EXPANSION OF THE *FMR1* CGG REPEAT IN 2789 BIOPSIED EMBRYO SAMPLES UNDERGOING PREIMPLANTATION GENETIC TESTING

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Objective: Determine if CGG repeat expansion in trophectoderm (TE) embryo biopsies is similar to repeat expansion in pre- or postnatal samples

Methods:

- Data from 2789 TE biopsies that underwent PGT-M for *FMR1* from January 2014 – December 2022
- Excluded from final analysis: Embryo samples from patients with premutation/full mutation mosaicism, those with no repeat numbers, and those with X chromosome abnormalities where inheritance of expansion was not clear
- Total number included in analysis: 2413

Results:

Expansion rates for maternal premutation alleles

Maternal allele	Total # of embryo samples	# of embryo samples with		% expanded to FM	Nolin *et al.* 2003	Nolin *et al.* 2015
		Premutation	Full mutation			
55-59	531	237	0	**0**	3.7 (n=27)	0.3 (n=299)
60-69	669	304	11	**3.5**	5.3 (n=113)	4 (n=200)
70-79	417	145	56	**27.3**	31.1 (n=90)	35.5 (n=183)
80-89	232	55	57	**49.1**	57.8 (n=140)	68 (n=138)
90-99	131	2	67	**97.1**	80.1 (n=111)	
100-139	264	0	118	**100**	100 (n=178)	
140-199	55	0	23	**100**	100 (n=19)	
>200	114	0	62			
Total	**2413**	**743**	**394**		N=678	N=820

+ For maternal alleles less than 90 repeats, 25 embryo samples (1.3%) exhibited a contraction to the intermediate or normal range

Expansion rates for maternal intermediate alleles

Maternal allele	Total # of embryo samples	# expanded to PM	% expanded to PM
45-50	179	0	0
51-54	197	36	33.0[S]
Total	**376**	**36**	

[S] All those that expanded to a premutation were from maternal alleles of 54 CGG repeats

Conclusions:

- Data represents larger sample size than in previous publications, but expansion and contraction percentages are similar to those in previous publications
- Ability to distinguish CGG repeat number provides more options and information for embryo transfer decisions
- More research and data required, but expansion data for intermediate alleles questions the benefit of PGT-M for intermediate alleles to reduce risk in the immediately following generation
- Limitation: AGG repeats were not included or assessed in analysis