February Update on Reprogenetics All Chromosome Analysis

In an effort to keep you informed on our progress with full chromosome analysis, we would like to update you on our fees and experience.

Fees for Clinic Billing as of February 1, 2010

$3,250 for up to 12 embryos
$200 per additional embryo analyzed over 12
No Cancellation fee

Important Note: Test can be ordered on the same day of the biopsy since there is no need to analyze the DNA of the parents beforehand. Please make sure to review all protocols and have an orientation with our team prior to your first case.

Full Chromosome Analysis by aCGH

Array CGH allows Reprogenetics to screen all 24 chromosomes in 24-30 hours of sample receipt. The array has many probes for each chromosome and enables simultaneous screening of many locations on each chromosome. Array CGH also detects all mitotic and meiotic abnormalities present in one cell or tissue sample. Unlike SNP arrays, aCGH does not require testing of the couple or the couple's parents prior to the IVF cycle. In addition, there are no set up fees associated with aCGH.

Our Experience – Clinical Results and Ongoing Validations

To date we have completed more than 400 procedures of standard CGH and 100 of 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. The frequency of single cells producing no results is 2%.

Reprogenetics routinely reanalyzes embryos that are not replaced for continual validation and assesment of tecnical error rates. We utilize FISH (Fluorsecent In Situ Hybridization) for reanalysis to ensure that the potential shortcomings of aCGH would be detected by a different technique. Using this approach the current error rate is 5%, which is the minimum expected on day 3 biopsies due to mosaicism. Error rates from the reanalysis of day 5 biopsies may be lower.

Day 3 Blastomere or Day 5 Trophectoderm Biopsy and Sample Preparation

Array CGH can be applied to polar bodies, a single cell from a day 3 embryo or trophectoderm tissue from day 5 or day 6 blastocysts. The single cell or 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. When needed, an experienced embryologist can be sent to your center to perform polar body, Day 3, or trophectoderm biopsy and/or sample preparation. In addition we can provide biopsy and cell preparation training in collaboration with Tyho-Galileo Research Laboratories.

Some patients prefer not to delay embryo transfers to accomodate analysis on trophectoderm tissue. Results are available for a fresh day 5 replacement when performing a biopsy on polar bodies or Day 3 embryos. In all cases,we recommend that only replacement quality embryos are slated for biopsy. The biopsy of poor quality embryos will increase the cost of the test and likely not provide results, as the quality of DNA will typically not amplify properly.

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Several recent studies support analysis on day 5 or 6 trophectoderm tissue for patients that are willing to cryopreserve embryos and delay the embryo transfer. At ASRM 2009 Wells et al (O-268) presented that standard CGH combined with day 5 trophetoderm biopsy and vitrification provided 80% delivery rates and 66% implantation rates (compared to 60% and 28%, respectively). Based on these studies, there may be advantages of trophectoderm biopsy for some cases. Even though trophectoderm biopsy presently requires cryopreservation, our experience is that more than 99% of embryos survive the trophectoderm biopsy and vitrification process. Additionaly, at ASRM 2009 Schlenker et al. (O-243) presented that CGH and SNP arrays provided the same impresive results since both analyze 24 chromosomes.

Simultaneous Detection of Single Gene Defects and Aneuploidy

Reprogenetics has partnered with Professor Alan Handyside to exclusively provide Karyomapping™ in the US. Karyomapping™ provides simultaneous analysis of single gene defects and 24 chromosome aneuploidy analysis using SNP arrays.

Abnormalities Ascertainment

Aneuploidy: Our current estimate, based on our validation experiments, is that aCGH will detect approximately 50% more abnormalities than 12 probe FISH and 20% more abnormal embryos (abnormalities tend to concentrate on the same embryos). Being quantitative, CGH and aCGH can detect all aneuploidies. In contrast, some SNP approaches relying on qualitative assesment of aneuploidy may miss trisomies of mitotic origin or originating from meiosis II aneuploidy without crossing-over. Out of 91,073 embryos analyzed by FISH with 9-12 probes at Reprogenetics in the last 11 years, 26,624 were complex abnormal (2 or more abnormal chromosomes), and of those 4,029 had only trisomies. From previous studies (Munne et al. 2002) we know that about 25% of mosaic embryos are also meiotically aneuploid, so we can estimate about 3.3% of these embryos to be missed as abnormal by qualitative SNP array methods.

Polyploidy: CGH and aCGH cannot detect polyploidy, but this would result in only 0.2% missed abnormalities. Reprogenetics extensive experience indicates that 7.7% (7,030/91,070) of tested embryos were polyploid or haploid, but of those, the majority had other abnormalities detectable by CGH and aCGH, and only 1.8% (1,641) were homogeneously polyploid or haploid. In addition, of those, only 13% were of good morphology and the others were arrested or dysmorphic. Thus, only 0.2% were homogeneously polyploid or haploid with good morphology and repleaceable, and likely to be misdiagnosed.

Structural abnormalities: Array CGH can detect deletions and duplications of small pieces of DNA. However, testing for such has not yet been fully validated. Presently, we are using aCGH to detect only whole chromosome numerical abnormalities (aneuploidy) and we expect to offer aCGH for translocations soon. However we expect that FISH will remain the less expensive method to perform PGD for translocations and structural abnormalities.