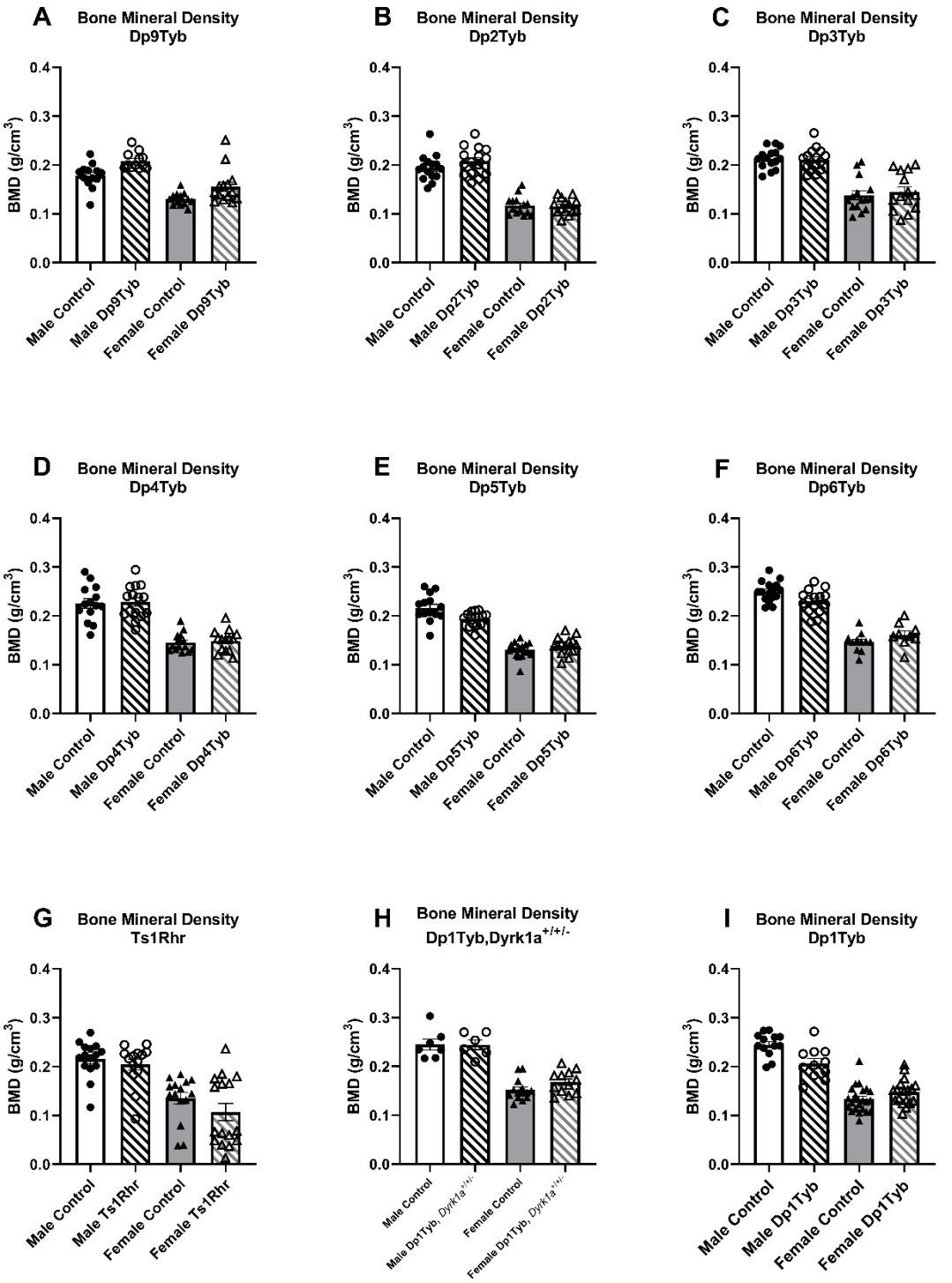

Fig. S1. Bone mineral density measurements in triplicated (Dp) mouse model and control mice. Animal numbers are as listed in Tables 1 and 2. Data are mean ± SEM. Dp1Tyb data comes from Thomas et al. (2020).

