VISTA carrier screening

This information is for
qualified healthcare professionals only

What is carrier screening?

Carrier screening is a type of genetic test that can tell a patient whether he/she carries a gene mutation for certain genetic disorders. When carrier screening is conducted before or during pregnancy, it allows a patient to find out his/her chances of having a child with a genetic disorder.
Previous studies have demonstrated that:

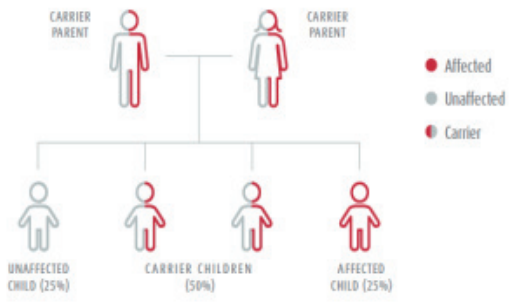
- An individual is a carrier of ~2.8 pathogenic variants on average [1]
- Approximately 1 in 4 (24%) individuals were carriers for at least 1 disorder and 1 in 20 (5.2%) were carriers for multiple disorders (of ~24000 individuals screened for 108 disorders) [2]
- 1 in 20 (5%) individuals (of 12,000 individuals screened for 3 disorders) were carriers, 88% had no previous family history and 1 in 240 were carrier couples with increased risk of having a child with a disorder [3]

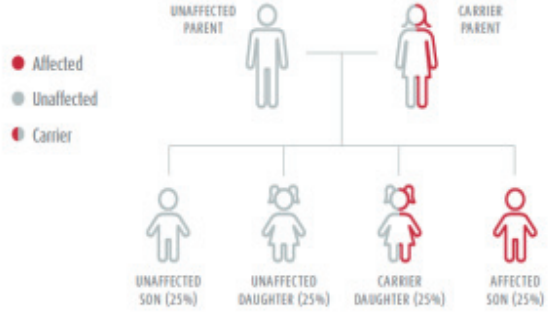
The American College of Obstetricians and Gynecology (ACOG) recommends expanded carrier screening to be offered to all pregnant women or couples considering pregnancy.

[1] Bell CJ, Dinwiddie DL, Miller NA, et al. Carrier testing for severe childhood recessive diseases by next-generation sequencing[J]. Sci Transl Med. 2011 Jan 12;3(65):65ra4.
[2] Lazarin GA, Haque IS, Nazareth S, et al. An empirical estimate of carrier frequencies for 400+ causal Mendelian variants: results from an ethnically diverse clinical sample of 23,453 individuals[J]. Genet Med. 2013 Mar;15(3):178-86.
[3] Archibald AD, Smith MJ, Burgess T, et al. Reproductive genetic carrier screening for cystic fibrosis, fragile X syndrome, and spinal muscular atrophy in Australia: outcomes of 12,000 tests[J]. Genet Med. 2018 Apr;20(5):513-523.

Why should patients consider carrier screening?

Everyone typically carries a gene mutation for at least one genetic disorder. So it is normal to be a carrier, even if people are healthy and do not experience any symptoms.
Genetic disorders usually follow standard patterns of inheritance. If both members of a couple are not carriers of the same genetic disorder, there is a low risk of having a child with a genetic condition. However, if the parents are carriers for the same genetic disorder, there is an increased risk of having a child with a genetic condition. Carrier screening before or during pregnancy therefore allows prospective parents to know ahead of time what their probability is of having an affected child.





What are the advantages of carrier screening?

- For couples who are not carriers
  Expanded carrier screening provides reassurance that their child will be at a significantly reduced risk of developing any of the included genetic disorders.
- For both parents who are found to be carriers for the same disorder

  I.They can choose assisted reproductive technologies to have a baby with a reduced risk of a disorder before pregnancy

  II.They can pursue prenatal testing to determine whether their pregnancy is affected, and to ensure the appropriate healthcare management for their baby during or after pregnancy

Who can be offered VISTA carrier screening?

