VERAgene comprehensive NIPT

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

FETAL FRACTION

8.9%

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
XYY Constitution	The results show very low risk for XYY constitution
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 not intended and not validated for a number of mutations which are associated with the monogenic diseases listed in Table1 but are not tested. Therefore, a very low risk result reduces but does not eliminate the possibility of the fetus to be affected or carry the mutation. A very high risk result for twin pregnancies indicates high risk for the presence of at least one affected fetus. In twin pregnancies, 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.

Approved by: Elena Kypri, Ph.D, ASCP

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

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

NIPD GENETICS
Neas Engomis, 31, Nicosia, 2409 Cyprus
Phone: +357 22266888 Fax: +357 22266899
Web: www.nipd.com
Email: info@nipd.com

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 (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 (GLDC-related)	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); Moorthie, 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 (LCA5-related)	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 (MMAA-related)	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 [MPV17-related 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 [Hyperornithinemia-Hyperammonemia-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)	Burstedt, M. et al. (2013); Burstedt, M. S. et al. (2001); Burstedt, 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_204delTG (p.Val68Alafs); c.193delG (p.Gly65Alafs); c.184A>T (p.Lys62Ter); c.143_144insA (p.Asp48Glufs); 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.Gln40Glufs); 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	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.Arg104Glufs); 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.Gly473Glufs); 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); c.3532_3535dupTCAA (p.Thr1179Ilefs);	>75% >70% >70%	General ppn EU US	Farrell, P. M. (2008); Elliott, A. M. et al. (2012); Bobadilla, J. L., et al. (2002)

		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			