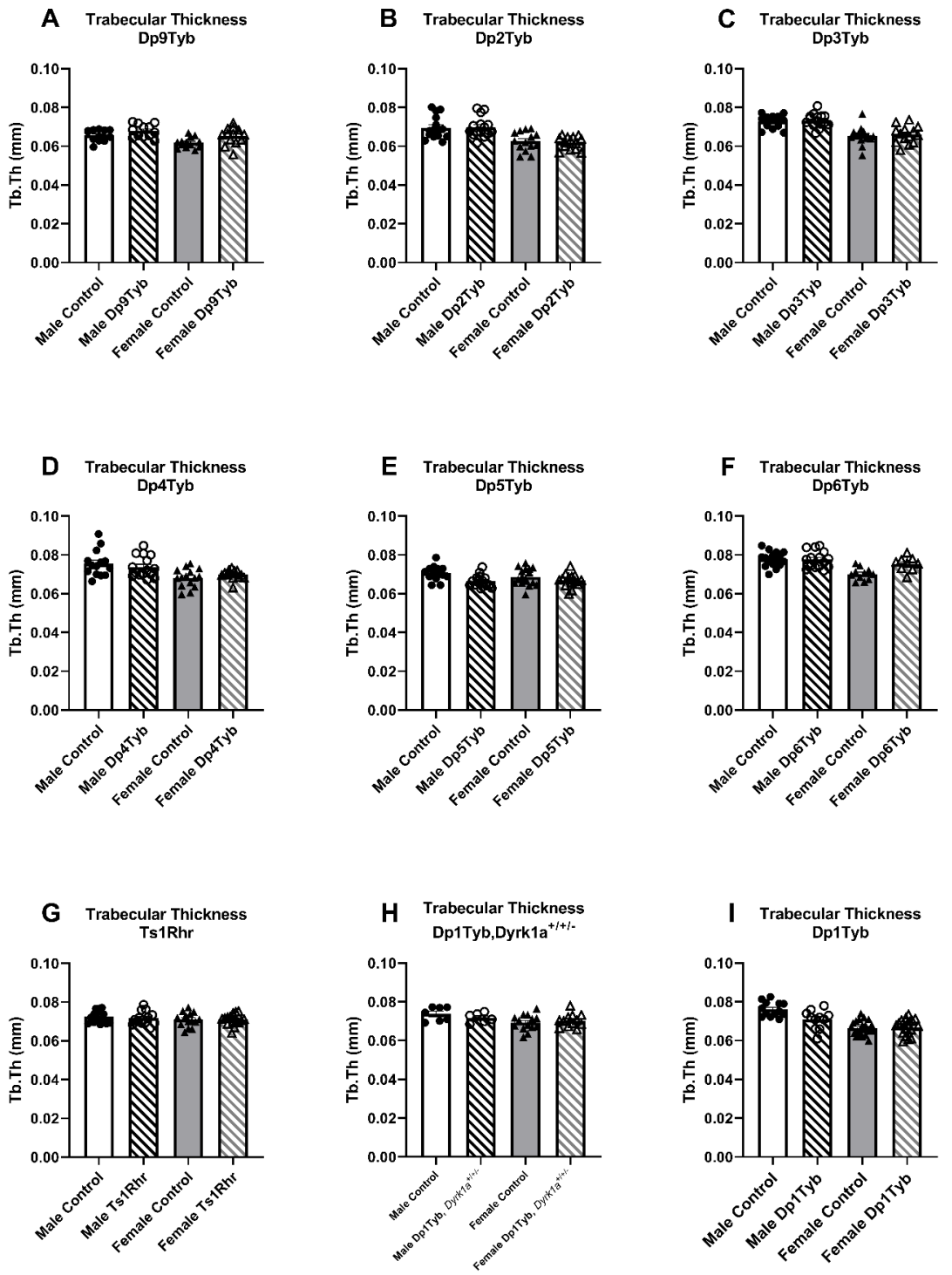

Fig. S2. Trabecular thickness measurements in triplicated (Dp) mouse models and control mice. Animal numbers are as listed in Tables 1 and 2. Data are mean ± SEM. Dp1Tyb data comes from Thomas et al. (2020).