BGI's VISTA Carrier Screening Test offers a comprehensive screening option for these disorders and a wider range of conditions. VISTA carrier screening can provide important information for people who:

1) are currently pregnant or planning a pregnancy

2) are at increased risk for a specific disorder based on their ethnicity

3) are planning to receive donor eggs, sperm, or embryos

4) would like additional information about the reproductive risks of having a child with a genetic disorder

Testing can be carried out either before or during pregnancy (before the 14th week), If a patient is already pregnant, the patient's reproductive partner can be tested together.

VISTA Carrier Screening offers a range of panels to suit a wide variety of screening needs. The largest panel screens for more than 11,000 mutations associated with 172 recessive monogenic diseases.

Why Choose BGI VISTA Carrier Screening?

VISTA Carrier Screening are expanded screening tests.

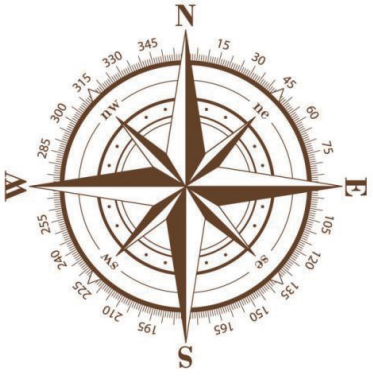
Comprehensive
Selecting conditions for carrier screening based on several professional guidelines could help to maximize the benefits and minimize the harms of screening tests

Accurate
Target region capture coupled with NGS and combined with conventional methods

Cost-effective
BGI's own proprietary DNBseq series sequencing platforms offer quality data at affordable pricing

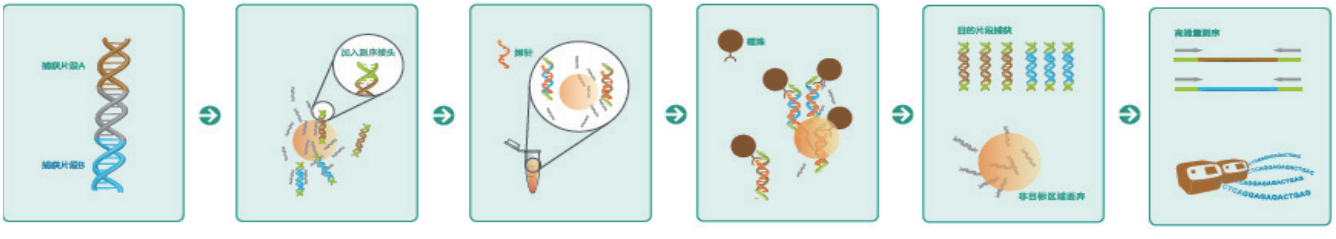
Risk Scores
Residual risk and reproductive risk are calculated in the repor

Comprehensive



In previous decades, carrier screening was typically performed for one or few relatively common recessive disorders. New genetic testing technologies have enabled the expansion of screening to multiple conditions, genes or sequence variants.
The ACMG and ACOG have published several professional guidelines addressing expanded carrier screening. Based on these professional guidelines, BGI's VISTA selects conditions for carrier screening.

Accurate



Using targeted region capture combined with NGS, BGI's VISTA carrier screening can detect pathogenic variants in the exon and splicing regions, and important variants in intronic regions and promoter regions.
Detected variants including: single nucleotide variant, small Indel (within 20bp), additional deletions in the HBA/HBB (--SEA, -α3.7, -α4.2, --FIL, --THAI, Chinese, SEA-HPFH), and deletion of exon 7 in the SMN1 gene and consecutive deletion or duplication of two or more exons in DMD.

Residual risk rate and reproductive risk rate

In the VISTA report residual risk rate and reproductive risk rate are calculated based on several professional guidelines.

