Genea BIOMEDX

Genie

COMPLETE SOLUTION FOR PGT

End to End solution for PGT labs

GENIE PLATFORM

Genie PGT-A Kit for PGT-A, Ploidy, and ROH

	Samples / run	Read lengths	Reads / sample
PGT-A	96	1x100 bp	2M Reads
PGT-A + PLOIDY, ROH	48	1x100 bp	10M Reads

Genie PGT Plus Kit for PGT-A, PGT-SR, and PGT-M

	Samples / run	Read lengths	Reads / sample
PGT-A, PGT-SR and PGT-M	12	2x100 bp	80M Reads
PGT-A, PGT-SR and PGT-M	48*	2x100 bp	80M Reads

* High throughput option available on request

Genie PGT Platform is supported by

1. Genie Data Analysis software

- Single software solution for Genie PGT solutions
- Software includes a review step to confirm sample details are correct

2. Genie Sequencer

- Generates 500M reads per run to support Genie PGT solutions
- High throughput sequencing (550M to 1600M reads) option available on request

GENIE PGT-A KIT

Offers two options with varying total reads per sample for greater flexibility.

Reads	Samples	Bioinformatics	Testing Content
2M	96 samples/run	• Circular binary segmentation (CBS) algorithm	• Aneuploidy • ≥4Mb CNVs • Mosaicism ≥30% & ≥10Mb • 1-4Mb known inherited CNVs
10M	48 samples/run	• Circular binary segmentation (CBS) algorithm • Log-likelihood ratio (LLR)	• Aneuploidy • ≥4Mb CNVs • Mosaicism ≥30% & ≥10Mb • 1-4Mb known inherited CNVs • Triploid • Whole-chromosome level ROH

Accurate detection of CNVs:

- Validated to detect CNVs ≥ 4Mb in size.
- Can detect known CNVs ≥1Mb in size.
- Can detect mosaicism ≥30% at a resolution of ≥10Mb.

For Research use Only (RUO). Not for use in diagnostic procedures.

Large-scale Randomized Clinical Trial with Genie PGT-A Solution.

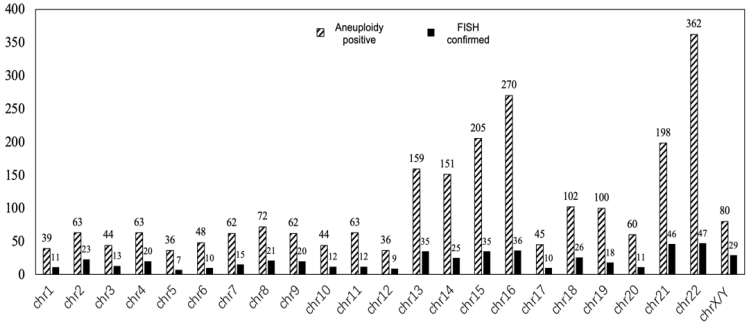
4 years

6 institutions

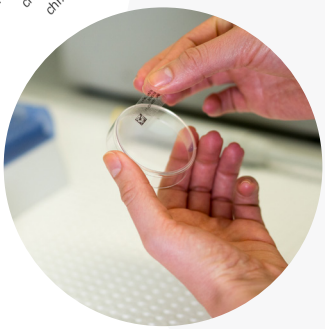
1482 couples

6282 embryos

- 1,672 positive, 4,483 negative for aneuploidy.
- 381 positive embryos underwent FISH with **100%** concordance (Kappa=1).
- 1,162 negative embryos transferred and 750 confirmed pregmancy.
- 291 women who had embryo transfer received karyotyping, **100%** concordance (Kappa=1).



FISH verification results of positive samples and karyotype analysis results of negative samples **are consistent with the detection results of this kit**, and **the accuracy, sensitivity and specificity are 100%**, with good detection consistency.



Large-scale clinical data from several assisted reproduction centers in China.
Data available upon request from manufacturer.

Use of Genie PGT-A showed an improved clinical pregnancy rate.

Clinical statistics on pregnancy rate and miscarriage rate in a single centre using Genie PGT-A Kit.

