Capital BIO
TECHNOLOGY

Pre-implantation Genetic Screening

PGS

Chromosome abnormality exists in around one-third of the embryos created through assisted reproductive technologies (such as IVF) and is a primary cause of pregnancy failure and miscarriage. Pre-implantation Genetic Screening (PGS) refers to the selection of one or more cells for chromosome number and structure abnormality testing during assisted reproductive technology and prior to embryo implantation in order to achieve a normal pregnancy, improve the patient's clinical pregnancy rate, and reduce the risk of early miscarriage. According to study, PGS can greatly boost IVF indices (see the Table 1).

Table 1 Index Comparison for IVF Combining or Not Combining with PGS Embryo Transplantation [1]

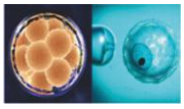
Technology	Transplantation Rate	Clinical Pregnancy Rate	Persistent Pregnancy Rate	Abortion Rate
IVF (-PGS)	19.15%	43.91%	32.49%	26.01%
IVF (+PGS)	52.63%	69.23%	61.54%	11.11%

References:

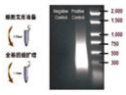
[1] Keltz, M.D., et al, Preimplantation genetic screening (PGS) with Comparative genomic hybridization (CGH) following day 3 single cell blastomere biopsy markedly improves IVF outcomes while lowering multiple pregnancles and miscarrlages. J Assist Reprod Genet, 2013.30(10): p.1333-9.

On the basis of the CapitalBio® BioelectronSeq 4000 Sequencer, CapitalBio Genomics successfully developed a PGS overall solution integrating test reagent, bioinformatics analysis, and data management software and combining with whole genome amplification (WGA) technology. The system can assist hospitals in conveniently and independently completing all PGS-related tasks such as testing, data review, and result reporting.

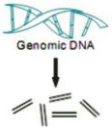
Workflow



Blastocyst trophoblast cells or cleft cells



Whole Genome Amplification

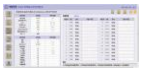


DNA Fragmentation

DNA Library Construction

BES 4000 Sequencing

Data Analysis



Data Review

Result Report

Sample Requirement

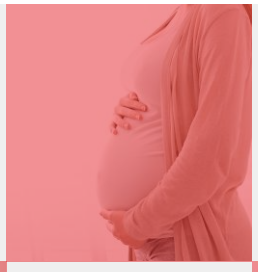
Sample Type	Collection	Storage
Blastomere cell	Using PBS buffer solution, rinse the individual blastomere cell and place it in the bottom of a 200uL PCR tube containing 2.5uL of buffer solution	Store it at –20˚C and use it within 48 hours
Blastocyst trophoblast cell	Using PBS buffer solution, rinse the multiple trophoblast cells and place them in the bottom of a 200uL PCR tube containing 2.5uL of buffer solution	Store it at –20˚C and use it within 48 hours
Unicellular whole genome amplification product*	Put it into 1.5mL EP tube	Refrigerate it at 2–4˚C for storage and use it within 72 hours
Multicellular whole genome amplification product*	Put it into 1.5mL EP tube	Refrigerate it at 2–4˚C for storage and use it within 72 hours

* Whole genome amplification product: the total amount of DNA should be at least 1.5ug, the concentration should be at least 30ng/uL, and $OD_{260/280}$ should be 1.7-2.0.

