfs); c.2017G>T (p.Gly673Ter); c.2036G>A (p.Trp679Ter); c.2051_2052delAAinsG (p.Lys684Serfs); c.2052dupA (p.Gln685Thrfs); c.2052delA (p.Lys684Asnfs); c.2053C>T (p.Gln685Ter); c.2053dupC (p.Gln685Profs); c.2083dupG (p.Glu695Glyfs); c.2125C>T (p.Arg709Ter); c.2128A>T (p.Lys710Ter); c.2175dupA (p.Glu726Argfs); c.2657+5G>A; c.2909G>A (p.Gly970Asp); c.2932A>T(p.Lys978Ter); c.2988G>A (p.Gln996=); c.2988+1G>A; c.3472C>T (p.Arg1158Ter); c.3484C>T (p.Arg1162Ter); c.3492dupT (p.Lys1165Terfs); c.3528delC (p.Lys1177Serfs);</p>	<p>>75% >70% >70%</p>	<p>General ppn EU US</p>	<p>Farrell, P. M. (2008); Elliott, A. M. et al. (2012); Bobadilla, J. L., et al. (2002)</p>
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		c.3532_3535dupTCAA (p.Thr1179Ilefs);			
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		<p>c.3536_3539delCCAA (p.Thr1179Asnfs); c.3587C>G (p.Ser1196Ter); c.3605delA (p.Asp1202Alafs); c.3611G>A (p. Trp1204Ter); c.3612G>A (p.Trp1204Ter); c.3659delC (p.Thr1220Lysfs); c.3691delT (p.Ser1231Profs); c.3700A>G (p. Ile1234Val); c.3712C>T (p.Gln1238Ter); c.3718-2477C>T; c.3731G>A (p. Gly1244Glu);c.3744delA (p. Lys1250Argfs); c.3747delG (p. Lys1250Argfs); c.3752G>A (p. Ser1251Asn); c.3761T>G (p. Leu1254Ter); c.3764C>A (p.Ser1255Ter); c.3764C>G (p.Ser1255Ter); c.3767dupC (p.Leu1258Phefs); c.3773dupT (p. Leu1258Phefs); c.3846G>A (p. Trp1282Ter);c.3848G>T (p.Arg1283Met); c.3873+1G>A; c.3873+2T>C</p>			
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ОБРАЗЕЦ АНОМАЛИИ ОБНАРУЖЕНЫ

2

PATIENT INFORMATION		REFERRAL INFORMATION	
NAME Sample 25		CLINIC NAME New Testing Clinic	
ID NUMBER 12390810		CLINIC ID 446	
DATE OF BIRTH (DD/MM/YYYY) 23/06/1985	GESTATIONAL AGE Week: 12 Day: 0	REFERRING CLINICIAN Dr. New Doctor	
IVF STATUS No	NUMBER OF FETUSES One	CLINIC FAX	
SAMPLE INFORMATION			
ORDER NUMBER V822956	LAB NUMBER 706	DATE OF COLLECTION (DD/MM/YYYY) 11/06/2018	DATE RECEIVED (DD/MM/YYYY) 11/06/2018
VERAgene PRENATAL SCREENING TEST RESULTS			
VERY HIGH RISK NIPT Results	CONDITION	REMARK	
	Trisomy 21	The results show very low risk for trisomy 21	
	Trisomy 18	The results show very low risk for trisomy 18	
	Trisomy 13	The results show very low risk for trisomy 13	
	Trisomy X	The results show very low risk for trisomy X	
	Monosomy X	The results show very low risk for monosomy X	
	XXY Constitution	The results show very low risk for XXY constitution	
FETAL FRACTION	XXY Constitution	The results show very low risk for XXY constitution	
6.2%	XXYY Constitution	The results show very low risk for XXYY constitution	
	Microdeletions: (DiGeorge,1p36 deletion syndrome,Smith-Magenis, Wolf Hirschhorn)	The results show very low risk for microdeletions (DiGeorge (22q11), 1p36 deletion syndrome, Smith-Magenis (17p11.2), Wolf Hirschhorn (4p16.3))	
	Panel of 50 single gene diseases	The results show very high risk for Beta thalassaemia	
	Presence/Absence of Y chromosome	The results show the presence of Y chromosome	
INTERPRETATION			
<p>The results show very high risk for Beta thalassaemia. The fetal fraction is 6.2%, which is sufficient for analysis. Please consult Test Method and Test Description sections below for information on the method, performance and limitations of the test. The results should be communicated by the referring clinician with appropriate counselling. Invasive prenatal diagnosis with amniocentesis is recommended before any medical decisions are made.</p>			

TEST METHOD

VERAgene is a Laboratory Developed Test (LDT) from NIPD Genetics Public Company Ltd for prenatal screening that analyses cell-free DNA (cfDNA) from maternal plasma and sample from biological father. Multiplexed parallel analysis of specific regions of interest was applied for the copy number determination of chromosomes 13, 18, 21, aneuploidies of X, Y, select microdeletions including, DiGeorge (22q11 deletion), 1p36 deletion syndrome, Smith-Magenis (17p11.2 deletion), Wolf Hirschhorn (4p16.3 deletion), Y detection and mutation detection for 50 single gene diseases (Table 1).