2013 — ACMG
- Mention the residual risk
- The calculation requires two factors

2015 — ACMG&ACOG
- Definition of residual risk
- In what condition the residual risk is not reliable
- How to calculate

2017 — ACOG No.690
- Residual risk should be provided
- Residual risk may not be reliable in some conditions

2017 — ACOG No.693
- Residual risks are outlined by ethnicity
- Residual risk in post-test counseling is important

VISTA Carrier Screening products list

Product type	Product Name	Product Details	Detection Techniques
INITIAL ANALYSIS	VISTA Carrier screening mini panel	• 11 of the most prevalent genetic conditions • 13 Genes • more than 5,400 pathogenic variations	Target region capture coupled with NGS
	VISTA Carrier screening targeted panel 2.0	• 172 common and severe genetic conditions • 164 Genes • more than 11000 pathogenic variations	
EXTRA	VISTA Hemophilia A	Point mutation, small fragment insertions and deletions, intron 1 and 22 inversion, located at F8	Target region capture coupled with NGS and Long-range PCR
	Fragile X Syndrome Test	FMR1 CGG repeat	TP-PCR and Fluorescence capillary electrophoresis

Note:

1, The diseases list for screening panel displayed on page 18-20.

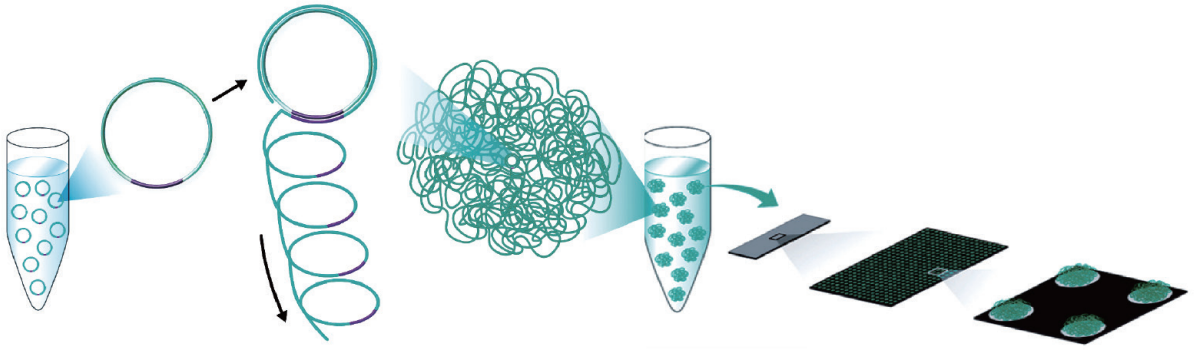
2, 3 optional types of genetic tests according to the situation.

3, Based on Target region capture coupled with high-throughput sequencing can detect deletion and repeat within the panel coverage range, such as, SMN1 exon 7 Deletion of Spinal Muscular Atrophy, large common fragment deletions of Thalassemia (--SEA, -α3.7, -α4.2, --FIL, --THAI, Chinese, SEA-HPFH, etc.)

How are conditions selected for screening?

Based on independent professional guidelines, the conditions selected for inclusion should meet several of the following consensus-determined criteria:
1) a high carrier frequency and a high disease incidence
2) a well-defined phenotype
3) an early onset in life, mostly fetal, neonatal or in childhood
4) a highly severe phenotype
5) a detrimental effect on quality of life, leading to birth defect, mortality or disability, require surgical or medical intervention
the conditions could be able to be diagnosed prenatally and may afford opportunities for antenatal intervention to improve perinatal outcomes

NGS combined with conventional methods



Proven DNBseq™ sequencing technology combines the power of DNA Nanoballs (DNB™), PCR-free Rolling Circle Replication, Patterned Nano Arrays and cPAS to deliver a new level of data clarity and affordability.
Long -range polymerase chain reaction is used to capture the functional gene for accurate analysis of genes with known pseudogenes, including HBA1 and HBA2
Multiplex ligation-dependent probe amplification (MLPA) is used to detect copy number changes for spinal muscular atrophy, alpha-thalassemia, and Duchenne and Becker muscular dystrophy.
Fragile X CGG repeat analysis is performed by PCR amplification followed by capillary electrophoresis for allele sizing.
Sanger sequencing may be used for select genes on the panel due to inadequate next-generation sequence coverage or for confirmation of variants identified by NGS

Sample Requirements

- Blood: one 5 ml EDTA tubes
- DNA: 3 ug
- Saliva: >2ml, Saliva specimens are accepted in specific Saliva kits.