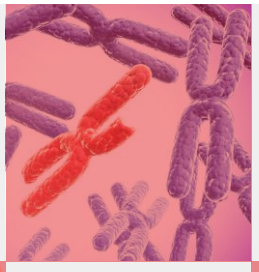
Target Population

PGS is applicable to all IVF couples, and it is especially recommended for the following communities:

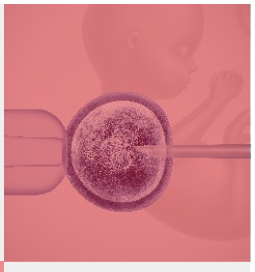
Pregnant woman after age 35

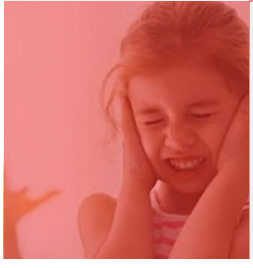


Couple with abnormal chromosome number and structure

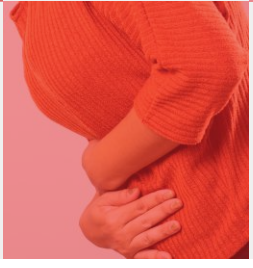


Pregnant women who have had multiple embryo implantation failures

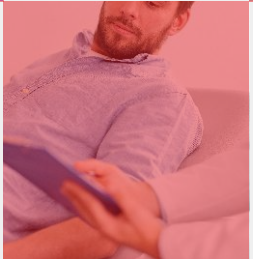




Pregnant woman with a history of recurrent miscarriages



Pregnant woman who delivered infants with chromosomal abnormalities



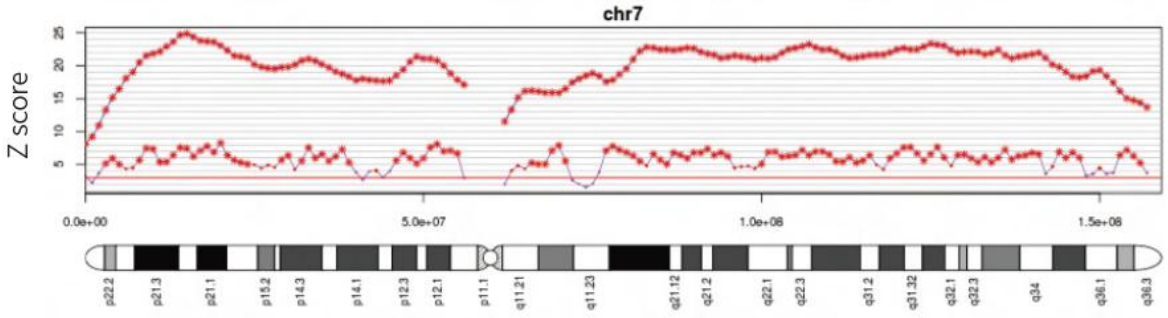
Severe male infertility (SMF): oligospermia, teratosis

What are the benefits of PGS?

High Accuracy: the test accuracy is ⩾99.9%.

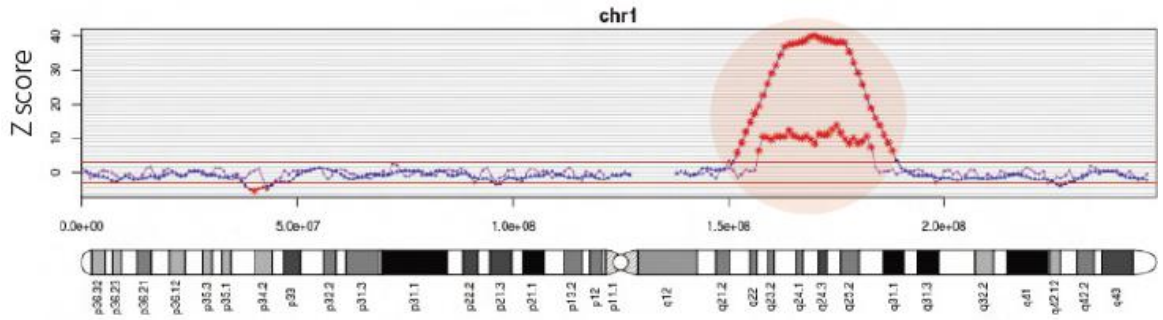
Comprehensive Test: it can test 23 pairs of chromosome aneuploidy and copy number variation in 5Mb area above of chromosome submicroscopic level.