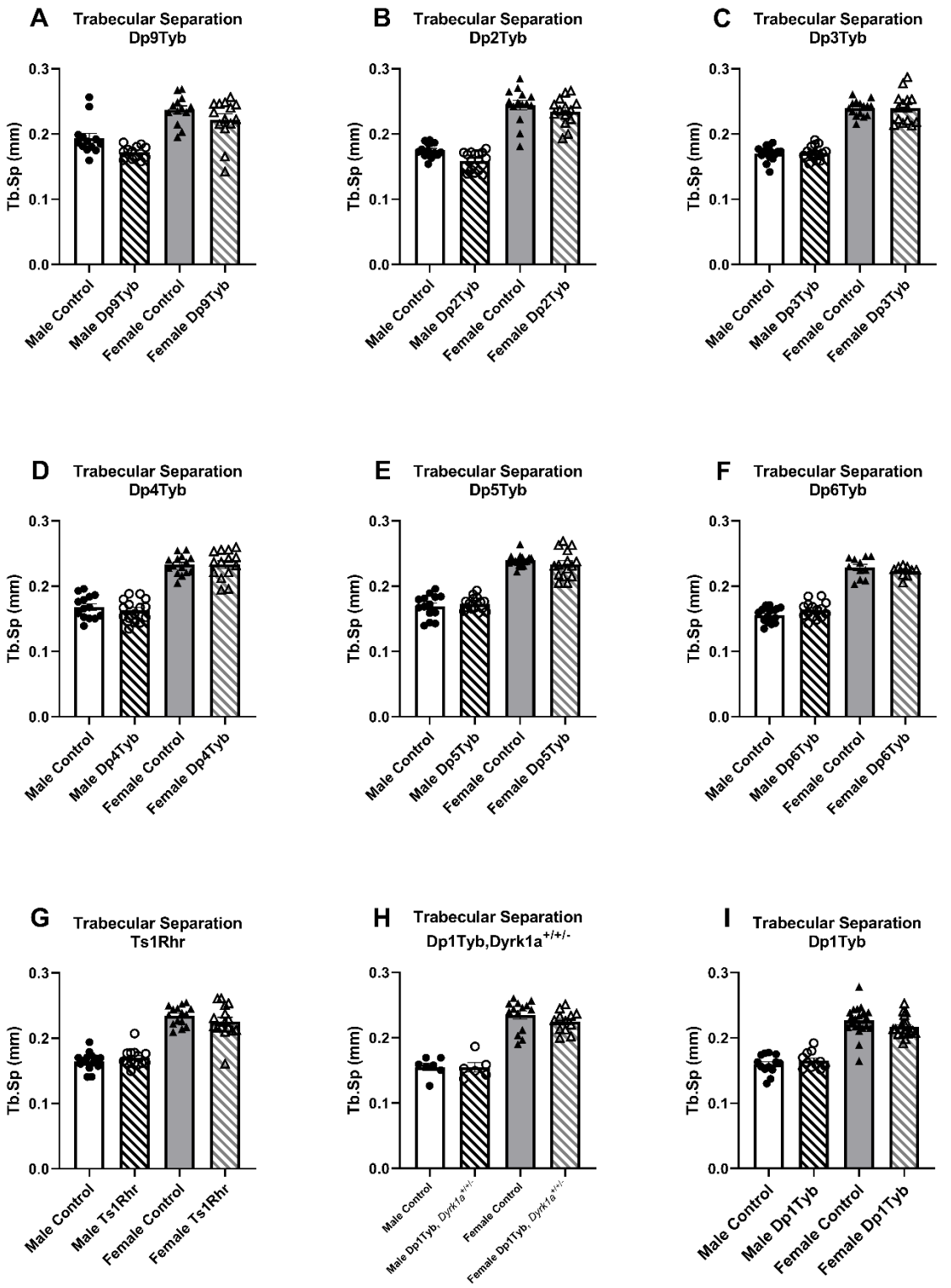

Fig. S3.Trabecular separation measurements in triplicated (Dp) mouse models and control mice. Animal numbers are as listed in Tables 1 and 2. Data are mean ± SEM. Dp1Tyb data comes from Thomas et al. (2020).