TEST DESCRIPTION

Test performance is valid only for full chromosomal aneuploidies for chromosomes 21, 18, and 13 aneuploidies of X, Y, select microdeletions, Y detection and a number of pathogenic and likely pathogenic mutations associated with monogenic diseases listed in Table 1. It does not exclude other chromosomal disorders, birth defects or other complications. VERAgene is available for singleton and twin pregnancies only, including in-vitro fertilization (IVF) pregnancies of at least 10 weeks of gestation. Sex chromosome aneuploidies are not reportable for twin gestations. The VERAgene test cannot be performed on pregnancies achieved with egg/sperm donation or surrogacy or vanished twin pregnancies. Patients with malignancy or history of malignancy, patients with bone marrow or organ transplant are not eligible for the test. Furthermore, samples from both biological parents are required for the test to be performed. In a small number of cases the amount of fetal DNA present in maternal blood (fetal fraction), is not sufficient for analysis and a redraw maybe requested.

Validation studies are carried out for all conditions by NIPD Genetics Public Company Ltd. The test is not intended and not validated for mosaicism, triploidy, partial trisomy or translocations. This test has been validated on full region deletions and maybe unable to detect deletion of smaller regions. The test will not identify all deletions associated

with each microdeletion syndrome. Furthermore, the test is mutations which are associated with the monogenic diseases risk result reduces but does not eliminate the possibility of the result for twin pregnancies indicates high risk for the presence detection of Y indicates the presence of at least one Y chromosome. Although this test is highly accurate, there is still a small possibility for false positive or false negative results. This may be caused by technical and/or biological limitations, including but not limited to confined placental mosaicism (CPM) or other types of mosaicism, maternal constitutional or somatic chromosomal abnormalities, residual cfDNA from a vanished twin or other rare molecular events. The VERAgene test is not diagnostic but a screening test and results should be considered



not intended and not validated for a number of listed in Table1 but are not tested. Therefore, a very low fetus to be affected or carry the mutation. A very high risk of at least one affected fetus. In twin pregnancies,

not intended and not validated for a number of listed in Table1 but are not tested. Therefore, a very low fetus to be affected or carry the mutation. A very high risk of at least one affected fetus. In twin pregnancies,

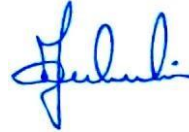
in the context of other clinical criteria. Clinical correlation and tests is recommended. If definitive amniocentesis is necessary. The referral clinician is including the provision of advice regarding the need

with ultrasound findings, and other clinical data diagnosis is desired, responsible for counselling before and after the test for additional invasive genetic testing.