Average Female Age	Average Number Eggs	Percent Euploid Embryos	Thawed Graft Cycle	Clinical Pregnancy Rate	Sustained Pregmancy Rate
37.34±4.37	11.24±7.16	40.7% (327/803)	112	75.89% (85/112)	64.29% (72/112)

PGT follow-up data (2018-2022) showed a **clinical pregnancy rate of 75.89%** in those who underwent PGT-A testing.

- Of the **803** blastocysts tested by the Genie-PGT-A kit, **327 (40.7%)** were haploid embryos.
- Of **112 thawed transplant cycles**, **85 (75.89%) resulted in clinical pregnancies** and **8 (9.41%) had early miscarriages**.
- The **sustained pregnancy rate of 64.29%** is much higher than that of conventional IVF cycles.

PGT-A data from a hospital in Shenyang, Liaoning, China.
Data available upon request from manufacturer.

GENIE PGT PLUS

Comprehensive PGT solution:
A single workflow for combined PGT-A, PGT-SR and PGT-M.

- Patented sample preparation method requiring **only 1/10th of 30x WGS** data for analysis.
- Genie PGT plus reports **Kinship, Mosaicism, ROH, Ploidy and CNV** in addition to linkage analysis.
- Where available, **the SNP sequence** (A, T, G and C) **is reported by the software.**
- Genie PGT plus detects **reciprocal and Robertsonian translocations including inversions Consanguinity and UPD**.
- **Haplotyping can be done without a proband (reference)** when there are more than 5 embryo samples in an analysis.
- **All available SNPs are Key SNPs** as the non-informative alleles are also being sequenced.

CONTENT	GENIE-PLUS
Total number of SNPs available	**1,000,000**
Average No. of SNPs in each 2Mb Window	**417.5**
SNP locus	**Stochasticity**
No. of informative SNPs	**75524**
Ratio of ≥2 Informative SNPs in 1 Mb Window	98.69
Sensitivity for Mosaic CNV	**High**
Sensitivity for ROH	**High**
Kinship	**Yes**

GENIE PGT PLUS VALIDATION

In September 2022, **REPRODUCTIVE GENETIC HOSPITAL OF CITIC-XIANGYA** published an article on Genie PGT-Plus.

By retrospectively analysing **188 embryonic samples** from **43 families**, Genie platform revealed **100% concordance** with the available results obtained from reference methods, including PGT-A, PGT-M, PGT-SR and PGT-HLA.

Summary of samples used in this study

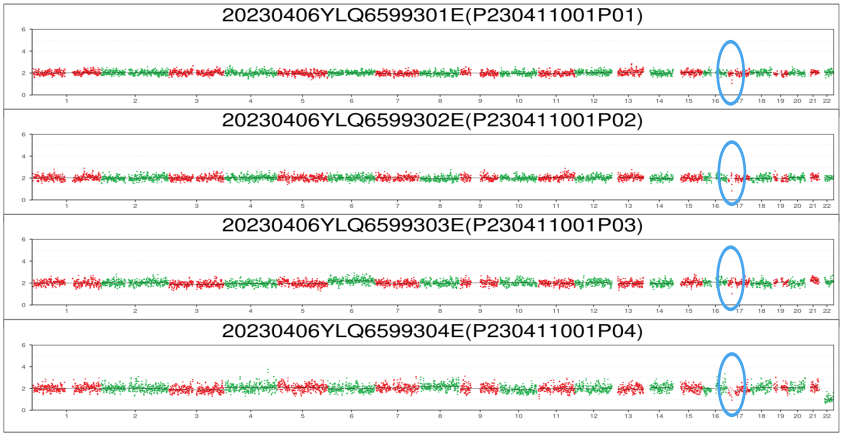
DETECTION	FAMILIES	EMBRYOS
PGT-A+SR	12	115
PGT-A+M/HLA	7	26
PGT-A+M+SR	3	26
1PN	12	12
Suspected triploid	9	9
TOTAL	**43**	**188**

Sensitivity (100%), Specificity (100%)

Xie P, et al. Hum Reprod. 2022;37(11):2546-2559.