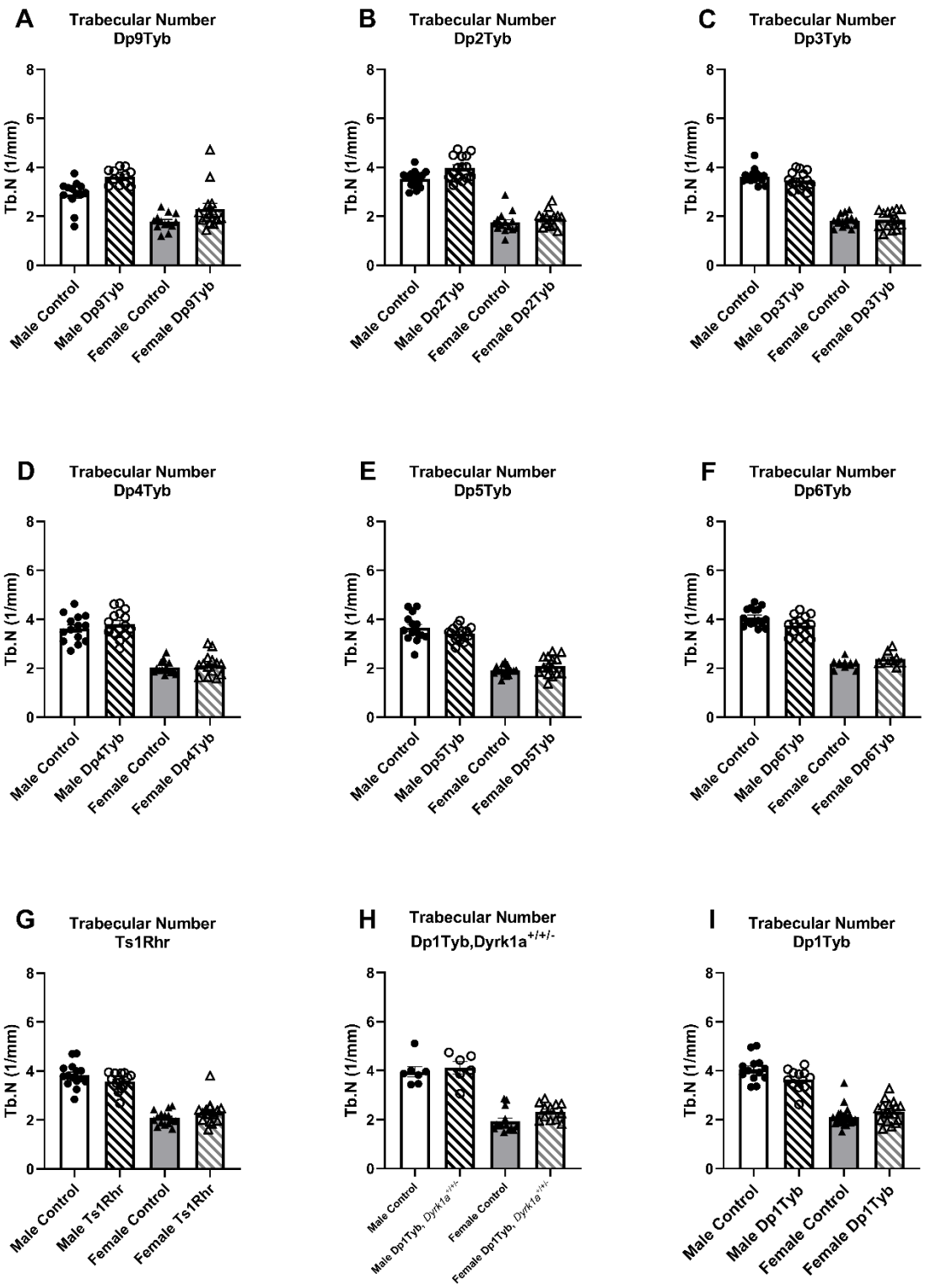

Fig. S4. Trabecular number measurements in triplicated (Dp) mouse models and control mice. Animal numbers are as listed in Tables 1 and 2. Data are mean ± SEM. Dp1Tyb data from Thomas et al. (2020).