Shipping requirements

- Blood and DNA: Stored at -20°C for short term, -80°C for long term, Shipped with dry ice. Please avoid vibrations or shock
- Saliva: Shipped at room temperature in 7 days

Turnaround time

21 days after receipt of samples

Service Workflow

01 Pretest genetic counseling with your doctor and sign consent form

02 Doctor draws blood

03 Ship sample to BGI

04 Test report is created 21 days later

05 Share the test report with your doctor

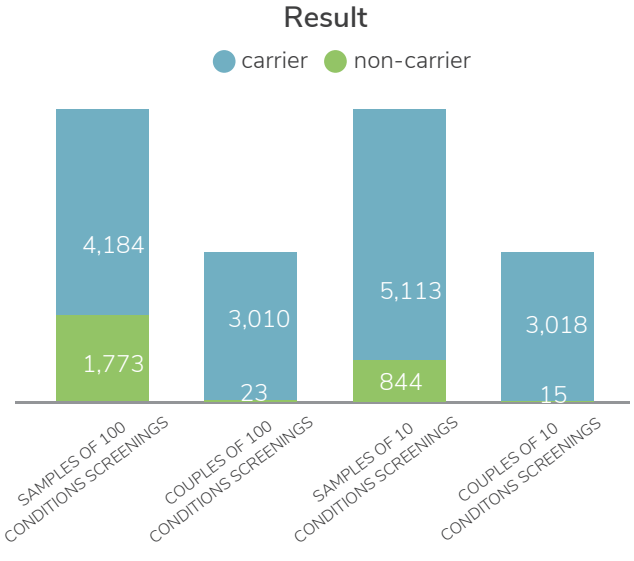
Basic research

BGI is dedicated to reducing the negative impact of genetic disease and ensuring that the benefits of genomics technology are available to all. Monogenic disease research forms an important part of BGI's research direction and BGI has a long history of important work in the field. Since the launch of the "Chinese Thousand Monogenetic Diseases Program" in 2010, BGI has cooperated with more than 150 research and medical organizations in China and internationally, and has published more than 200 papers.

Multi-Center Research Cooperation in China

A multi-center carrier screening program for common monogenic disease in pregnancy population of China was launched, led by Peking Union Medical College Hospital and BGI.
Sample size: 5,957 individuals, comprised 2924 couples and 109 pregnant women.

1,773 samples (29.76%, 1773/5957) and 23 couples (0.76%,23/3033, excluding 5 couples with standard thalassemia) tested positive after screening 100 conditions, 844 samples (14.17%, 844/5957) and 15 couples (0.49%, 15/3033) tested positive after screening 11 conditions. 5 affected fetuses was confirmed by prenatal diagnosis after Informed selection, the incidence is 1/607 (5/3033), equally important as Down's syndrome, demonstrating the clinical utility of expanded carrier



The first expanded carrier screening report in China

European Journal of Human Genetics (2019)-27(2):254-262
https://doi.org/10.1038/s41431-018-0253-9

ARTICLE

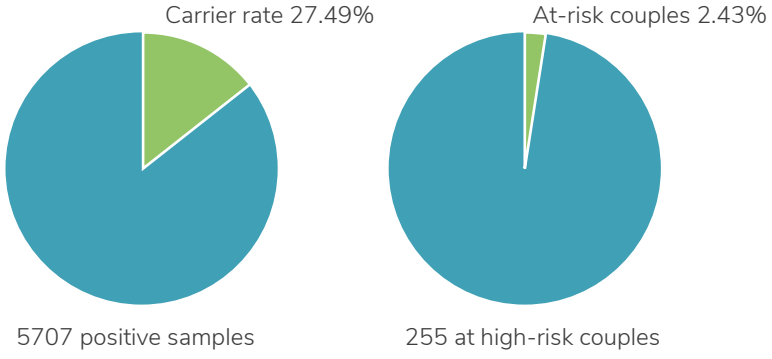
Pilot study of expanded carrier screening for 11 recessive diseases in China: results from 10,476 ethnically diverse couples