Approved by: Elena Kypri, Ph.D, ASCP

Approved



by: Philippos Patsalis, Ph.D, HCLD, Laboratory Director

DATE OF REPORT (DD/MM/YYYY): 11/06/2018

TABLE 1

Condition	Gene	Mutations	Det Freq	Area	References
3 Methylcrotonyl CoA Carboxylase Deficiency 1	MCCC1	c.1310T>C (p.Leu437Pro); c.1155A>C (p.Arg385Ser)	28% >35%	European ppn General ppn	Baumgartner, M. R. et al. (2001); Fonseca, H. et al.(2016); Grünert, S. C. et al. (2012)
3 Methylcrotonyl CoA Carboxylase Deficiency 2	MCCC2	c.295G>C (p.Glu99Gln); c.464G>A (p.Arg155Gln); c.499T>C (p.Cys167Arg); c.569A>G (p.His190Arg); c.803G>C (p.Arg268Thr); c.838G>T (p.Asp280Tyr); c.929C>G (p.Pro310Arg); c.1309A>G (p.Ile437Val)	>35%	General ppn	Baumgartner, M. R. et al. (2001); Fonseca, H. et al.(2016); Grünert, S. C. et al. (2012)
Abetalipoproteinemia	MTTP	c.2593G>T (p.Gly865Ter)	95%	Ashkenazi Jewish	Benayoun, L. et al. (2007)
Arthrogryposis Mental Retardation Seizures	SLC35A3	c.514C>T (p.Gln172Ter)	>50%	Ashkenazi Jewish	Edvardson, S. et al. (2013)
Autosomal recessive polycystic kidney disease	PKHD1	c.10658T>C (p.Ile3553Thr); c.10444C>T (p.Arg3482Cys); c.10412T>G (p.Val3471Gly); c.10219C>T (p.Gln3407Ter); c.10174C>T (p.Gln3392Ter); c.9689delA (p.Asp3230Valfs); c.9530T>C (p.Ile3177Thr); c.9053C>T (p.Ser3018Phe); c.8870T>C (p.Ile2957Thr); c.8581A>G (p.Ser2861Gly); c.8011C>T (p.Arg2671Ter); c.6992T>A (p.Ile2331Lys); c.5895dupA (p.Leu1966Thrfs); c.5513A>G (p.Tyr1838Cys); c.5236+1G>A; c.4991C>T (p.Ser1664Phe); c.4870C>T (p.Arg1624Trp); c.3761_3762delCCinsG (p.Ala1254Glyfs); c.3407A>G (p.Tyr1136Cys); c.3367G>A (p.Gly1123Ser); c.2854G>A (p.Gly952Arg); c.2414C>T (p.Pro805Leu); c.2341C>T (p.Arg781Ter); c.2279G>A (p.Arg760His); c.1486C>T (p.Arg496Ter); c.1068dup (p.Asn3571IlefsX57); c.664A>G (p.Ile222Val); c.383delC (p.Thr128IlefsX25); c.370C>T (p.Arg124Ter); c.107C>T (p.Thr36Met)	90% 69% 70%	Ashkenazi Jewish General ppn Caucasian	Sweeney, W. E. & Avner, E. D. (1993); Shi, L. et al.(2017).
Bardet Biedl syndrome 12	BBS12	c.335_337delTAG (p.Val113del); c.865G>C (p.Ala289Pro); c.1063C>T (p.Arg355Ter); c.1483_1484delGA (p.Glu495Argfs)	>50%	European ppn	Stoetzel, C. et al. (2007); Burstedt, M. et al. (2013); Burstedt, M. S. et al. (2001); Muller, J. et al. (2010)
Canavan disease	ASPA	c.433-2A>G; c.693C>A (p.Tyr231Ter); c.854A>C (p.Glu285Ala); c.914C>A (p.Ala305Glu)	97-98% 60%	Ashkenazi Jewish EU	Feigenbaum, A. et al. (2004); Kaul, R. et al. (1994); Matalon, R. & Matalon, K. M. (Elsevier, 2015)
Choreacanthocytosis	VPS13A	c.6059delC (p.Pro2020fs)	66.67%	Ashkenazi Jewish (founder)	Rampoldi, L. et al. (2001); Dobson-Stone, C. et al. (2002); Siegl, C. et al. (2013); Lossos, A. et al. (2005)
Crigler Najjar syndrome, Type I	UGT1A1	c.513_515delCTT (p.Phe171del); c.524T>A (p.Leu175Gln); c.840C>A (p.Cys280Ter); c.923G>A (p.Gly308Glu); c.991C>T (p.Gln331Ter); c.992A>G (p.Gln331Arg); c.1021C>T (p.Arg341Ter); c.1070A>G (p.Gln357Arg); c.1124C>T (p.Ser375Phe); c.1198A>G (p.Asn400Asp)	>99% >70%	Tunisia (founder) Sardinia	Francoual, J. et al. (2002)

