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Time-lapse monitoring: an adjunct tool to select embryos for preimplantation genetic testing

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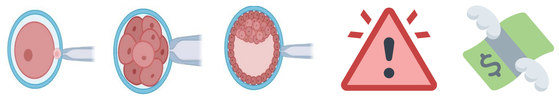
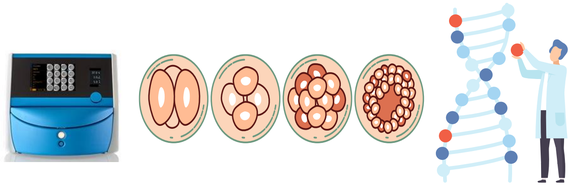
Introduction

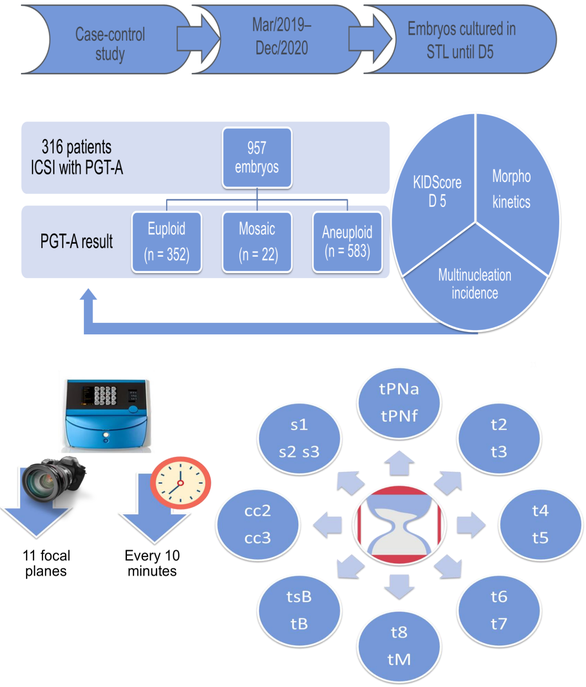
The preimplantation genetic testing (PGT) emerged as an approach to analyse embryos' DNA for determining genetic abnormalities, distinguishing chromosomally normal embryos, considered to have high developmental potential, from their aneuploid siblings. Although shown to be efficient and clinically relevant, the invasive nature of the technique limits its success. Given the challenges associated with invasive embryo biopsy, ongoing studies are now seeking for non-invasive assessments of the embryo DNA.



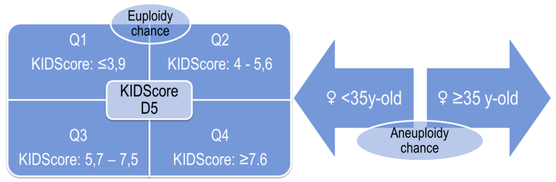
Timelapse imaging (TLI) may allow the identification of morphokinetics events affected by aneuploidy, which could be a powerful tool for improving embryo selection for transfer, without the detrimental effects of embryo biopsy. The objective of this study was to investigate embryo aneuploidy have any impact on embryo morphokinetic events in a time-lapse imaging (TLI) culture system.



Methods



Generalized linear models (GzLM) followed by Bonferroni post hoc were used to compare timing of specific events in euploid, aneuploid, and mosaic embryos.



