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Preimplantation Genetic Screening in the age of 23-chromosome evaluation Why FISH is no longer an acceptable technology?

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Abstract

Preimplantation Genetic Screening (PGS) has been used for some time with fluorescence in situ hybridization (FISH) technology with marginal success. Newer modalities capable of evaluating all 23 pairs of chromosomes are now available for PGS and are superior to PGS with FISH.

Keywords: PGS; FISH; "23 chromosome" microarrays

Capsule: Modalities using 23 chromosome evaluation are superior to 9-12 probe FISH in performing PGS.

In Vitro Fertilization (IVF) is a technology that has transformed the field of infertility medicine. Literally millions of individuals who could never have conceived naturally are now parents thanks to this technology. As the technology has matured, other applications that utilize IVF have emerged. One such technology is preimplantation genetic screening (PGS). The traditional modality for performing PGS has been through fluorescence in situ hybridization (FISH) of 9-12 chromosomes. Given newer technologies able to simultaneously evaluate all 23 pairs of chromosomes, however, FISH is no longer an optimal technology in the context of PGS.

Spontaneous miscarriages in human pregnancies are documented to be associated with chromosomal aneuploidy [1,2]. PGS was introduced to minimize aneuploidy in certain patient populations. PGS is a procedure in which single cells can be biopsied from cultured early embryos and tested for their chromosome complement prior to uterine transfer [3]. PGS is generally performed on polar bodies or Day-3 biopsies of 1 or 2 totipotent blastomere cells [3]. The traditional modality for evaluating the chromosomal makeup of these cells has been by fluorescence in situ hybridization (FISH) of 9-12 chromosomes [3].

Despite initial excitement generated by the potential of PGS by FISH on Day-3 blastomeres to improve pregnancy outcome, randomized controlled trials have failed to demonstrate a significant clinical benefit [4-6]. Consequently, major professional societies have discouraged its use [4-6]. Potential reasons for the lack of predictive value from karyotyping Day-3 blastomeres using FISH could be damage caused to the developing embryo during biopsy, testing of only a subset of chromosomes, or the presence of mosaicism within the Day-3 cleaving embryo. Indeed, studies have documented mosaicism rates of between 17%-50% in Day-3 preimplantation embryos [7,8].

For several years, comparative genomic hybridization (CGH) on metaphase chromosomes, real-time polymerase chain reaction (PCR), or microarray platforms using single nucleotide polymorphism (SNP) or CGH have been utilized to evaluate all 23 pairs of chromosomes simultaneously [9-12]. These techniques are capable of identifying only euploid embryos for transfer. This has resulted in significant improvement in clinical pregnancy rates when compared to 9-12 chromosome FISH methods [3,12-15]. Recently, the aforementioned technologies have been employed to evaluate Day-5 blastocyst TE cells without disturbing the ICM, with promising results [3,12-15].

The superior results obtained through PGS using simultaneous evaluation of all 23 pairs of chromosomes are not surprising. Indeed, many cases of aneuploidy exist on chromosomes simply not evaluated by 9-12 probe FISH. The use of FISH PGS in the current environment should be questioned. 23 Chromosome evaluation for PGS seems, based on intuition and the evidence, to be superior to FISH and should become the new standard in PGS testing in almost all clinical cases.

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