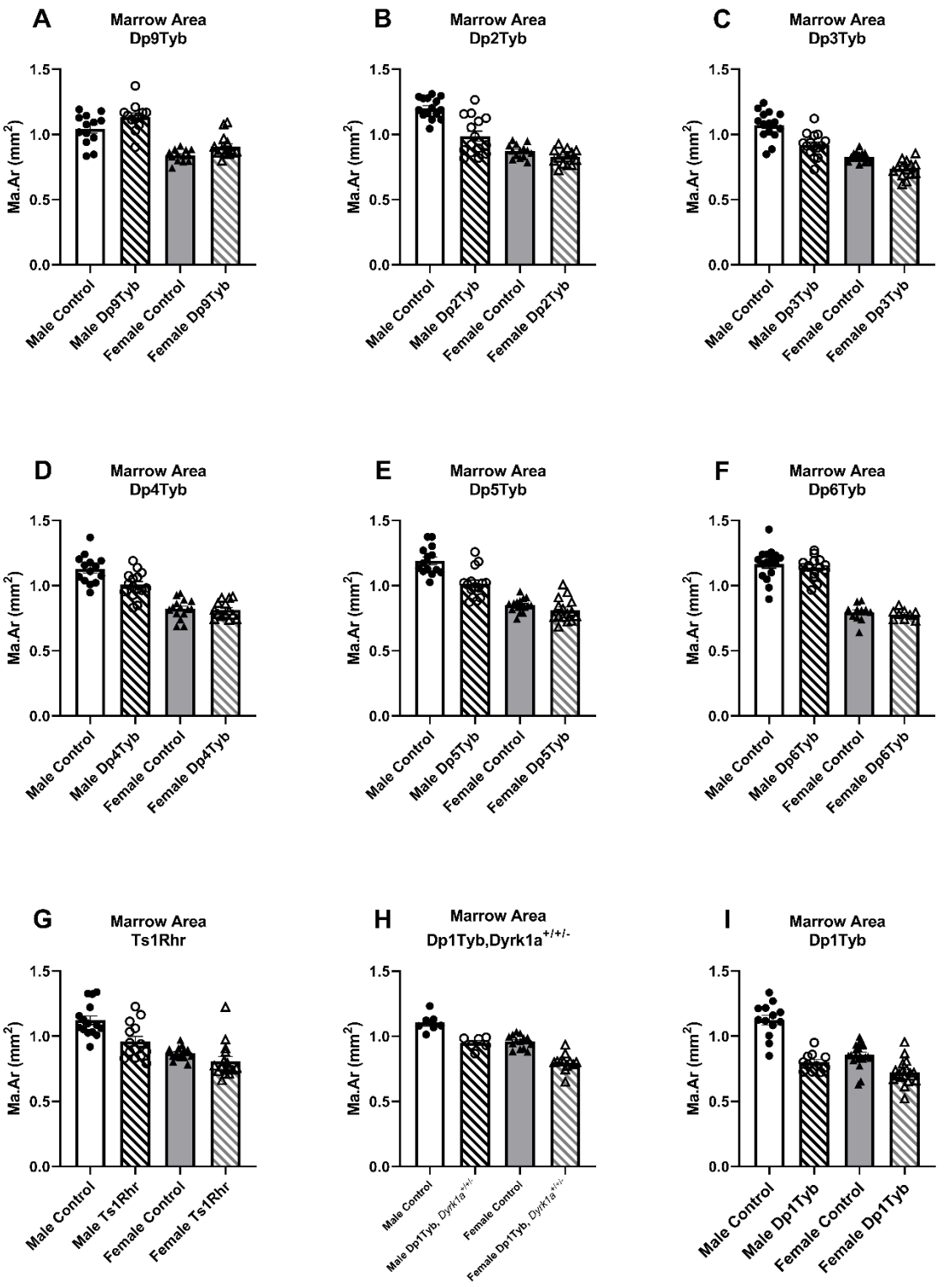

Fig. S5. Marrow area measurements in triplicated (Dp) mouse models and control mice. Animal numbers are as listed in Tables 1 and 2. Data are mean ± SEM. Dp1Tyb data comes from Thomas et al. (2020).

