

# The type of chromosomal alteration that is detected in aneuploid embryos is related to maternal age

Ortiz, J.A., PhD<sup>b</sup>, Lledo, B. PhD<sup>b</sup>, Morales, R. PhD<sup>b</sup>, Ochando I.<sup>a</sup>, Llacer, J. MD<sup>a</sup> and Bernabeu, R. MD PhD<sup>a,b</sup>.  
a: Reproductive Medicine, Instituto Bernabeu, Alicante, Spain. b: Instituto Bernabeu Biotech, Alicante, Spain.

## INTRODUCTION

The aneuploidy is one of the major factors affecting the embryo outcome. The rate of embryonic aneuploidy increases with maternal age. Discarding affected embryos, after a Comprehensive Chromosome Screening (CCS) by array Comparative Genomic Hybridization (aCGH) give us an implantation rate that does not depend on maternal age. Thus, CCS corrects the effect of maternal age in embryo implantation.

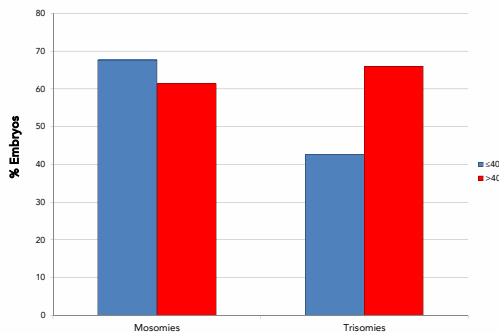


Fig. 1. Percentage of embryos with trisomies-monosomies and depending on maternal age

## METHODS

This is a retrospective observational study performed between January 2013 and January 2015 at Instituto Bernabeu. Alicante. Spain. The study includes the data analysis of 585 blastocysts with conclusive CCS results obtained from 197 patients. We included 518 blastocysts from patients aged ≤40 years old and 67 over 40 years old. Whole chromosome imbalances by array-CGH in trophoctoderm cells from D5 embryos were detected. Array-CGH analysis were performed using Agilent SurePrint G3 8x60K. The association between variables was analyzed using Logistic Regression and Chi-square Test.

## RESULTS

41.4% of the embryos analyzed were aneuploids of which 65.3% had monosomy and 46.2% trisomy. There was no significant difference in the number of monosomies in aneuploid blastocysts between patients ≤40 years old (67.7 %) and >40 years old (61.4%)  $p=0.422$ . On the other hand, trisomies increase in a statistically significant way between both age groups (42.6 % vs 65.9% ;  $p=0.005$ ).

After the individual analysis of chromosome, it was observed that most do not modify their levels of alteration with increasing maternal age, only on chromosomes 2, 11, 13, 15, 16, 21 and 22 a statistically significant increase was observed. Surprisingly, on chromosome 3, the opposite effect is observed, this chromosome appears altered less frequently in aneuploid embryos with higher maternal age.

Chromosome	% Aneuploid Embryos			
	Maternal Age			
	<30 (n=251)	30-35 (n=132)	35-40 (n=96)	>40 (n=102)
2	2.4	0	4.2	5.9*
3	5.2	0.8	1	0*
11	2	2.3	1	10.8*
13	2.4	1.5	3.1	8.8*
15	2	0.8	3.1	11.8*
16	5.6	3.8	10.4	12.7*
21	0.8	2.3	4.2	8.8*
22	0.8	6.8	10.4	17.6*

Table 1. Percentage of embryos with chromosome aneuploidy and depending on maternal age.

\*  $\chi^2$  Test ( $p<0.05$ ).

## CONCLUSIONS

This investigation reveals that all types of embryonic aneuploidies are not equiprobables. Trisomies are less frequent than monosomies but trisomies augment with increasing maternal age mainly on chromosomes 2, 11, 13, 15, 16, 21 and 22. The study is limited by its retrospective nature. A higher sample size or a prospective randomized design should be used in future studies to corroborate the current findings.