Factor V Leiden thrombophilia	F5	c.1601G>A (p.Arg534Gln)	100% 100% 100% 100%	General ppn European ppn US (caucasian) US (Afr-Am) US (Hisp)	Kujovich, J. L. (2011)
Factor XI deficiency	F11	c.400C>T (p.Gln134Ter); c.403G>T (p.Glu135Ter); c.408C>A (p.Cys136Ter); c.901T>C (p.Phe301Leu)	>95%	Ashkenazi Jewish	Peretz, H. et al. (2013); Asakai, R., et al. (1991); Shpilberg, O. et al. (1995)
Familial dysautonomia	IKBKAP	c.2741C>T (p.Pro914Leu); c.2204+6T>C; c.2087G>C (p.Arg696Pro)	>99.5%	Ashkenazi Jewish	Chaverra, M. et al. (2017); Shohat, M. & Weisz Hubshman, M. (2003); Peters, N. et al. (Springer Berlin Heidelberg, 2009)
Familial Mediterranean fever	MEFV	c.1437C>G (p.Phe479Leu); c.2177T>C (p.Val726Ala); c.2082G>A (p.Met694Ile); c.2080A>G (p.Met694Val); c.2076_2078delAAT (p.Ile692del); c.2040G>C (p.Met680Ile); c.2040G>A (p.Met680Ile); c.1958G>A (p.Arg653His)	>70% >85% >75% 64%	Mediterranean Middle Eastern Cypriot Turkish	Fujikura, K. (2015); Shohat, M. (2000); Neocleous, V. et al. (2015); Ben-Chetrit, E. & Touitou, I. (2009); Mikula, M. et al. (2008)
Fanconi anemia (FANCG-related)	FANCG	c.1480+1G>C; c.925-2A>G; c.307+1G>C	>80% >65% >80%	French-Canadian Korean/Japanese Portuguese-Brazilian	Auerbach, A. D. et al. (2003); Mehta, P. A. & Tolar, J. (2002); Fanconi Anemia: Guidelines for Diagnosis and Management, Fourth Edition (2014)
Glycine encephalopathy (GLDCrelated)	GLDC	c.2284G>A (p.Gly762Arg); c.1691G>T (p.Ser564Ile)	78% 10%	Finland General ppn	Van Hove, J., Coughlin, C. & Scharer, G. (2002)
Glycogen storage disease, Type 3	AGL	c.16C>T (p.Gln6Ter); c.18_19delGA (p.Gln6Hisfs); c.1222C>T (p.Arg408Ter); c.1384delG (p.Val462Terfs); c.2039G>A (p.Trp680Ter); c.2590C>T (p.Arg864Ter); c.2681+1G>A; c.3439A>G (p.Arg1147Gly); c.3682C>T (p.Arg1228Ter); c.3965delT (p.Val1322Alafs); c.3980G>A (p.Trp1327Ter); c.4260-12A>G; c.4342G>C (p.Gly1448Arg); c.4456delT (p.Ser1486Profs)	>99% >99%	Sephardic Jewish - Moroccan Faroese	Kishnani, P. S. et al. (2010); Santer, R. et al. (2001); Goldstein, J. L. et al. (2010); Parvari, R. et al. (1997)
Glycogen storage disease, Type 7	PFKM	c.329G>T (p.Arg110Leu); c.450+1G>A; c.496C>T (p.Arg166Ter)	>95%	Ashkenazi Jewish	Sherman, J. B. et al. (1994)
GRACILE Syndrome	BCS1L	c.103G>C (p.Gly35Arg); c.133C>T (p.Arg45Cys); c.148A>G (p.Thr50Ala); c.166C>T (p.Arg56Ter); c.232A>G (p.Ser78Gly); c.296C>T (p.Pro99Leu); c.464G>C (p.Arg155Pro); c.547C>T (p.Arg183Cys); c.548G>A (p.Arg183His); c.550C>T (p.Arg184Cys)	>95%	Finland	de Lonlay, P. et al. (2001); Visapää, I. et al. (2002)
Inclusion body myopathy, Type 2	GNE	c.2228T>C (p.Met743Thr); c.1714G>C (p.Val572Leu)	>95% 48.3% 50%	Iranian Jewish Japanese Korean	Haghighi, A. et al. (2015); Cho, A. et al. (2014); Park, Y.-E. et al. (2012)
Isovaleric acidemia	IVD	c.941C>T (p.Ala314Val)	>50%	General ppn	Vockley, J. & Ensenauer, R. (2006); Mohsen, A.-W. A. et al. (1998); Moorithie, S., et al. (2014); Ensenauer, R. et al. (2004)
Joubert syndrome, Type 2	TMEM216	c.218G>A (p.Arg73His); c.218G>T (p.Arg73Leu)	>99%	Ashkenazi Jewish	Edvardson, S. et al. (2010)
Junctional epidermolysis bullosa, Herlitz type	LAMC2	c.283C>T (p.Arg95Ter)	>30%	Italian	Posteraro, P. et al. (2004); Castori, M. et al. (2007)
Leber congenital amaurosis (LCA5related)	LCA5	c.1476dupA (p.Pro493Thrfs); c.1151delC (p.Pro384Glnfs); c.835C>T (p.Gln279Ter)	unknown >80%	General ppn Pakistani	Weleber, R. G. et al. (2004); Mackay, D. S. et al. (2013); Corton, M. et al. (2014)

