

Preimplantation Genetic Diagnosis (PGD) **Practitioner Information**

CHROMOSOMAL MICROARRAY (CMA) PGD FOR ANEUPLOIDY SCREENING

Chromosomal microarray (CMA) testing is designed for full and balanced coverage of all chromosomal regions and has a much higher genomic coverage and resolution for detecting chromosomal defects compared to standard FISH testing. This is ideal for cases of repeated pregnancy loss, advanced reproductive age, and multiple IVF failures despite the presence of morphologically good embryos. CMA testing is performed following whole genome amplification using the 24Sure™ array kit (BlueGnome Ltd., Cambridge, UK). This array is composed of over 5,000 bacterial artificial chromosome (BAC) DNA probes spanning all 24 chromosomes with an average resolution of 10Mb. This array is designed to identify whole chromosome aneuploidy in samples obtained from embryo biopsy. Results are interpreted using BlueFuse Multi data analysis software, which compares embryo samples to a normal reference sample optimized for preimplantation genetic diagnosis testing. Testing is available for Day 3 single cell blastomeres and fresh transfer and for Day 5/6 trophectoderm biopsy and frozen transfer. Results are available the next day following sample receipt.

PGD FOR GENDER TESTING

For gender determination, CMA or FISH tests [XY/XX or XY/XX,21) are available.

CHROMOSOMAL MICROARRAY (CMA) PGD FOR PATIENTS WITH CHROMOSOME REARRANGEMENTS

Recent research studies indicate enhanced pregnancies rates with CMA when compared to FISH testing. No pre-test workup is needed but advanced notification of the rearrangement along with submission of a laboratory report documenting the rearrangement is required. The array has expanded genomic coverage and resolution for detecting small unbalanced chromosome segments. The microarray test is performed following whole genome amplification using the 24Sure+™ array kit (BlueGnome Ltd., Cambridge, UK). This array has a backbone screening resolution of approximately 0.5Mb and approximately 0.25Mb in the pericentromeric and subtelomeric regions. This array is designed to identify whole chromosome aneuploidy and large unbalanced rearrangements in samples obtained from embryo biopsy. Results are interpreted using BlueFuse Multi data analysis software, which compares embryo samples to a normal reference sample optimized for preimplantation genetic diagnosis testing. Testing is available for Day 3 single cell blastomeres and fresh transfer and for Day 5/6 trophectoderm biopsy and frozen transfer. Results are available the next day following sample receipt.

SINGLE GENE DISORDER TESTING

GIVF has expanded our team of molecular geneticists devoted to single gene disorder PGD. Recent advances in medical genetics have now identified the molecular basis for over 3,000 Mendelian diseases and for most of these disorders a genetic test can be designed. Our test design takes into account the affected gene and specific mutation as well as flanking polymorphic markers for added diagnostic accuracy. Single gene disorder testing can also be coupled with CMA analysis for chromosome aneuploidy detection. Due to the complexity of genetic testing for these disorders, patients should have a full consultation with a medical geneticist to determine if this option would fit their family's needs. Prior to the PGD cycle, the laboratory must be notified in order to develop a patient-specific test for each disorder. In addition to testing for the inherited disorder, aneuploidy screening can also be performed on the same sample.

ACCURACY AND TEST LIMITATIONS

The DNA probes used in this array do not target known copy number variation (CNV) or genetic diseases. This test cannot detect all types of polyploidy, balanced chromosome abnormalities such as translocations or inversions, low-level mosaicism, microdeletions, microduplications, point mutations, uniparental disomy, or genomic imbalances that are not represented in the array. It is estimated that about 5% of the time the biopsied cell(s) fails to get into the buffer solution or the DNA is degraded to the point where it cannot be analyzed. As performed at Genetics & IVF Institute (GIVF), the technical accuracy of CMA and FISH testing is about 98% for whole chromosome aneuploidy and unbalanced rearrangements. The technical accuracy for single gene disorder and aneuploidy testing is also about 98%. Genetic counseling is recommended to discuss test results with patients. The use of intracytoplasmic sperm injection (ICSI) is recommended to reduce the risk of misdiagnosis due to contamination by sperm DNA. Preimplantation genetic diagnosis (PGD) is not intended to replace prenatal testing. These tests are validated and their performance is determined by GIVF.