

ARRAY CGH (aCGH) – All Chromosome Analysis



In an effort to provide you with the best testing and service available, we would like to notify you that array CGH (aCGH) is available to offer to patients pursuing preimplantation genetic screening (PGS). Array CGH allows Reprogenetics to screen all chromosomes in 24-30 hours of sample receipt. We are providing the details below to assist you in discussing aCGH with patients.

Case Preparation

Unlike SNP arrays, aCGH does not require testing of the couple or the couple's parents prior to the IVF cycle. Array CGH can therefore be scheduled just a few days prior to embryo biopsy and there are no set-up fees.

Biopsy Stage - Day 3 or Day 5 biopsy?

Based on the studies of Wells and Schoolcraft (ASRM 2008, 2009) regarding standard CGH, there may be advantages of blastocyst stage trophectoderm biopsy. However, aCGH can be applied to either a single cell from a day 3 embryo or trophectoderm tissue from day 5 or day 6 blastocyst. Day 3 blastomere biopsy facilitates result availability for a fresh day 5 replacement and eliminates the necessity of cryopreservation which is necessary when trophectoderm tissue is biopsied. We recommend that you only biopsy good quality embryos that you would consider for embryo replacement. Poor quality and arrested embryos will have high failure rates as a result of DNA degradation. An experienced embryologist can be sent to your center to perform Day 3 or Day 5 biopsy. In addition we provide biopsy and cell preparation training in collaboration with Tyho-Galileo Research Laboratories.

Sample Preparation

A single cell or a tissue sample from each embryo is loaded into PCR tubes; this is similar to sample preparation for molecular testing methods used in single gene disorder PGD. While the quality of the results are technician dependent, some embryologists find it easier to load PCR tubes than perform the cell fixation required for PGS utilizing FISH. If your embryology staff needs assistance or training we can provide this service.

Cost

As of August 1, 2009, the published fee is a \$2,500 base fee plus \$200 per embryo analyzed.

Reprogenetics is offering a discounted fee for the first 1000 samples received. All cycles must be paid by October 15, 2009 and completed by December 1, 2009. If a Reprogenetics embryologist is utilized to perform the biopsy and cell preparation for aCGH we will also discount this service. To utilize these discounted cycles, please notify Client Services at 973-436-5013 or clientservices@reprogenetics.com.

Our Experience

To date we have completed more than 300 cases of standard CGH and aCGH. The CGH and aCGH techniques are very similar and detect the same types of abnormalities. The major difference is that aCGH is faster and compatible with day 3 biopsy and day 5 replacement. At ASRM 2009 we will present the validation results for aCGH.

Abnormality Ascertainment

Aneuploidy

Our current estimate, based on our validation experiments, is that aCGH will detect approximately 20% more abnormalities on average than 12 probe FISH.

Structural abnormalities

Array CGH can theoretically detect deletions and duplications of small pieces of DNA. However, testing for such has not been fully validated. Presently, we are using aCGH to detect only whole chromosome numerical abnormalities (aneuploidy).

Polyploidy

There are three types of polyploid embryos:

1. Those developing from 3PN zygotes (i.e. polyspermic or through retention of second polar body). These embryos are detected by embryologists and discarded, and therefore would not be biopsied or tested.
2. Those produced by diploid sperm or diploid eggs. Diploid eggs are giant eggs and should be discarded; they should not be available for biopsy or testing. One-percent of sperm are diploid. As these are megaloccephalic, they are discriminated against when doing ICSI; they can however fertilize eggs in conventional IVF. Array CGH cannot detect this type of polyploidy.
3. Polyploidy arising post-meiotically. About 5% of 2PN zygotes (embryos starting with two homologous chromosomes) may become polyploid through endoreduplication and cytokinesis failure. The majority of these polyploid embryos will have other chromosome abnormalities detectable by aCGH. Only 1% of these polyploid cells derived from 2PN zygotes are purely polyploid (no other abnormalities). These cannot be detected by aCGH or SNP arrays. Embryos that are of poor quality, small, arrested or dysmorphic are likely to have degraded DNA. Testing of these embryos can give a chaotic profile.