Chromosome Aneuploidy



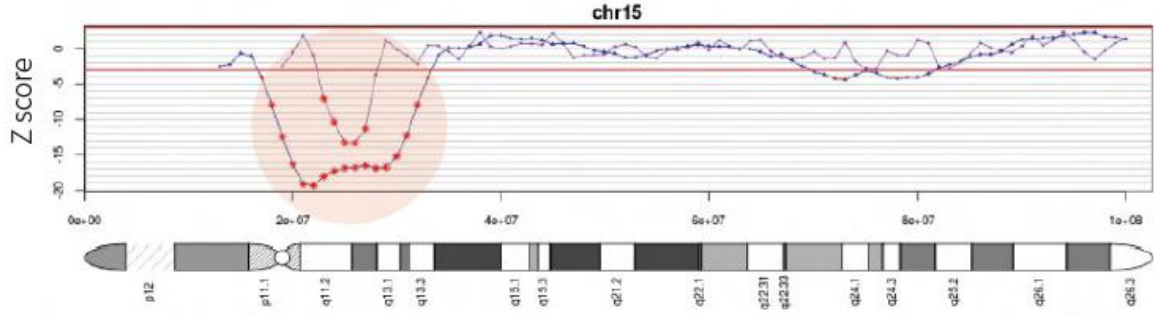
Trisomy 7

Copy Number Variation (⩾10Mb) of Chromosome Microscopic Level



20Mb microdulication at the long arm of Chromosome 1

Copy Number Variation (⩾5Mb)



5Mb microdeletion at the long arm of Chromosome 15

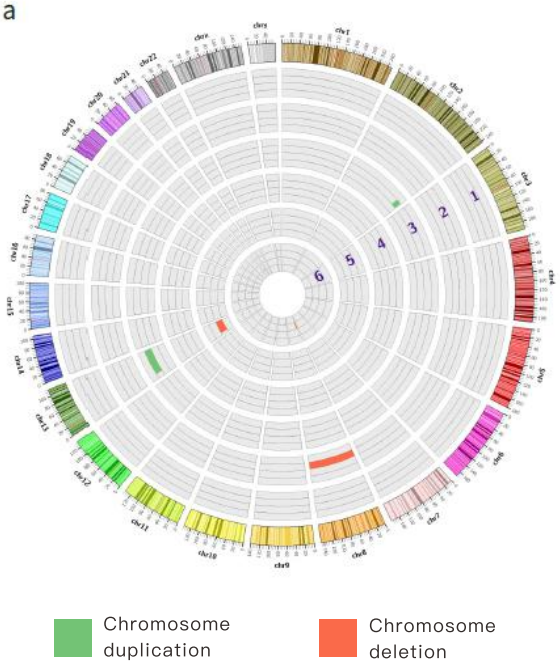
Note: in the above result diagram, the abscissa represents the chromosome location and the ordinate represents the Z-score; the purple line represents the original Z-score of read_ ratio in chromosome areas; the blue line represents the Stouffer's Z-score read_ ratio in chromosome areas.

Classic Test Case

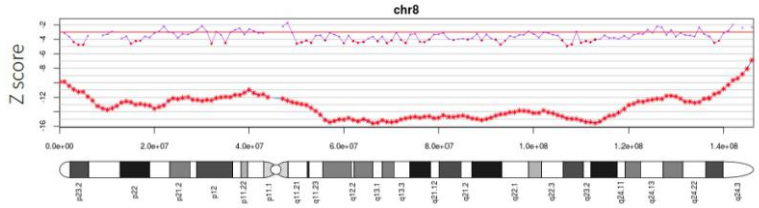
Case 1

29–year–old patient, husband chromosome karyotype 45, XY, rob (13; 21)(q10; q10). Six embryonic trophoblast cells developed to the fifth day after IVF surgery were chosen for PGS testing, and the results are shown in the figure below. Two of the embryos have normal chromosomes, and one is implanted into the mother's uterus. A urine test two weeks after embryo transfer confirms pregnancy, and chorionic gonadotropin (HCG) testing and ultrasound testing at 12 weeks confirm successful pregnancy. The baby's development indicators are normal after a later stage follow–up.

