

Multicenter prospective study of concordance between embryo cell-free DNA and trophoctoderm biopsies from 1,301 human blastocysts

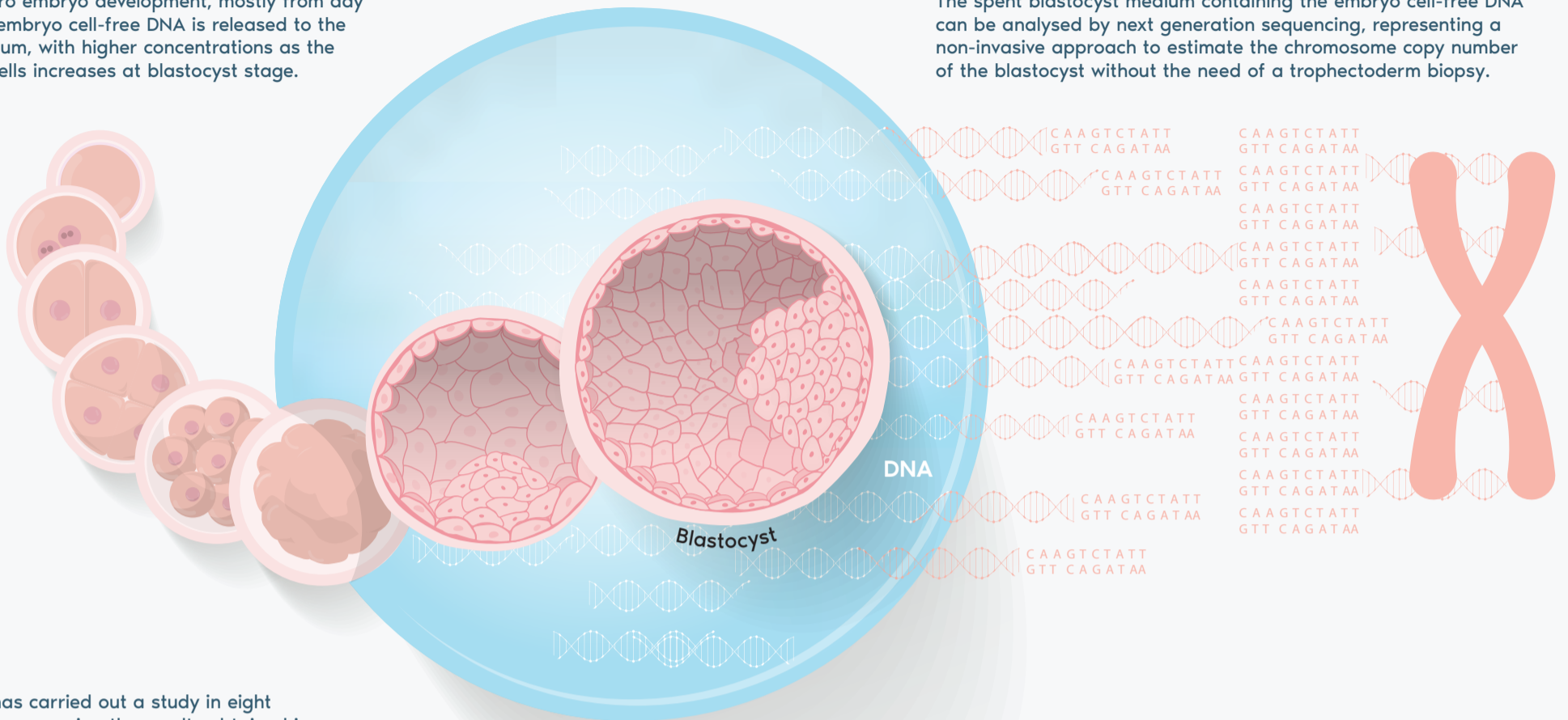
The recent identification of embryo cell-free DNA in the spent blastocyst media opened a new era of possibilities for non-invasive embryo aneuploidy testing in assisted reproductive technologies.

1

During in vitro embryo development, mostly from day 4 to day 6, embryo cell-free DNA is released to the culture medium, with higher concentrations as the number of cells increases at blastocyst stage.