Higher accuracy of CNV detection

Detection of 1-4Mb of pathogenic CNV.



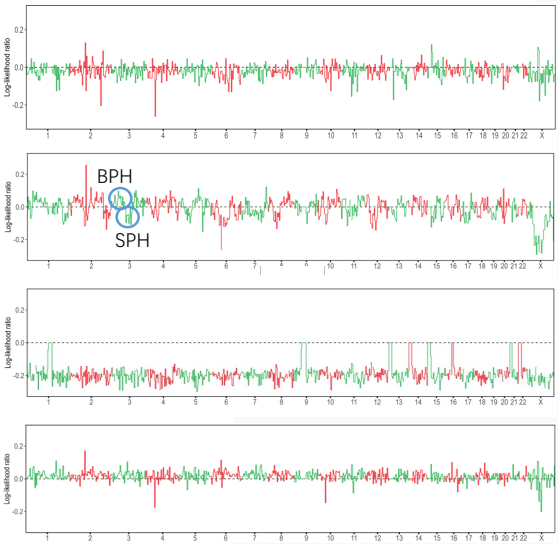
A 1.40Mb deletion was detected by Genie PGT-A in the chr17p12 region, involving 9 protein-coding genes. Among them, 3 are pathogenic genes recorded in OMIM (COX10, PMP22, and TEKT3).

Detects Origin of Aneuploidies, Contamination and UPD

Genie PGT solution uses **Linkage Disequilibrium (LD)** to identify the number of haplotypes inherited from each parent.

Both Parental Haplotype (BPH), refers to both haplotypes from the same parent.

Single Parental Haplotype (SPH), refers to one haplotype from one parent.



Triploid

Diploid

Haploid

Contamination

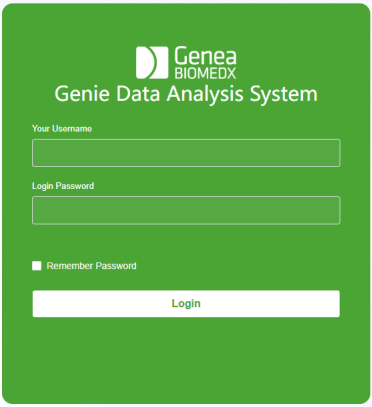
Log-likelihood ratio, the likelihood of the reads in the sample containing BPH and/or SPH for each parental haplotypes

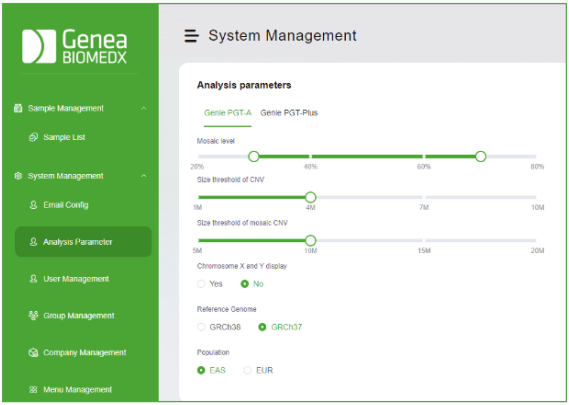
In a normal diploid sample, the LLR is 0, due to the presence of SPH from each parent. When the LLR is >0, the likelihood of BPH from at least one parent is higher, i.e., the region may contain three haplotypes.

GENIE PGT ANALYSIS SOFTWARE

A single software solution for Automated PGT analysis & reporting.

- Genie Software has **8 CNV annotations**, including UCSC, NCBI, DECIPHER, DGV and ClinGen.
- Genie analysis software supports **both hg19 and hg38** as the reference databases for data analysis.
- **Analysis Parameters can be optimised** as per user requirement (eg, define mosaic percentages).
- Genie analysis software supports **customised report generation**.