Leydig cell hypoplasia [Luteinizing Hormone Resistance]	LHCGR	c.1505T>C (p.Leu502Pro); c.1847C>A (p.Ser616Tyr); c.1777G>C (p.Ala593Pro); c.1660C>T (p.Arg554Ter); c.1635C>A (p.Cys545Ter); c.1627T>C (p.Cys543Arg); c.1060G>A (p.Glu354Lys); c.1027T>A (p.Cys343Ser); c.430G>T (p.Val144Phe); c.391T>C (p.Cys131Arg)	>90%	Brazilian	Latronico, A. C. et al. (1996); Laue, L. et al. (1995)
Limb girdle muscular dystrophy, Type 2E	SGCB	c.452C>G (p.Thr151Arg); c.341C>T (p.Ser114Phe); c.323T>G (p.Leu108Arg); c.299T>A (p.Met100Lys); c.272G>C (p.Arg91Pro); c.272G>T (p.Arg91Leu)	>99% >55% 25% 12.5%	US Amish Brazilian EU General ppn	Duclos, F. et al. (1998); Semplicini, C. et al. (2015); Vainzof, M. et al. (1999); Bönnemann, C. G. et al. (1996)
Lipoamide Dehydrogenase Deficiency [Maple syrup urine disease, Type 3]	DLD	c.214A>G (p.Lys72Glu); c.685G>T (p.Gly229Cys); c.1081A>G (p.Met361Val); c.1123G>A (p.Glu375Lys); c.1178T>C (p.Ile393Thr); c.1463C>T (p.Pro488Leu); c.1483A>G (p.Arg495Gly)	>85%	Ashkenazi Jewish	Scott, S. A. et al. (2010); Quinonez, S. C. & Thoene, J. G. (2014); Shaag, A. et al. (1999)
Lipoprotein lipase deficiency	LPL	c.644G>A (p.Gly215Glu)	23%	General ppn	Monsalve, M. V et al. (1990); Gilbert, B. et al. (2001)
Long chain 3-hydroxyacyl-CoA dehydrogenase deficiency	HADHA	c.1528G>C (p.Glu510Gln); c.1132C>T (p.Gln378Ter)	>80%	EU	IJlst, L. et al. (1996); Nedoszytko, B. et al. (2017); IJlst, L. et al. (1994)
Maple syrup urine disease, Type 1B	BCKDHB	c.548G>C (p.Arg183Pro); c.832G>A (p.Gly278Ser); c.853C>T (p.Arg285Ter); c.970C>T (p.Arg324Ter); c.1114G>T (p.Glu372Ter)	>95%	Ashkenazi Jewish	Baskovich, B. et al. (2016); Edelmann, L. et al. (2001); Scott, S. A. et al. (2010)
Methylmalonic acidemia (MMAArelated)	MMAA	c.64C>T (p.Arg22Ter); c.161G>A (p.Trp54Ter); c.266T>C (p.Leu89Pro); c.283C>T (p.Gln95Ter); c.358C>T (p.Gln120Ter); c.397C>T (p.Gln133Ter); c.433C>T (p.Arg145Ter); c.503delC (p.Thr168Metfs); c.562G>C (p.Gly188Arg); c.650T>A (p.Leu217Ter); c.653G>A (p.Gly218Glu); c.733+1G>A; c.988C>T (p.Arg330Ter); c.1076G>A (p.Arg359Gln)	>80%	General ppn	Manoli, I., Sloan, J. L. & Venditti, C. P. (2005); Lerner-Ellis, J. P. et al. (2004)
Multiple sulfatase deficiency	SUMF1	c.463T>C (p.Ser155Pro)	95%	Ashkenazi Jewish	Shi, L. et al. (2017)
Navajo neurohepatopathy [MPV17related hepatocerebral mitochondrial DNA depletion syndrome]	MPV17	c.149G>A (p.Arg50Gln)	>99%	Navajo ppn	El-Hattab, A. W., Scaglia, F., Craigen, W. J. & Wong, L.-J. C. (2012)
Neuronal ceroid lipofuscinosis (MFSD8-related)	MFSD8	c.881C>A (p.Thr294Lys); c.754+2T>A; c.894T>G (p.Tyr298Ter); c.929G>A (p.Gly310Asp)	55% 70%	General ppn Turkish	Kousi, M., Lehesjoki, A.-E. & Mole, S. E. (2012)
Nijmegen breakage syndrome	NBN	c.657_661delACAAA (p.Lys219Asnfs)	100% 70%	Slavic N American	Varon, R., Demuth, I. & Chrzanowska, K. H. (1999)
Ornithine translocase deficiency [HyperornithinemiaHyperammonemia-Homocitrullinuria (HHH) Syndrome]	SLC25A15	c.95C>G (p.Thr32Arg); c.535C>T (p.Arg179Ter); c.562_564delTTC (p.Phe188del)	95% >50%	French-Canadian Japanese	Debray, F.-G. et al. (2008); Miyamoto, T. et al. (2001); Salvi, S. et al. (2001); Salvi, S. et al. (2001); Sokoro, A. A. H. et al. (2010); Camacho, J. & Rioseco-Camacho, N. (2012)
Peroxisome biogenesis disorders Zellweger syndrome spectrum (PEX1-related)	PEX1	c.2916delA (p.Gly973Alafs); c.2528G>A (p.Gly843Asp); c.2097dupT (p.Ile700Tyrfs)	>70% >70%	General ppn Caucasian	Walter, C. et al. (2001); Maxwell, M. A. et al. (1999); Walter, C. et al. (2001); Maxwell, M. A. et al. (2002); Weller, S., Gould, S. J. & Valle, D. P. (2003); Steinberg, S. et al. (2004)
Peroxisome biogenesis disorders Zellweger syndrome spectrum (PEX2-related)	PEX2	c.355C>T (p.Arg119Ter)	95%	Ashkenazi Jewish	Shi, L. et al. (2017)