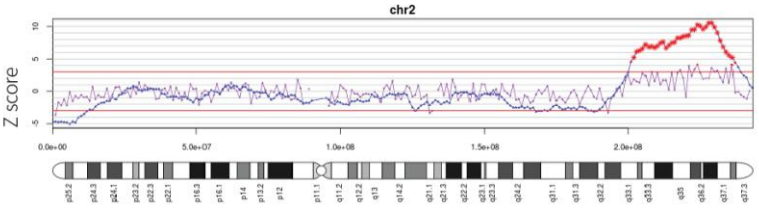
a

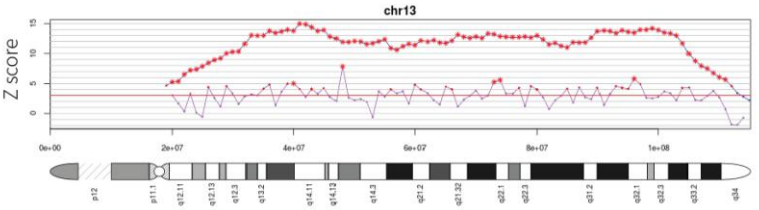


b

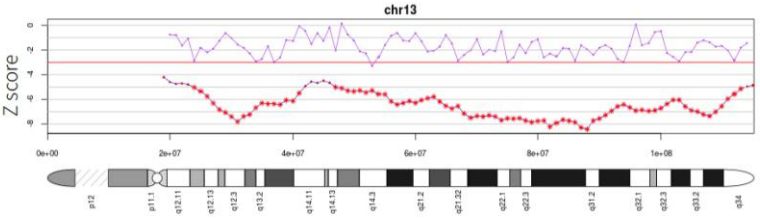


2# embryo: 8# chromosome monomer

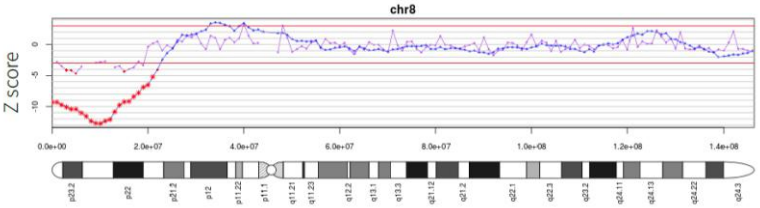




3# embryo: 20Mb duplication exists in 2# chromosome long arm q23.1–q37.2 and the duplication exists in 13# chromosome long arm.



5# embryo: the duplication exists in 13# chromosome long arm.



6# embryo: a 20Mb deletion on the short arm of chromosome 8 (p.23.3–p22)

6# embryo: 20Mb deletion exists in 8# chromosome short arm p23.3–p22.

Fig. PGS Test Results of 6 Embryo Single Cells in Case 12

a. PGS test result diagram of 6 embryo single cells. 1# and 4# embryo have no abnormality found; 2# embryo is the 8# chromosome monomer; 3# embryo has chromosome duplication; 5# embryo has chromosome deletion; 6# embryo has chromosome deletion.

b. Z–score Distribution Diagram of Chromosome Abnormality in 2#, 3#, 5# and 6# Embryo. The abscissa represents the chromosome location and ordinate represents the Z–score. The purple line represents the original Z–score of read_ ratio in chromosome areas; the blue line represents the Stouffer's Z–score read_ ratio in chromosome areas.