Sumin Zhao[1,2] · Jiale Xiang[3] · Chunna Fan[1,2] · Asan[1,2] · Xuan Shang[4] · Xinhua Zhang[5] · Yan Chen[6] · Baosheng Zhu[7] · Wangwei Cai[8] · Shaoke Chen[9] · Ren Cai[10] · Xiaoling Guo[11] · Chonglin Zhang[12] · Yuqiu Zhou[13] · Shuodan Huang[14] · Yanhui Liu[15] · Biyan Chen[16] · Shanhuo Yan[17] · Yajun Chen[18] · Hongmei Ding[19] · Fengyu Guo[1,2] · Yaoshen Wang[1,2] · Wenwei Zhong[1,2] · Yaping Zhu[1,2] · Yaling Wang[1,2] · Chao Chen[1,2] · Yun Li[20] · Hui Huang[3] · Mao Mao[3] · Ye Yin[3] · Jian Wang[21,22] · Huanming Yang[21,22] · Xiangmin Xu[4] · Jun Sun[1,2] · Zhiyu Peng[3,23]

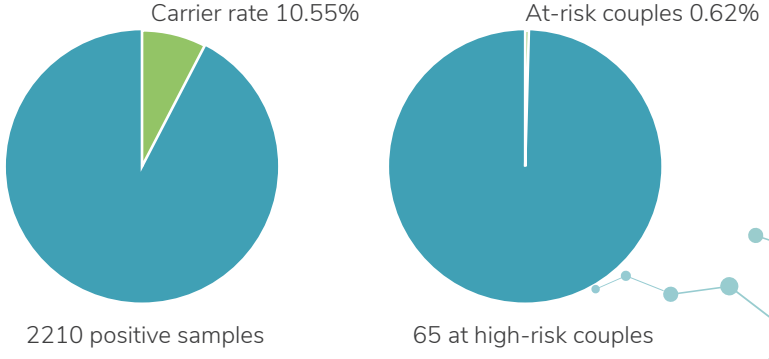
Received: 15 February 2018 / Revised: 20 July 2018 / Accepted: 9 August 2018 / Published online: 1 October 2018

Sample: A total of 10,476 prenatal/preconception couples from 34 self-reported ethnic groups

Testing conditions: 11 Mendelian disorders



Excluding α、β thalassemia



Comprehensive carrier genetic test using next-generation deoxyribonucleic acid sequencing in infertile couples wishing to conceive through assisted reproductive technology

Julio Martin, Ph.D., [a] Asan, Ph.D.,[b] Yuting Yi, M.S., [b] Trinidad Alberola, Ph.D., [a] Beatriz Rodríguez-Iglesias, Ph.D.,[a] Jorge Jim énez-Almazán, Ph.D.,[a] Qin Li, B.S.,[c] Huiqian Du, M.S., [b] Pilar Alama, M.D., [d] Amparo Ruiz, M.D., [d] Ernesto Bosch, M.D.,[d] Nicolas Garrido, Ph.D., [c] and Carlos Simon, M.D. [a,d,e]

[a] IGenomix, Parc Cienti fic Univeristat Valencia, Valencia, Spain; [b] Binhai Genomics Institute and Tianjin Translational Genomics Center, BGI-Tianjin, Tianjin, People's Republic of China; [c] BGI-Shenzen, Shenzhen, People's Republic of China; [d] Instituto Valenciano de Infertilidad Valencia and Fundaci ón Instituto Valenciano de Infertilidad, Valencia, Spain; and [e] Department of Obstetrics and Gynecology, Valencia University, Instituto Universitario IVI/INCLIVA, Valencia, Spain

Sample: 2570 samples

Testing conditions: The gene panel covers a total of 549 genes implicated in 623 disease phenotypes

84% (2161 / 2570)

were positive for at least one pathogenic variant
An average carrier burden of 2.3 per sample

