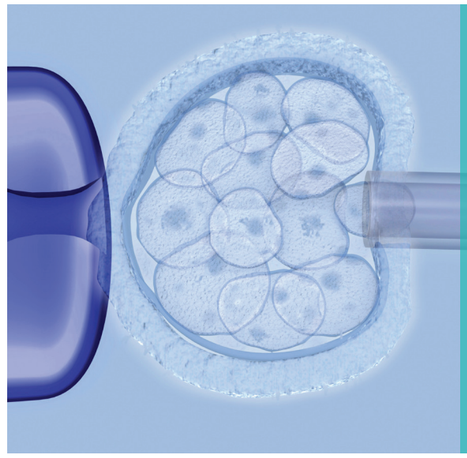
Agilent
Trusted Answers

Agilent solutions for preimplantation genetic testing

Make informed choices with technologies that fit your needs

Brief history of IVF

The first applications of *in vitro* fertilization (IVF) date back 40 years[1]. Since then, the introduction of new procedures and technologies have drastically changed the way we approach IVF. In the early 1990s, the first successful clinical preimplantation genetic testing (PGT) was applied to eliminate the transmission of X-linked conditions and cystic fibrosis transmembrane conductance regulator (CFTR) mutations[2,3]. Today, PGT is commonly used to test a few cells from embryos before embryo transfer to detect aneuploidy (PGT-A), translocations (PGT-SR), and/or more than 400 monogenic disorders (PGT-M). It has been estimated that approximately 100,000 PGT cycles have been performed worldwide over the past 23 years, the vast majority being PGT-A (www.pgdis.org).



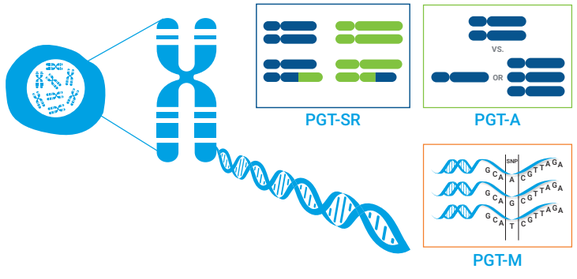
The benefits of embryo testing

To increase the success of IVF procedures, embryo testing[4,5] and ranking is a routine clinical procedure in cytogenetic laboratories and IVF clinics prior to implantation. The benefits include:

- Reduction in miscarriage rate
- Increased pregnancy rate
- Increased likelihood of healthy birth
- Reduced risk of multiple pregnancies
- Optimization of time and resources

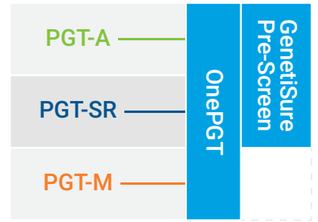
Informed testing, that can be detected with available technologies

Current PGT nomenclature highlights the different applications of preimplantation genetic testing of embryos. The new definitions highlight all the genetic anomalies tested:



Agilent is innovating the path for embryo testing and ranking

Agilent is your trusted partner for embryo testing and ranking. Our mission is to accelerate informed decisions by providing tools and solutions that address laboratory needs in terms of throughput, effectiveness, completeness and ease of use.



Agilent provides two complementary integrated solutions for the detection of aneuploidies, chromosomal rearrangements and single gene disorders or a combination thereof.

- GenetiSure Pre-Screen kits
- CGH array platform solution
- OnePGT Solution - Genome-wide next-generation sequencing (NGS) solution

By providing highly accurate and comprehensive genetic data, Agilent enables fertility specialists to make better-informed decisions on embryo ranking and selection—thereby increasing the chances of a successful and healthy pregnancy.

In addition, Agilent's product portfolio provides a full spectrum of solutions linked to human reproductive genetics.

Prenatal and postnatal genome analysis with a full suite of technologies from Agilent

NGS

Agilent's market-leading hybrid capture method, SureSelect, offers NGS target enrichment solutions including custom & catalog panels to analyze a few genes to full exomes.

SureMASTR catalog panels are based on multiplex amplification of selected genomic targets through a simple PCR assay. Panels are focused on specific diseases or conditions (e.g. CFTR, BRCA) and come with MASTR Reporter, a dedicated data analysis tool.

CGH

Industry-leading catalog and custom CGH microarrays are able to detect whole genome CNVs and absence of heterozygosity (AOH) in a single experiment using blood, CVS, or amniotic fluid as starting samples. The CGH and CGH+SNP platform offers real comparative genomic data due to the 2-color approach, and unlimited flexibility in terms of format and content.