Classic Test Case

Case 2

The 32–year–old patient had been induced once in the second trimester of her pregnancy and then miscarried twice due to embryo suspension. Following IVF, embryonic trophoblast cells that have reached the fifth day are chosen for pre–implantation PGS testing. The figure below depicts some of the test results, where embryos 6 and 7 have normal chromosomes and can be used for transfer.

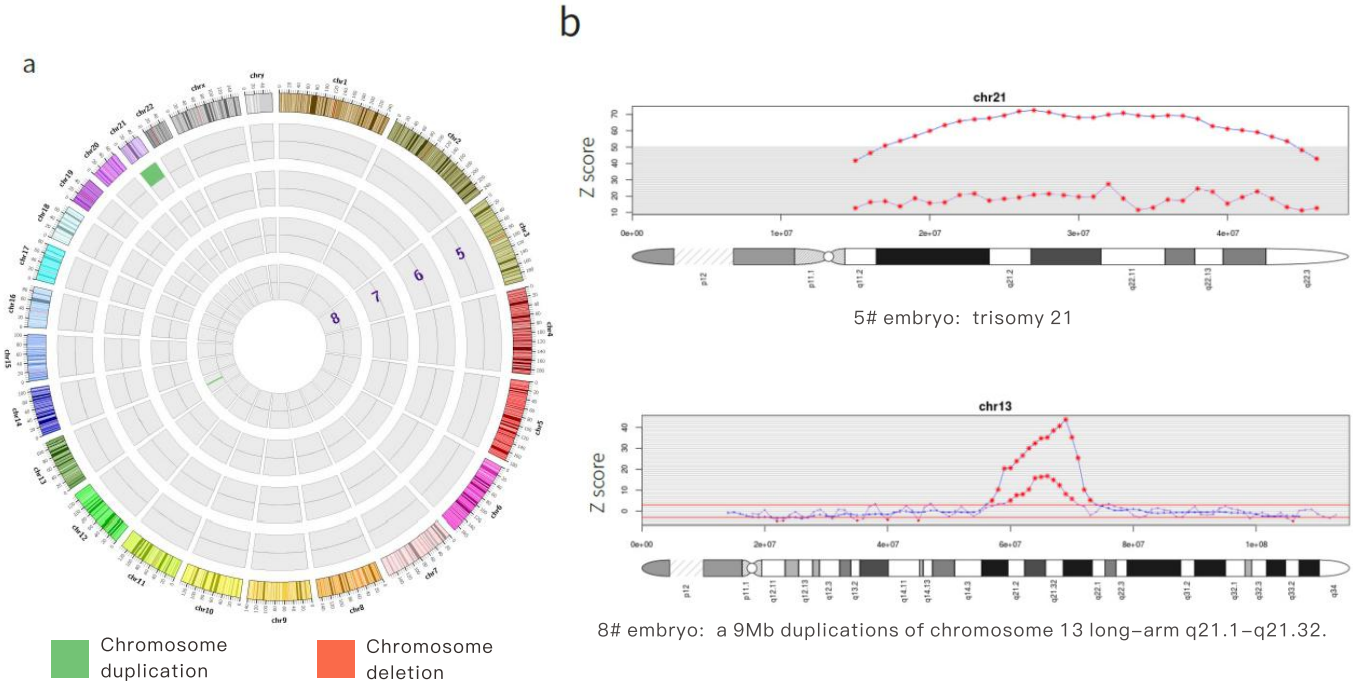


Fig. PGS Test Results of 4 Embryo Single Cells in Case 13

a. PGS Test Result Diagram of 4 Embryo Single Cells. 6# and 7# embryo are no abnormality found, 5# embryo is chromosome trisomy and 8# embryo has chromosome duplication.

b. Z–score Distribution Diagram of Chromosome Abnormality in 5# and 8# Embryo. The abscissa represents the chromosome location and ordinate represents the Z–score. The purple line represents the original Z–score of read_ ratio in chromosome areas; the blue line represents the Stouffer's Z–score read_ ratio in chromosome areas.

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