Phenylketonurea	PAH	c.1315+1G>A; c.1301C>A (p. Ala434Asp); c.1243G>A (p. Asp415Asn); c.1241A>G (p. Tyr414Cys); c.1238G>C (p. Arg413Pro); c.1223G>A (p. Arg408Gln); c.1222C>T (p. Arg408Trp); c.1220C>T (p. Pro407Leu); c.1208C>T (p. Ala403Val); c.1200-1G>A; c.1169A>G (p. Glu390Gly); c.1162G>A (p. Val388Met); c.1157A>G (p. Tyr386Cys); c.1139C>T (p. Thr380Met); c.1129delT (p. Tyr377Thrfs); c.1068C>G (p. Tyr356Ter); c.1068C>A (p. Tyr356Ter); c.1066-3C>T; c.1066-11G>A; c.1055delG (p. Gly352Valfs); c.1045T>C (p. Ser349Pro); c.1042C>G (p. Leu348Val); c.932T>C (p. Leu311Pro); c.926C>T (p. Ala309Val); c.912+1G>A; c.898G>T (p. Ala300Ser); c.896T>G (p. Phe299Cys); c.856G>A (p. Glu286Lys); c.842+5G>A; c.842+2T>A; c.842+1G>A; c.842C>T (p. Pro281Leu); c.838G>A (p. Glu280Lys); c.829T>G (p. Tyr277Asp); c.818C>T (p. Ser273Phe); c.814G>T (p. Gly272Ter); c.782G>A (p. Arg261Gln); c.781C>T (p. Arg261Ter); c.770G>T (p. Gly257Val); c.764T>C (p. Leu255Ser); c.755G>A (p. Arg252Gln); c.754C>T (p. Arg252Trp); c.745C>T (p. Leu249Phe); c.728G>A (p. Arg243Gln); c.727C>T (p. Arg243Ter); c.722G>A (p. Arg241His); c.721C>T (p. Arg241Cys); c.688G>A (p. Val230Ile); c.611A>G (p. Tyr204Cys); c.581T>C (p. Leu194Pro); c.561G>A (p. Trp187Ter); c.473G>A (p. Arg158Gln); c.442-1G>A; c.442-2A>C; c.331C>T (p. Arg111Ter); c.311C>A (p. Ala104Asp); c.284_286delTCA (p. Ile95del); c.204A>T (p. Arg68Ser); c.194T>C (p. Ile65Thr); c.143T>C (p. Leu48Ser); c.136G>A (p. Gly46Ser); c.116_118delTCT (p. Phe39del); c.117C>G (p. Phe39Leu)	>75% >70%	General ppn EU	van Wegberg, A. M. J. et al. (2017); Brauner-Falco, M. et al. (Springer Berlin Heidelberg, 2009)
Pontocerebellar hypoplasia, Type 2E	VPS53	c.2084A>G (p. Gln695Arg); c.1556+5G>A	99%	Moroccan Jewish	Ben-Zeev, B. et al. (2003); Feinstein, M. et al. (2014)
Pycnodysostosis	CTSK	c.990A>G (p. Ter330Trp); c.926T>C (p. Leu309Pro)	87.5%	Danish	Haagerup, A. et al. (2000)
Pyruvate dehydrogenase deficiency (PDHB-related)	PDHB	c.1030C>T (p. Pro344Ser); c.395A>G (p. Tyr132Cys)	20%	General ppn	Brown, R. et al. (2004); Okajima, K. et al. (2008)
Retinal Dystrophy (RLBP1-related) [Bothnia retinal dystrophy]	RLBP1	c.700C>T (p. Arg234Trp)	>99%	Sweden (founder)	Burststedt, M. et al. (2013); Burststedt, M. S. et al. (2001); Burststedt, M. S. et al. (1999)
Retinitis pigmentosa (DHDDS-related)	DHDDS	c.124A>G (p. Lys42Glu)	95%	Ashkenazi Jewish	Shi, L. et al. (2017); Zelinger, L. et al. (2011)
Sanfilippo syndrome, Type D [Mucopolysaccharidosis IIID]	GNS	c.1226dupG (p. Ser410Ilefs); c.1169delA (p. Gln390Argfs); c.1168C>T (p. Gln390Ter); c.1138_1139insGTCCT (p. Asp380Glyfs); c.1063C>T (p. Arg355Ter)	>80%	General ppn	Jansen, A. C. M. et al. (2007); Mok, A., Cao, H. & Hegele, R. A. (2003)
Sickle-cell disease	HBB	c.80A>G (p. Glu27Gly); c.247A>G (p. Lys83Glu); c.82G>T (p. Ala28Ser); c.4G>T (p. Val2Leu); c.70G>T (p. Val24Phe); c.103G>T (p. Val35Phe); c.263C>T (p. Thr88Ile); c.19G>A (p. Glu7Lys); c.220G>A (p. Asp74Asn); c.364G>C (p. Glu122Gln); c.79G>A (p. Glu27Lys); c.184A>G (p. Lys62Glu); c.364G>A (p. Glu122Lys); c.184A>C (p. Lys62Gln); c.20A>T (p. Glu7Val)	100%	Severe pathogenic alleles	Rees, D. C., Williams, T. N. & Gladwin, M. T. (2010); Stuart, M. J. & Nagel, R. L. (2004); Leung, A. K. C. et al. (Springer Berlin Heidelberg, 2009)