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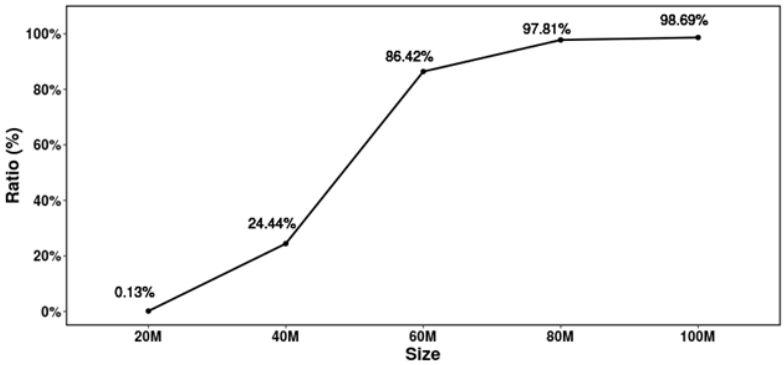
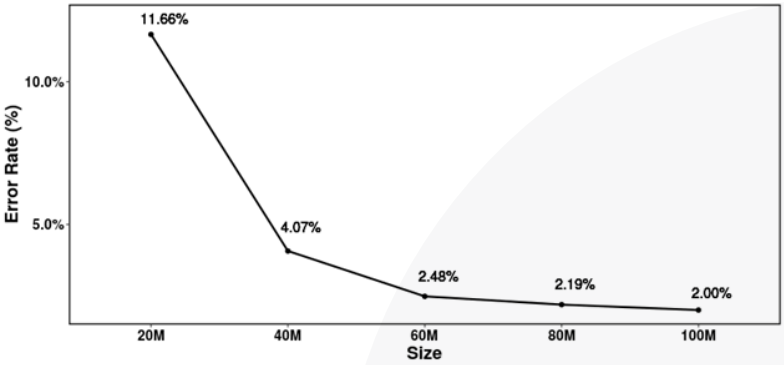
PGT Plus: Genome-wide SNP coverage enables better haplotyping



The proportion of windows containing two or more informative SNPs for haplotyping at different data sizes



The error rate of Genie PGT-Plus at different data sizes

With 80M reads per sample, we are able to get 1M SNPs for haplotyping. The proportion of windows containing two or more informative SNPS for haplotyping was almost saturated at 80M (~97.81%). Meanwhile, the genotyping error rate was stabilised at a low level (2.19%).

Xie P, et al., Hum Reprod. 2022; 37(11):2546-2559.

PGT Plus: Deep sequencing enables the detection of nucleotides (A, T G and C) in SNPs

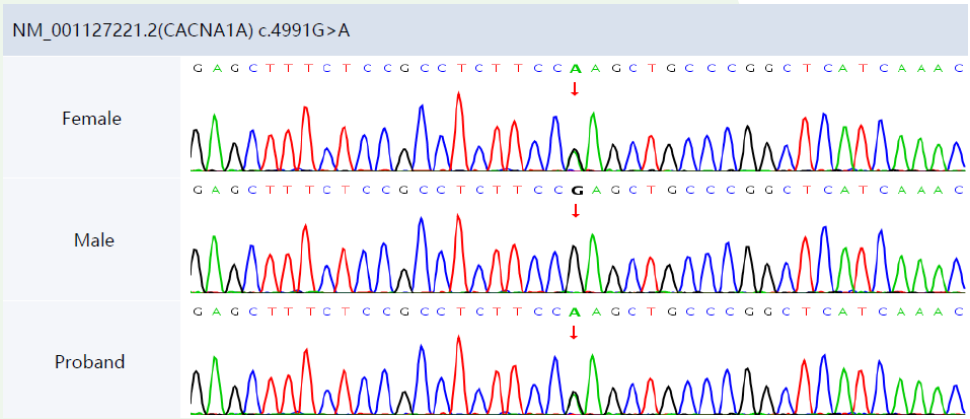
SNP		Female		Male		Proband	
		M0	M1	F0	F1	M1	F1
chr19	13129932	A	AT	AT	AT	AT	AT
chr19	13296650	C	C	C	T	C	T
chr19	13312377	G	G	T	G	G	G
chr19	13312429	C	C	T	C	C	C
chr19	13313232	C	G	G	G	G	G
chr19	13326140	T	G	G	G	G	G
chr19	13326155	C	T	T	T	T	T
chr19	13336705	C	T	T	T	T	T
Pathogenic variation (chr19:13346507)							
chr19	13368588	G	A	G	G	A	G
chr19	13391286	C	C	T	C	C	C
chr19	13396110	T	T	C	T	T	T
chr19	13404415	C	C	C	T	C	T
chr19	13433348	C	C	T	C	C	C
chr19	13442779	G	G	A	G	G	G
chr19	13442795	G	G	C	G	G	G
chr19	13475028	T	T	C	T	T	T
chr19	13492857	C	C	G	C	C	C
chr19	13496908	T	T	C	T	T	T