Results

Morphokinetics (h)	Euploid embryos (n=352)	Aneuploid embryos (n=583)			Mosaic embryos (n=22)			p-value
	Mean ± SE	Mean ± SE	B	95% CI	Mean ± SE	B	95% CI	
tPNf	22.50±0.157[a]	24.01±0.16[b]	0.997	0.48-1.51	24.81±0.79[a,b]	1.867	0.251-3.482	< 0.001
t2	24.99±0.0[a]	26.8±0.172[b]	1.2	0.69-1.80	27.23±0.86[a,b]	1.68	-0.70-3.41	< 0.001
t3	36.14±0.0[a]	38.08±0.20[b]	1.14	0.47-1.80	39.42±1.02[a,b]	2.47	0.40-4.54	< 0.001
t4	37.25±0.22[a]	39.52±0.21[b]	1.55	0.85-2.24	39.75±1.07[a,b]	1.78	-0.39-3.9	< 0.001
t6	50.78±000[a]	53.20±0.29[b]	1.42	0.450-2.39	55.26±1.49[a,b]	3.48	0.45-6.51	< 0.001
t7	52.56±0.35[a]	53.65±0.42[b]	1.65	0.616-2.68	57.00±1.59[a,b]	1.65	0.11-6.58	< 0.001
t8	55.43±0.51[a]	58.87±0.39[b]	2.22	0.95-3.49	60.4±1.94[a,b]	3.78	-0.17-7.73	< 0.001
tM	88.05±0.63[a]	88.0±0.48[b]	1.03	0.534-2.596	90.6±2.5[a,b]	5.56	0.50-10.62	0.024
tsB	96.68±0.69[a]	91.34±3.32[b]	2.23	0.53-3.92	98.90±0.52[a,b]	-5.33	-11.98-1.30	0.03
tB	105.31±0.00[a]	109.64±0.477[b]	3.54	2.00-5.07	110.59±2.44[a,b]	4.49	0.45-9.44	<0.001
s2	1.0±0.12[a]	1.3±0.09[b]	0.40	0.07-0.73	1.43±0.10[a,b]	-0.69	-1.71-0.33	0.022
s3	7.0±0.38[a]	8.37±0.30[b]	1.28	0.30-2.26	9.35±1.50[a,b]	2.26	-0.79-5.32	0.006
KIDScore	6.52±0.13[a]	5.54±0.10[b]	-0.97	-1.30 - -0.64	4.62±0.49[a,b]	-1.89	-2.89 - -0.88	< 0.001

Table 1. Results from GzLM followed by Bonferroni post hoc for embryonic morphokinetics among aneuploid, euploid and mosaic embryos.

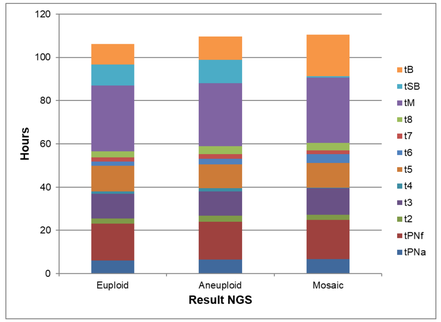


Figure 1. A comparison of the cumulative morphokinetic development of euploid, aneuploid and mosaic embryos.

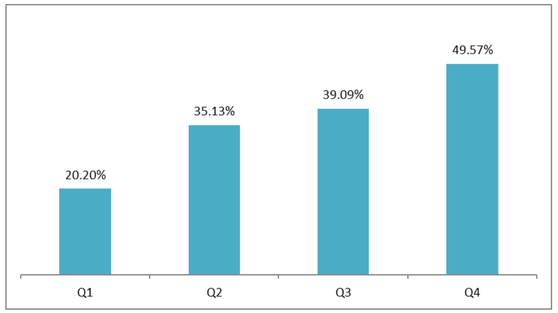


Figure 2. Distribution of the percentage of euploid embryos in KIDScore D5 categories: Q1 ≤3.9, Q2, between 4 and 5.6, Q3 between 5.7 and 7.5, and Q4 ≥7.6.

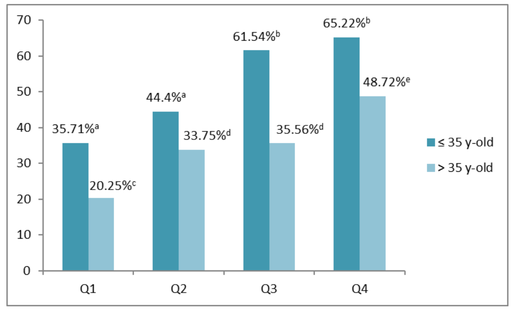


Figure 3. Distribution of the chances of being euploid according to the KIDScore D 5 category: Q1 ≤3.9, Q2 between 4 and 5.6, Q3 between 5.7 and 7.5, and Q4 ≥7.6. a≠b≠c≠d≠e.

Conclusions

Aneuploidy had a significant impact on early and late embryo morphokinetic events. Mosaic and aneuploid embryos behaved similarly in terms of morphokinetics. Our evidence suggests that TLI monitoring may be an adjunct approach to select embryos for PGT, however, cautious investigation is still needed. The mechanism by which embryo aneuploidy may alter the cleavage timing of embryos is undefined, but disruptions of mitosis, cell-cell interactions and blastocyst differentiation are possible candidates.