Sjögren-Larsson syndrome	ALDH3A2	c.943C>T (p.Pro315Ser); c.1297_1298delGA (p.Glu433Argfs)	>95% 69%	Swedish Dutch	Jagell, S., Henrik, K. & Holmgren, G. (2008); Willemsen, M. A. A. P. et al. (1999)
Tay-Sachs disease	HEXA	c.745C>T (p.Arg249Trp); c.739C>T (p.Arg247Trp); c.1330+1G>A; c.1307_1308delTA (p.Ile436Serfs); c.1302C>G (p.Phe434Leu); c.1274_1277dupTATC (p.Tyr427Ilefs); c.1260G>C (p.Trp420Cys); c.1178G>C (p.Arg393Pro); c.1177C>T (p.Arg393Ter); c.1176G>A (p.Trp392Ter); c.1073+1G>A; c.987G>A (p.Trp329Ter); c.805G>A (p.Gly269Ser)	81% 32%	Ashkenazi Jewish non-Jewish	Scott, S. A. et al. (2010); Kaback, M. et al. (1993)
Usher syndrome, Type 1F	PCDH15	c.733C>T (p.Arg245Ter); c.7C>T (p.Arg3Ter)	64%	Ashkenazi Jewish	Ben-Yosef, T. et al. (2003); Brownstein, Z. et al. (2004)
Beta thalassemia	HBB	c.316-3C>G; c.316-3C>A; c.316-106C>G; c.316-146T>G; c.93-21G>A; c.92+6T>C; c.75T>A (p.Gly25=); c.-29G>A; c.-50A>C; c.-78A>G; c.-50-29A>G; c.-80T>A; c.-81A>G; c.-136C>G; c.-137C>A; c.-137C>G; c.-50-88C>T_c.-138C>T; c.-138C>A; c.316-197C>T; c.92+5G>T; c.92+5G>A; c.383_385delAGG (p.Gln128_Ala129delinsPro); c.316-2A>G; c.316-2A>C; c.315+1G>A; c.287dupA (p.Leu97Alafs); c.271G>T (p.Glu91Ter); c.257T>C (p.Phe86Ser); c.251delG (p.Gly84Alafs); c.230delC (p.Ala77Valfs); c.217_221delAGTGAinsT; c.216_217insA (p.Ser73Lysfs); c.216dupT (p.Ser73Terfs); c.203_204delITG (p.Val68Alafs); c.193delG (p.Gly65Alafs); c.184A>T (p.Lys62Ter); c.143_144insA (p.Asp48Glu fs); c.135delC (p.Phe46Leufs); c.130G>T (p.Glu44Ter); c.126_129delCTTT (p.Phe42fs); c.114_120delGACCCAG (p.Trp38Terfs); c.118C>T (p.Gln40Ter); c.116_117delCC (p.Gln40Glu fs); c.114G>A (p.Trp38Ter); c.113G>A (p.Trp38Ter); c.112delT (p.Trp38Glyfs); c.108C>A (p.Tyr36Ter); c.108delC (p.Pro37Leufs); c.93-22_95del25 no_chnage; c.93-1G>C; c.93-1G>A; c.92+5G>C; c.92+2T>A; c.92+2T>C; c.92+1G>T; c.92+1G>A; c.92+1G>C; c.92G>C (p.Arg31Thr); c.85dupC (p.Leu29Profs); c.52A>T (p.Lys18Ter); c.51delC (p.Lys18Argfs); c.47G>A (p.Trp16Ter); c.45dupG (p.Trp16Valfs); c.36delT (p.Thr13Leufs); c.27dupG; c.25_26delAA; c.20delA; c.17_18delCT (p.Pro6Argfs); c.4delG (p.Val2Cysfs); c.2T>G (p.Met1Arg); c.2T>C (p.Met1Thr); c.93_94insCGG (p.Arg31_Leu32insArg); c.93G>T (p.Arg31Ser); c.415G>C (p.Ala139Pro); c.127_129delTTT (p.Phe43del); c.182T>A (p.Val61Glu); c.176C>G (p.Pro59Arg); c.70_72delGTT (p.Val24del); c.169G>C (p.Gly57Arg);	91-95% 91-95% 91-95% 91-95% 75-80%	Mediterranean Middle-Eastern Thai Chinese African-American	Origa, R. (2000)
		c.34G>A (p.Val12Ile); c.128T>C (p.Phe43Ser); c.298G>A (p.Asp100Asn); c.295G>A (p.Val99Met); c.277C>T (p.His93Tyr); c.59A>G (p.Asn20Ser); c.86T>A (p.Leu29Gln); c.127T>G (p.Phe43Val); c.199A>G (p.Lys67Glu)			

