

# Morphological biomarkers for aneuploidy and embryo quality

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## ABSTRACT

The selection of chromosomally normal and viable embryos for transfer is crucial for couples' success rate in IVF treatment. The selection is commonly based on morphological evaluations which do not incorporate a chromosomal evaluation of the embryos. In addition, a chromosomal evaluation is time consuming and most IVF centres do not have the possibility to include this analysis in their IVF programme. A combination of morphological parameters and the chromosome content in embryos seems, therefore, to be a scientific challenge in terms of determining the extent to which certain morphological characteristics correlate with chromosome abnormalities.

The thesis includes a methodological part of introducing a new method for characterizing chromosome aberrations in single blastomere nuclei. In addition, it includes an analytical part of using this method to enumerate chromosomes and to determine the correlation between selected morphological characteristics and the chromosome content.

The methodological part involved a FISH set-up based on the peptide nucleic acid (PNA) probes in combination with competitive displacement which enabled us to perform five consecutive FISH cycles on a single nucleus almost without loss of signals. It should therefore, in principle, be possible to enumerate all chromosomes in a single blastomere. The method is a good alternative to PGD with DNA probes especially in aneuploidy screening where the number of chromosomes analyzed is correlated with success rate.

The analytical part included morphological evaluation of different parameters in fresh and frozen-thawed embryos. All parameters were related to the chromosome content classified for 13 chromosomes using the PNA probes and competitive displacement.

The combined morphological and chromosomal evaluation of the fresh embryos showed the number of nuclei in the blastomeres was strongly correlated to aneuploidy. In contrast to the binucleated fresh embryos the binucleated frozen-thawed embryos include several binucleated blastomeres for which the chromosome content was normal. These findings suggest that different mechanisms might be involved in the multinucleated condition in fresh and frozen-thawed embryos. The combination of morphological and chromosomal evaluation including several chromosomes is important and will lead to an increase in the selection of the most viable and chromosomally normal embryos.