5% (7 / 138)

were at high risk because partners shared recessive mutations in the same gene

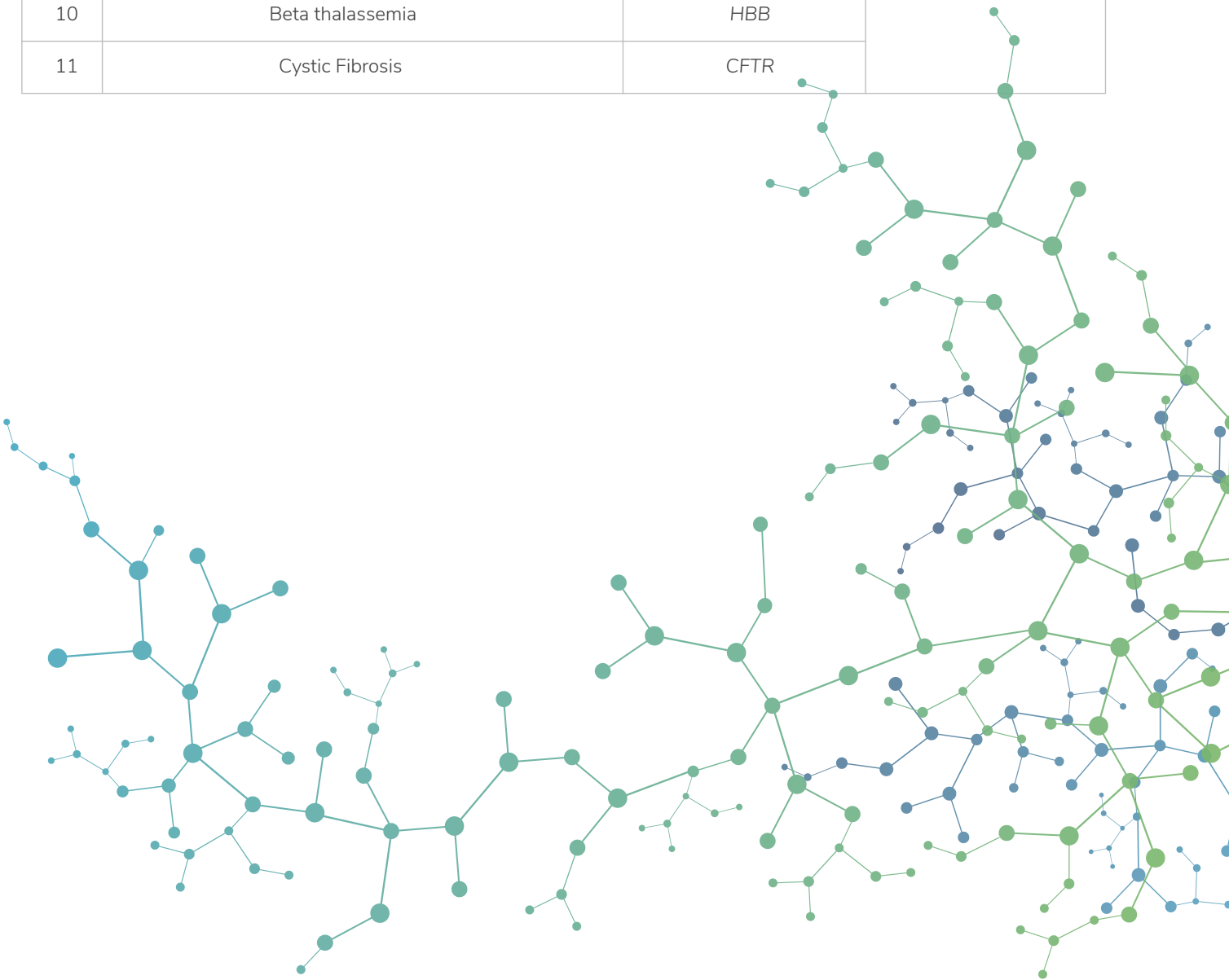
1.94% (18 / 926)

were positive for X-linked conditions for female donors

Result: The implementation of carrier screening for couples and patients requiring gamete donation may have potentially prevented 1.25% affected babies born after assisted reproductive technology.

