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THE NATURE OF SEX CHROMOSOME ANEUPLOIDIES IN HUMAN BLASTOCYSTS

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OBJECTIVE:

Post-implantation studies suggest that certain sex chromosome aneuploidies (SCA) do not result from maternal meiotic non-disjunction and hence may have different characteristics than autosomal trisomies. Our aim was to characterize SCA in the human blastocyst in terms of frequency, relationship with female age, and association with day of development.

MATERIALS AND METHODS:

Retrospective analysis of consecutive trophectoderm biopsies performed between August 2015 and March 2022 evaluated with Next Generation Sequencing by a single genetics laboratory. Biopsy results were examined by age of female and day of biopsy using Chi-square goodness-of-fit. The SCA group included all embryos with X, XXX, XYY, and XXY results. Embryos with indeterminate results or segmental abnormalities involving sex chromosomes were excluded.

RESULTS:

A total of 36,841 SCA results were obtained from an analysis of 249,274 embryos (incidence 147.8/1,000 blastocysts). The most frequent SCA was X followed by XXY, XXX, and XYY (145.2, 1.3, 0.7, and 0.6/1,000 blastocysts, respectively). The proportion of X significantly increased with advancing female age ($p<0.001$); however, there was no age association for other SCAs

(Table 1). When excluding embryos with autosomal aneuploidy from the X category, the association differed with a lower proportion in the ≥40 age group (p<0.001). Analogous to autosomal aneuploidies, there was a significantly greater proportion of X blastocysts biopsied on day 6/7 compared to day 5 (p<0.001).

Age group (yrs)	X*	XXX	XXY	XYY	XX/XY* (Euploid)	XX/XY* (Aneuploid)	Ploidy Error[1]	Total
≤30	3,695 (10.9)	31 (0.1)	45 (0.1)	22 (0.1)	21,219 (62.5)	8,509 (25.0)	454 (1.3)	33,975
31-33	6,007 (11.9)	39 (0.1)	68 (0.1)	45 (0.1)	29,623 (58.8)	13,943 (27.7)	644 (1.3)	50,369
34-36	8,875 (14.0)	40 (0.1)	81 (0.1)	33 (0.1)	32,466 (51.4)	20,870 (33.0)	827 (1.3)	63,192
37-39	9,843 (17.0)	41 (0.1)	74 (0.1)	25 (0.0)	22,458 (38.7)	24,776 (42.7)	825 (1.4)	58,042
≥40	7,769 (17.8)	27 (0.1)	64 (0.1)	17 (0.0)	9,611 (22.0)	25,376 (58.1)	832 (1.9)	43,696

* p<0.05 using Chi-square

1. Haploid, triploid, tetraploid embryos

2. Counts (% total for age group)

CONCLUSIONS:

A notable proportion of human embryos carry SCAs at the blastocyst stage, predominantly X. There is an association between X embryos and advancing female age that is not seen with other SCAs. When excluding embryos with autosomal aneuploidies, the relationship between X embryos and age changes, indicating that X embryos without other abnormalities may be less frequent in older women. The higher proportion of X embryos biopsied on day 6/7 suggest delayed embryo development.

IMPACT STATEMENT:

At the human blastocyst stage, there is an association between X embryos and advancing female age that is not evident with other SCAs.

REFERENCES:

N/A