M0 for female normal chromosome.

M1 for female risk chromosome.

F0 and **F1** for male normal chromosome.

Sanger sequencing



The haplotype results were consistent with those verified by Sanger sequencing.

PGT Plus: Genome wide Linkage Analysis is supported by the exact nucleotides (A, T, G and C)

SNP	Chrom	Position	F-M0_M0	M-M0_M0	F-F0_F0	M-F0_F0	F-P01_S1	M-P01_S1	P02_P01	P02_P01	P03_P02	P03_P02	P04_P03	P04_P03	P05_P04	P05_P04
chr14_92	chr14	92870233	A	T	A	A	T	A	T	A	A	A	A	A	T	A
chr14_92	chr14	92870285	G	A	G	G	A	G	A	G	G	G	G	G	A	G
chr14_92	chr14	92876580	T	T	C	T	T	T	T	T	T	T	T	T	T	T
chr14_92	chr14	92878489	A	A	G	A	A	A	A	A	A	A	A	A	A	A
chr14_92	chr14	92878794	G	A	G	G	A	G	A	G	G	G	G	G	A	G
chr14_92	chr14	92884446	G	T	G	G	T	G	T	G	G	G	G	G	T	G
chr14_92	chr14	92889211	G	A	G	G	A	G	A	G	G	G	G	G	A	G
chr14_92	chr14	92891153	G	C	G	G	C	G	C	G	G	G	G	G	.	.
chr14_92	chr14	92891292	G	T	G	G	T	G	T	G	.	.	G	G	.	.
chr14_92	chr14	92924556	C	A	C	C	A	C	A	C	C	C	C	C	A	C
chr14_92	chr14	92939023	G	C	C	C	C	C	C	C	G	C	G	C	C	C
chr14_92	chr14	92942795	A	AT	A	A	AT	A	AT	A	A	A	A	A	AT	A
chr14_92	chr14	92974439	T	C	C	C	C	C	C	C	T	C	T	C	C	C
chr14_92	chr14	92974445	C	T	T	T	T	T	T	T	C	T	C	T	T	T
chr14_92	chr14	92985875	C	T	T	T	T	T	T	T	C	T	C	T	T	T
chr14_92	chr14	92986169	G	A	A	A	A	A	A	A	G	A	G	A	A	A
chr14_93	chr14	93003092	G	A	A	A	A	A	A	A	.	.	A	A	A	A
chr14_93	chr14	93010820	A	A	G	A	A	A	A	A	A	A	A	A	A	A
chr14_93	chr14	93044798	G	G	G	A	G	A	G	A	G	A	G	A	G	A
chr14_93	chr14	93046467	A	A	A	G	A	G	A	G	A	G	A	G	A	G
chr14_93	chr14	93066363	G	G	G	A	G	A	G	A	.	.	G	A	G	G
chr14_93	chr14	93067262	G	G	G	A	G	A	G	A	G	A	G	A	G	G
chr14_93	chr14	93070764	T	T	C	T	T	T	T	T	T	T	T	T	T	C
chr14_93	chr14	93071337	T	T	C	T	T	T	T	T	T	T	T	T	T	C
chr14_93	chr14	93082160	G	G	G	A	G	A	G	A	.	.	G	A	G	G
chr14_93	chr14	93084800	G	G	G	A	G	A	G	A	G	A	G	A	G	G
chr14_93	chr14	93095146	T	T	T	A	T	A	T	A	.	.	T	A	.	.
chr14_93	chr14	93095284	G	G	G	A	G	A	G	A	.	.	G	A	G	G
chr14_93	chr14	93103250	T	T	T	TA	T	TA	T	TA	T	TA	T	TA	T	T

The SNPs detected with Genie PGT plus can be linked for genome-wide SNP analysis and haplotype construction.