NIPT

Clarigo* is a unique, NGS-based, CE-marked noninvasive prenatal test (NIPT) solution validated for detection of trisomy 13, 18, 21 with optional gender calling in cell-free DNA from maternal blood.

*The product referenced above is not available for sale in all countries or jurisdictions. Please contact your local sales representative for additional information.

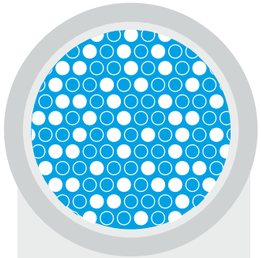
GenetiSure Pre-Screen solution – rapid and reliable identification of aneuploidies and chromosomal rearrangements

GenetiSure Pre-Screen Complete kit with QIAGEN REPLI-g is a cost-effective and a highly sensitive array CGH solution. The assay includes all the reagents and the software with dedicated analysis workflow.

Microarrays can be applied in PGT when high resolution and fast results are requested. Variable array formats enable scalable throughput using blastomere or trophectoderm biopsies from fresh or frozen embryos.

Protocol workflow

Sample preparation	20 min
REPLI-g WGA	140 min
Labeling	80 min
Purification	20 min
Preparation for hybridization	35 min
Hybridization	2 hr
Washing, scanning, analysis	45 min
Total:	7 hr 40 min



Advantages

- **Easy**
  Based on Agilent CGH platform
- **High resolution**
  Ability to call aberrations down to >1 Mb
- **Fast**
  From sample to results in less than 8 hours
- **Low-cost**
  Cost-effective, starting from 6 samples/run

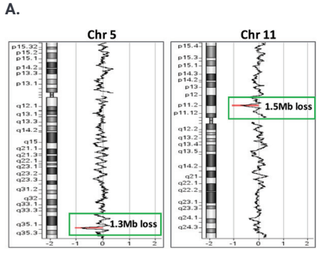
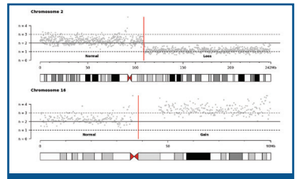


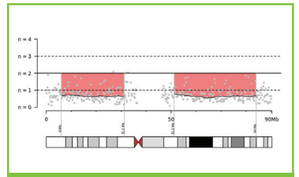
Figure 1. A) Thanks to higher data quality linked to MDA amplification, the new kit enables calling with higher confidence small aberrations, in the range of 1-5 Mb, above an example of two deletion < 2 Mb detected with the platform. **B)** Working with single cells provides extra flexibility to the solution, allowing to work with day 3 embryo biopsy if needed. The pre-screen complete platform is robust enough to call with confidence aberrations > 5 Mb also starting from such limited starting material. Above is an example of a gain and a loss detected starting from a single cell (cell line GM14485). **C)** The ability to call mosaic is extremely important to properly rank embryo quality. We mixed two cell lines both carrying a gain of approx. 30 Mb to test ability of the assay to detect low level mosaic down to 20%.

OnePGT: Comprehensive insight for every IVF transfer

Agilent OnePGT solution is a universal genome-wide NGS-based solution that integrates preimplantation genetic testing (PGT) for single gene disorders (PGT-M), translocations (PGT-SR) and aneuploidies (PGT-A) in a single workflow with verified automated calling.

OnePGT is developed to help fertility specialists and laboratories achieve comprehensive insights to guide embryo ranking. This all-in-one solution enables labs to concurrently test for three PGT applications using a single biopsy sample.





1. Genome-wide NGS
2. Comprehensive automatic calling
3. Single, universal workflow
4. Verified on clinical samples
5. Embedded QC metrics
6. On-boarding program

Figure 2. OnePGT can be used to determine the genetic profile of an embryo with regard to an inherited single gene disorder (PGT-M) or translocation (PGT-SR) as well as chromosomal copy number aberrations (PGT-A) using a single optimized NGS workflow.

Advantages

Comprehensive insights

- Facilitates multiple requests on same biopsy
- Complete report to improve cycle management

Easy

- Eliminates test development
- One workflow for PGT-M/SR/A
- Automated calling, including segmentals

Reliable

- Verified on clinical samples
- Embedded QC metrics
- Scalable and flexible

Fast implementation

- Optimized workflow
- Proven performance
- Onboarding program

Comprehensive insights to facilitate embryo ranking and detection of monogenic disorders

Two technologies – Comprehensive preimplantation genetic testing

Agilent is the only commercial manufacturer offering two reliable technologies (CGH and NGS) for universal genome-wide comprehensive preimplantation genetic testing. We offer a complete solution with reagents and software for both CGH and NGS workflows, including sample preparation, quality control and data analysis.