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The spent blastocyst medium containing the embryo cell-free DNA can be analysed by next generation sequencing, representing a non-invasive approach to estimate the chromosome copy number of the blastocyst without the need of a trophoctoderm biopsy.

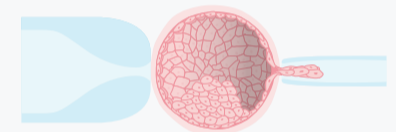


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Igenomix has carried out a study in eight IVF centres comparing the results obtained in embryo cell-free DNA from 1,301 spent blastocyst media and the corresponding trophoctoderm biopsies in couples undergoing preimplantation genetic testing for aneuploidy PGT-A.

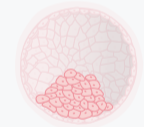


The study was designed with two main objectives:



Trophoctoderm DNA

To evaluate the concordance and reproducibility of testing embryo cell-free DNA versus trophoctoderm DNA obtained from the same embryo in a large sample of 1,301 day 6 and day 7 human blastocysts,



Inner cell mass DNA

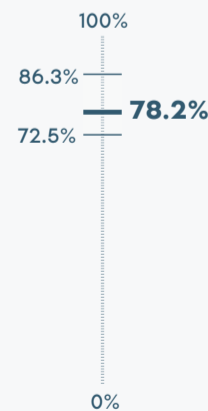
and to assess the concordance rates with the inner cell mass of the blastocyst in a subset of 81 aneuploid blastocysts donated for research.

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Concordance rates of 1,301 embryo cell-free DNA and trophoctoderm DNA

The results of the non-invasive analysis of embryo cell-free DNA from spent blastocyst medium demonstrated a high concordance rate with the trophoctoderm biopsy results.

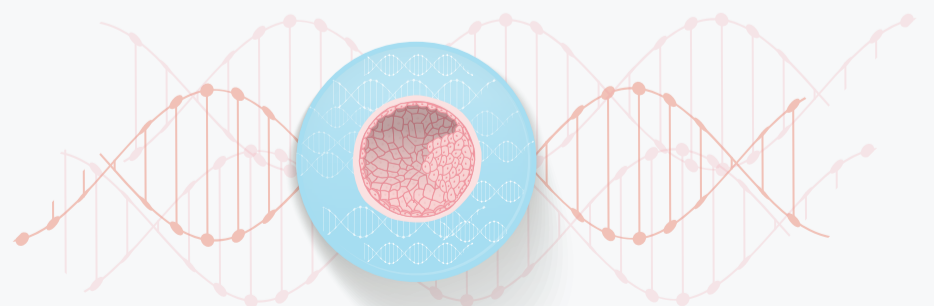
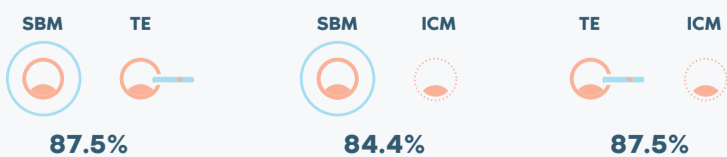
	Center 1	Center 2	Center 3	Center 4	Center 5	Center 6	Center 7	Center 8	TOTAL
Concordance	75.6	77.1	81.8	86.3	84.2	85.0	72.5	77.0	78.2
Sensitivity	80.5	84.8	88.2	86.7	91.3	76.7	76.5	78.9	81.7
Specificity	69.9	72.7	85.2	87.5	80.0	93.3	64.7	78.1	77.4



The concordance rate was on average 78.2% ranging from 72.5% to 86.3% in different centers, without significant differences among centers related to culture conditions or blastocyst quality.

Concordance rates with inner cell mass of 81 blastocysts

In addition, in a subgroup of 81 blastocysts, the comparison of the inner cell mass with the embryo cell-free DNA and the trophoctoderm biopsies has shown similar concordance rates, 84.4% and 87.5% respectively.



We can conclude that this non-invasive approach could avoid embryo biopsies and reduce costs, while democratizing its use and increasing accessibility for a wider population of patients. **Nevertheless, more studies are needed to understand the origin of the embryo cell-free DNA and the mechanisms involved.**