Cystic fibrosis	CFTR	<p>c.1000C>T (p.Arg334Trp); c.489+1G>T; c.165-1G>A; c.170G>A (p.Trp57Ter); c.171G>A (p.Trp57Ter); c.175dupA (p.Arg59Lysfs); c.178G>T (p.Glu60Ter); c.200C>T (p.Pro67Leu); c.223C>T (p.Arg75Ter); c.233dupT (p.Trp79Leufs); c.254G>A(p.Gly85Glu); c.262_263delTT (p.Leu88Ilefs); c.263T>G (p.Leu88Ter); c.271G>A (p.Gly91Arg); c.273+1G>A; c.273+3A>C; c.274-1G>A; c.274G>A (p.Glu92Lys); c.274G>T (p.Glu92Ter); c.292C>T (p.Gln98Ter); c.293A>G (p.Gln98Arg); c.310delA (p.Arg104Glu fs); c.313delA (p.Ile105Serfs); c.325_327delTATinsG (p.Tyr109Glyfs); c.328G>C (p.Asp110His); c.349C>T (p.Arg117Cys); c.350G>A (p.Arg117His); c.366T>A (p.Tyr122Ter); c.409delC (p.Leu137Serfs); c.424delA (p.Ile142Phefs); c.429delT (p.Phe143Leufs); c.442delA(p.Ile148Leufs); c.550delC (p.Leu184Phefs); c.579+1G>T; c.1364C>A (p.Ala455Glu); c.1397C>A (p.Ser466Ter); c.1397C>G (p.Ser466Ter); c.1400T>C (p.Leu467Pro); c.1418delG (p.Gly473Glu fs); c.1438G>T (p.Gly480Cys); c.1466C>A (p.Ser489Ter); c.1475C>T (p.Ser492Phe); c.1477_1478delCA (p.Gln493Valfs); c.1477C>T (p.Gln493Ter); c.1519_1521delATC (p.Ile507del); c.1518C>G (p.Ile506Met); c.1521_1523delCTT (p.deltaF508); c.1520_1522delTCT (p.deltaF508); c.1545_1546delTA (p.Tyr515Terfs); c.1558G>T (p.Val520Phe); c.1572C>A (p.Cys524Ter); c.1573C>T (p.Gln525Ter); c.1584+1G>A; c.1585-8G>A; c.1585-1G>A; c.1601C>A (p.Ala534Glu); c.1624G>T (p.Gly542Ter); c.1645A>C (p.Ser549Arg); c.1646G>A (p.Ser549Asn); c.1646G>T (p.Ser549Ile); c.1647T>G (p.Ser549Arg); c.1648G>T(p.Gly550Ter); c.1650delA (p.Gly551Valfs); c.1651G>A (p.Gly551Ser); c.1652G>A (p.Gly551Asp); c.1654C>T (p.Gln552Ter); c.1657C>T (p.Arg553Ter); c.1658G>A (p.Arg553Gln); c.1675G>A (p.Ala559Thr); c.1679G>A (p.Arg560Lys); c.1679G>C (p.Arg560Thr);c.1679+1G>A; c.1679+1G>C; c.1766+1G>A; c.1973_1985del13insAGAAA (p.Arg658Lysfs); c.1986_1989delAACT (p.Thr663Argfs); c.2012delT (p.Leu671Terfs); c.2017G>T (p.Gly673Ter); c.2036G>A (p.Trp679Ter); c.2051_2052delAAinsG (p.Lys684Serfs); c.2052dupA (p.Gln685Thrfs); c.2052delA (p.Lys684Asnfs); c.2053C>T (p.Gln685Ter); c.2053dupC (p.Gln685Profs); c.2083dupG (p.Glu695Glyfs); c.2125C>T (p.Arg709Ter); c.2128A>T (p.Lys710Ter); c.2175dupA (p.Glu726Argfs); c.2657+5G>A; c.2909G>A (p.Gly970Asp); c.2932A>T(p.Lys978Ter); c.2988G>A (p.Gln996=); c.2988+1G>A; c.3472C>T (p.Arg1158Ter); c.3484C>T (p.Arg1162Ter); c.3492dupT (p.Lys1165Terfs); c.3528delC (p.Lys1177Serfs);</p>	<p>>75% >70% >70%</p>	<p>General ppn EU US</p>	<p>Farrell, P. M. (2008); Elliott, A. M. et al. (2012); Bobadilla, J. L., et al. (2002)</p>
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		c.3532_3535dupTCAA (p.Thr1179Ilefs);			
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	<p>c.3536_3539delCAA (p.Thr1179Asnfs); c.3587C>G (p.Ser1196Ter); c.3605delA (p.Asp1202Alafs); c.3611G>A (p. Trp1204Ter); c.3612G>A (p.Trp1204Ter); c.3659delC (p.Thr1220Lysfs); c.3691delT (p.Ser1231Profs); c.3700A>G (p. Ile1234Val); c.3712C>T (p.Gln1238Ter); c.3718-2477C>T; c.3731G>A (p. Gly1244Glu);c.3744delA (p. Lys1250Argfs); c.3747delG (p. Lys1250Argfs); c.3752G>A (p. Ser1251Asn); c.3761T>G (p. Leu1254Ter); c.3764C>A (p.Ser1255Ter); c.3764C>G (p.Ser1255Ter); c.3767dupC (p.Leu1258Phefs); c.3773dupT (p. Leu1258Phefs); c.3846G>A (p. Trp1282Ter);c.3848G>T (p.Arg1283Met); c.3873+1G>A; c.3873+2T>C</p>			
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