Both technologies include the same DNA amplification protocol, based on the QIAGEN REPLI-g kit MDA technology. This protocol gives you flexibility to collect your embryo sample, perform Multiple Displacement Amplification (MDA), and then choose between the CGH or NGS workflow based on your needs.

Sample collection
(Day 3 to day 5)

Benefits of MDA

Non PCR based amplification	CN information is retained
Optimized Φ29 enzyme	Strong strand displacement activity & high fidelity DNA synthesis
Optimized alkaline incubation	Very low DNA fragmentation, longer fragments
Single cell buffer system	Secondary structures resolved for easier amplification
Average product length 10 Kb	Minimum bias in genome coverage

Highlights of MDA

REPLI-g Single Cell kit

CGH

Data analysis

Wash & scan

Hybridization

Labeling

- Results in 8 h
- Resolution down to less than 2 Mb
- Cost-effective (start with as few as 6 samples/run)

NGS

NGS library prep

NGS

Automated data analysis

- Flexible genome-wide NGS-based solution with onboarding program
- Universal workflow for all PGT applications
- Comprehensive automated calling verified on clinical samples

GenetiSure Pre-Screen kit ordering information

Product number	Product	Description
G9500A	GenetiSure Pre-Screen Complete kit 8x60K	Array and reagents to analyze 42 samples and 6 controls
G9501A	GenetiSure Pre-Screen Complete kit 4x180K	Array and reagents to analyze 32 samples and 12 controls
G9502A	GenetiSure Pre-Screen Amplification & Labeling kit	Amplification and labeling reagents to process 48 samples (samples and controls)
G5963A	GenetiSure Pre-Screen Array kit 8x60K	3 slides – 48 samples
G5962A	GenetiSure Pre-Screen Array kit 4x180K	3 slides – 24 samples
G5972A	GenetiSure Pre-Screen kit 8x60K - X/Y	3 slides – 48 samples
G5973A	GenetiSure Pre-Screen kit 8x60K - X/Y	3 slides – 24 samples

Product number	Product
5190-4240	SureTag Complete DNA Labeling kit† (including Agilent M/F Reference, 100 rxn 8x, 50 rxn 4x)
5190-3393	Human Cot-1 DNA
Low 5188-5220 High 5188-5380	Agilent Oligo aCGH Hybridization kit to process 25 (low) or 100 (high) slides
5188-5226	Agilent Oligo aCGH Wash Buffer 1 and 2 Set
G2534-60018	Hybridization Chamber Gasket Slide kit 8-pack, 3 gasket slides
G2534-60011	Hybridization Chamber Gasket Slide kit 4-pack, 5 gasket slides

† The SureTag Complete DNA Labeling kit includes 50 SureTag purification columns. Use p/n 5190-3391 to purchase additional columns needed to process 8x microarray.

Product number	Product
G2534A	Hybridization chamber, stainless
G2545A	Hybridization oven
G2530-60029	Hybridization oven rotator rack
G4900DA	SureScan microarray scanner*

** G5761AA SureScan Dx available in select countries.*

Agilent CytoGenomics software v5.0 license (free)
Download: https://www.agilent.com/en/download-agilent-cytogenomics-software

OnePGT ordering information

Product	Description	Part number
Agilent OnePGT solution	Includes reagents for genome-wide amplification and library preparation, software and cloud services	G9426AA
Agilent OnePGT solution without REPLI-g	Includes reagents for library preparation, software and cloud services	G9427AA
Agilent OnePGT HOT workshop	Hands-On-Training workshop in Agilent facility to train customers on OnePGT workflow and data analysis	R2600A

[1] *Steptoe PC & Edwards RG 1978 Birth after the reimplantation of a human embryo. Lancet 2 366. (https://doi.org/10.1016/S0140-6736(78)92957- 4)*
[2] *A review of the modern approach to in vitro fertilization Susan M. Maxwell, MD *, James A. Grifo, MD, PhD*
[3] *Chromosomal analysis in IVF: just how useful is it? Darren K Griffin$_1$ and Cagri Ogur$_{2,3}$ $_1$School of Biosciences, Centre for Interdisciplinary Studies of Reproduction, University of Kent, Canterbury, UK, $_2$Bahceci Genetic Diagnosis Center, İstanbul, Turkey and $_3$Department of Bioengineering, Yildiz Technical University, İstanbul, Turkey*
[4] *Goldman KN., J Genet Couns. 2016 Dec;25(6):1327-1337;*
[5] *Rechitsky S., Fertil Steril. 2015 Feb;103(2):503-12*

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This information is subject to change without notice.

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