PGT Plus provides the number of SNPs supporting the haplotyping results

Paternal and Maternal SNP Table:

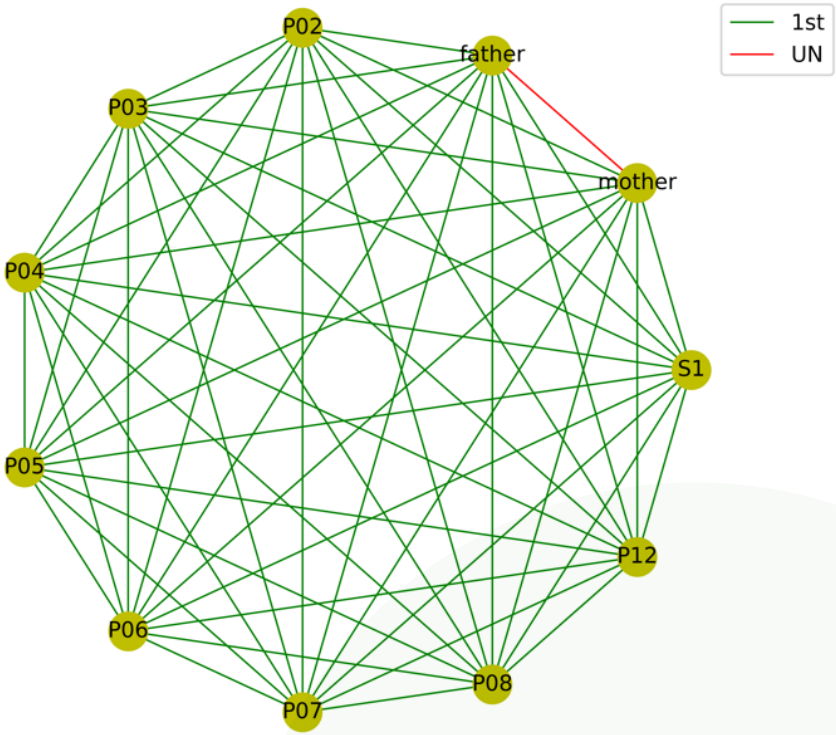
the number of SNPs supporting/unsupporting the haplotyping in the region of interest and 2 Mb flanking regions on both sides.

Haplotype QC

SERPINA1 chr14:94844947-94847262	Paternal SNPs				Maternal SNPs			
	Support		Unsupport		Support		Unsupport	
Region	key	Non-Key	key	Non-Key	key	Non-Key	key	Non-Key
Left Flanking(5`)	13	7	0	0	24	18	0	0
Main	0	0	0	0	0	1	0	0
Right Flanking(3`)	20	23	0	0	48	28	0	1
Count	33	30	0	0	72	47	0	1

1q23.1 chr1:155500000-160100000	Paternal SNPs				Maternal SNPs			
	-		-		Support		Unsupport	
Region	key	Non-Key	key	Non-Key	key	Non-Key	key	Non-Key
Left Flanking(5`)					19	12	0	1
Main					85	28	4	2
Right Flanking(3`)					14	17	1	0
Count					118	57	5	3

PGT Plus provides Kinship graph (Sibling QC)



The **green line** represents the first degree of kinship.
The **red line** represents unrelatedness.

- Identity By Descent (IBD): a concept used in genetics to measure the proximity of kin pairs.

- Family relationships are examined by estimating kinship coefficients and inferring IBD for all individuals in pairs.

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