# Improvements in embryonic preimplantation genetic screening techniques

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A Short Comparative Genomic Hybridisation (CGH) method has been developed to carry out preimplantation genetic screening (PGS) by analysing all chromosomes and transferring selected embryos to the recipient uterus in the same in vitro fertilisation cycle. This eliminates the need to freeze them.

The technique has been applied to the screening of chromosomal anomalies in cases of advanced maternal age, recurrent miscarriages or repeated implantation failures.

Short-CGH achieved, as part of a PGS programme, the pregnancy of a woman whose partner is carrier of two chromosomal translocations, a very rare case which commonly causes infertility, miscarriages or physical and/or mental malformations in the newborn.

The technique developed is the result of a doctoral thesis by Mariona Rius, member of the research team belonging to the Cell Biology and Medical Genetics Unit of the Department of Cell Biology, Physiology and Immunology at Universitat Autònoma de Barcelona (UAB). The project received funding from the Spanish Health Research Fund and was carried out under the Eugin Research Chair - UAB.

Preimplantation Genetic Screening (PGS), through in vitro fertilisation (IVF) treatment, allows selecting healthy embryos with no anomalies which are later transferred to the recipient uterus, thus increasing chances of implantation.

Presently, the methodology most frequently used is the analysis of one cell of the embryo the third day of its development through fluorescent in situ hybridisation (FISH), which routinely analyses only nine of the 24 different types of existing chromosomes. The selected embryos are transferred to the recipient uterus four days after beginning, in the same IVF cycle. The implantation rate using this technique is 14%.

An alternative technique, used in few centres in the world, is Comparative Genomic Hybridisation (CGH) which allows for a comprehensive cytogenetic analysis of all chromosomes to check for anomalies of full chromosomes (aneuploidy) or only of parts. This methodology, however, is highly complex and needs more time than the IVF cycle to yield results (72 hours). Therefore, the embryos analysed must be cryopreserved and transferred in a subsequent IVF cycle, which could affect their viability. The implantation rate using this technique ranges from 40 to 70 %.

In her doctoral thesis, Mariona Rius developed a short-CGH method which allows the full karyotype study of the cell (blastomere) with a very reduced hybridisation period (from 72 to 12 hours). Using only one procedure and with the same efficacy, short-CGH permits scientists to detect not only aberrations in the number of chromosomes (numerical), but also alterations in chromosome fragments (structural). Thus the embryos selected – chromosomally normal – can be transferred within the same IVF cycle.

The technique was applied clinically in the screening of chromosomal abnormalities in cases of advanced maternal age, recurrent miscarriages or repeated implantation failures. The implantation rate of transferred embryos reached 60%. It was also used, for the first time in a PGS programme, to obtain a successful pregnancy of a woman whose partner is carrier of two chromosomal translocations, one reciprocal and the other Robertsonian. This is a very rare case which frequently causes

infertility, miscarriages or physical and/or mental malformations in the newborn. Of the 16 embryos analysed in three consecutive IVF cycles, the only embryo without chromosomal imbalances was transferred to the woman, who is currently in the third trimester of her pregnancy.

Given the results obtained in this first research phase, researchers are confident that the short-CGH method will be applied in more PGS tests.

**More information:** Doctoral thesis articles:

M. Rius, A. Obradors, G. Daina, L. Ramos, A. Pujol, O. Martínez-Passarell, L. Marquès, M. Oliver-Bonet, J. Benet, J. Navarro.
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Fertility and Sterility (in press).

Rius M, Daina G, Obradors A, Ramos L, Velilla E, Fernández S, Martínez-Passarell O, Benet J, Navarro J.
"Comprehensive embryo analysis of advanced maternal age-related aneuploidies and mosaicism by short comparative genomic hybridization."
Fertility and Sterility 95(1):413-6 (2011).

Rius M, Obradors A, Daina G, Cuzzi J, Marquès L, Calderón G, Velilla E, Martínez-Passarell O, Oliver-Bonet M, Benet J, Navarro J.
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Human Reproduction 25(7):1824-35 (2010).