VISTA Carrier Screening Mini Panel, screens for more than 5,400 mutations associated with 11 recessive monogenic diseases.

No.	Product Name	Genes Tested	Inheritance Patterns
1	Dystrophinopathies	*DMD*	X-linked Recessive
2	Hemophilia B	*F9*	
3	Hereditary Hearing Loss and Deafness	*GJB2*、*SLC26A4*	Autosomal Recessive
4	Spinal Muscular Atrophy	*SMN1*	
5	Phenylketonuria	*PAH*	
6	Wilson Disease	*ATP7B*	
7	Glycogen Storage Disease	*GAA*	
8	Galactosemia	*GALT*	
9	Alpha thalassemia	*HBA1*、*HBA2*	
10	Beta thalassemia	*HBB*	
11	Cystic Fibrosis	*CFTR*	



VISTA Carrier Screening Targeted Panel 2.0, screens for more than 11,000 mutations associated with 172 recessive monogenic diseases.

System	Conditions	Num
Genetic Metabolic	Hepatolenticular degeneration, primary carnitine deficiency, phenylketonuria, BH4-deficient hyperphenylalaninemia A, B-type, methylmalonic acidemia Mut, cblA, cblB, cblC, cblD , MCEE-related, homocysteineuria with megaloblastic anemia CblE type, homocystinuria with megaloblastic anemia CblG type, hereditary fructose intolerance, Tay-Sachs disease, Smith-Lemli -Opitz syndrome, etc.	83
Neuromuscular & Skeletal	Progressive pseudohypertrophic muscular dystrophy, spinal muscular atrophy, Joubert syndrome 2,3,5,6,9,17, metachromatic leukodystrophy, X-linked central nuclear myopathy, neuronal ceroid lipofuscinosis type 1-7, etc.	31
Integumentary	Eye whitening disease 1-4,6,7, X-linked genetic eye whitening disease, Herman-sky-Pudlak syndrome type 1,3, autosomal recessive hereditary ichthyosis type 1,4a, borderline bullous epidermis release LAMA3 , LAMB3, LAMC2, COL17A1 related, etc.	18
Cardiovascular	Hemophilia B, α/β-thalassemia, sickle cell anemia, Fanconi anemia complement group A, C, D2, G, I, infant type generalized arterial calcification type 2	9
Immune & Endocrine	Familial hemophagocytic lymphohistiocytosis type 2-5, Omenn syndrome, autosomal recessive severe combined immunodeficiency (B/T cell negative, NK cell positive), X-linked severe combined immunodeficiency, X-chain Congenital adrenal insufficien-cy, etc	9
Digestive & Urinary	Progressive familial intrahepatic cholestasis type 2-4, autosomal recessive Alport syndrome type I, type II, nephrotic syndrome type 1, nephron pyelonephritis type 3, nephrotic cytinosis, etc	9
Multiple systems	Cystic fibrosis, autosomal recessive deafness type 1A, Pendred syndrome, Wolfram syndrome type 1, Wolfram Syndrome, osteoporosis - pseudoglioma syndrome, immunodeficiency-centromic instability-facial abnormalies syndrome type 1	13
Total		172

This test is used to identify people who carry one copy of a gene mutation that, when present in two copies, causes a genetic disorder.

Information is for qualified healthcare professionals only.

Information is not meant to substitute qualified medical advice and is for reference only.

If the test result returns as positive for a mutation, any patient treatment plans should only be undertaken by or in consultation with a qualified healthcare professional. Further, confirmatory diagnostic testing may need to be performed for final diagnosis of any condition.

BGI recommends that non-directive genetic counseling and guidance always be provided to patients prior to undertaking any genetic testing and when reviewing results with the patient.

Accuracy of genetic testing may be affected by certain clinical factors. Therefore, test results should always be interpreted in the context of other clinical and family information of the patient.

Informed consent should always be obtained from the patient prior to testing.

www.bgi.com
info@bgi.com