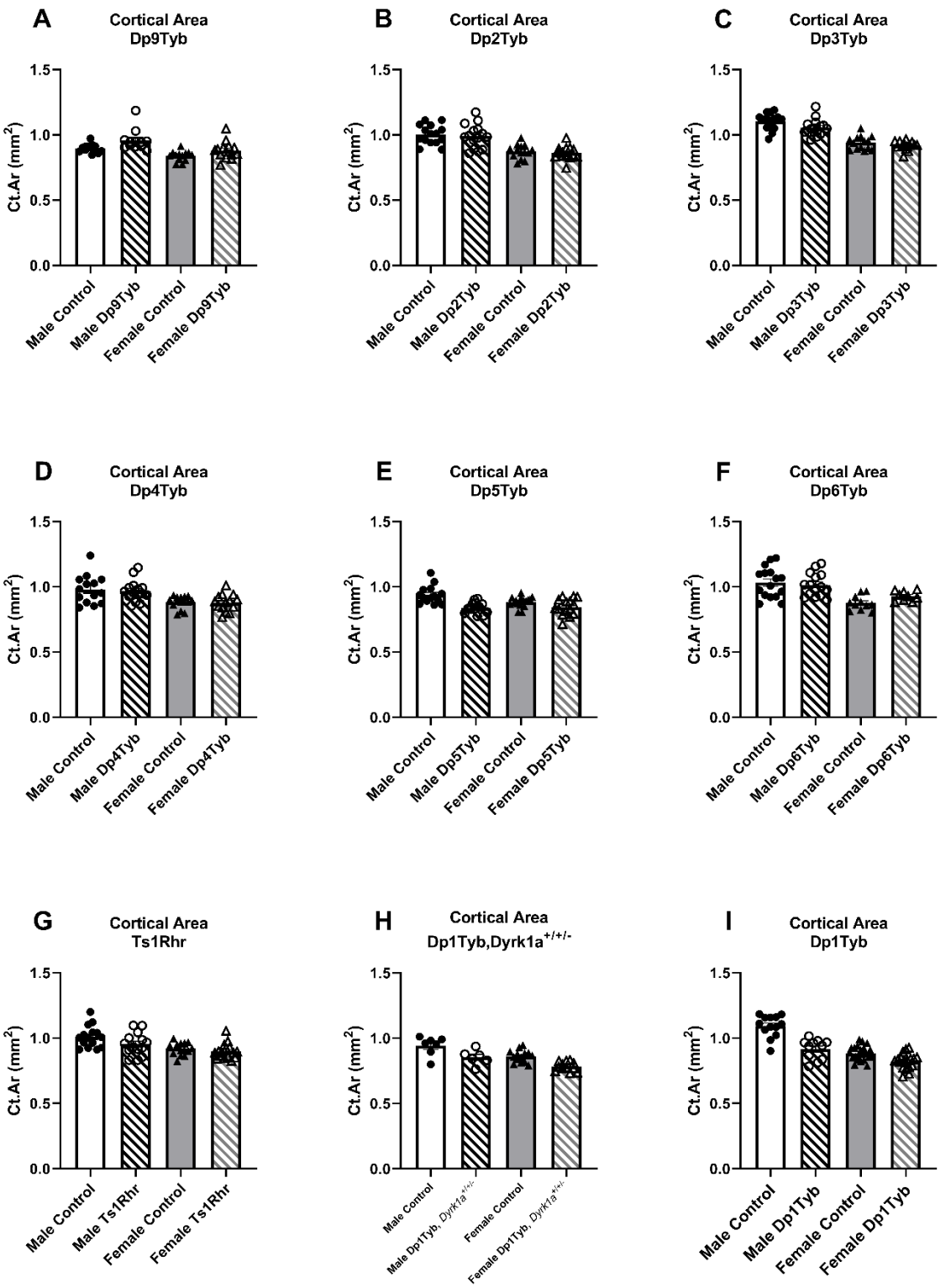

Fig. S6. Cortical area measurements in triplicated (Dp) mouse models and control mice. Animal numbers are as listed in Tables 1 and 2. Data are mean ± SEM. Dp1Tyb data comes from Thomas et al. (2020).

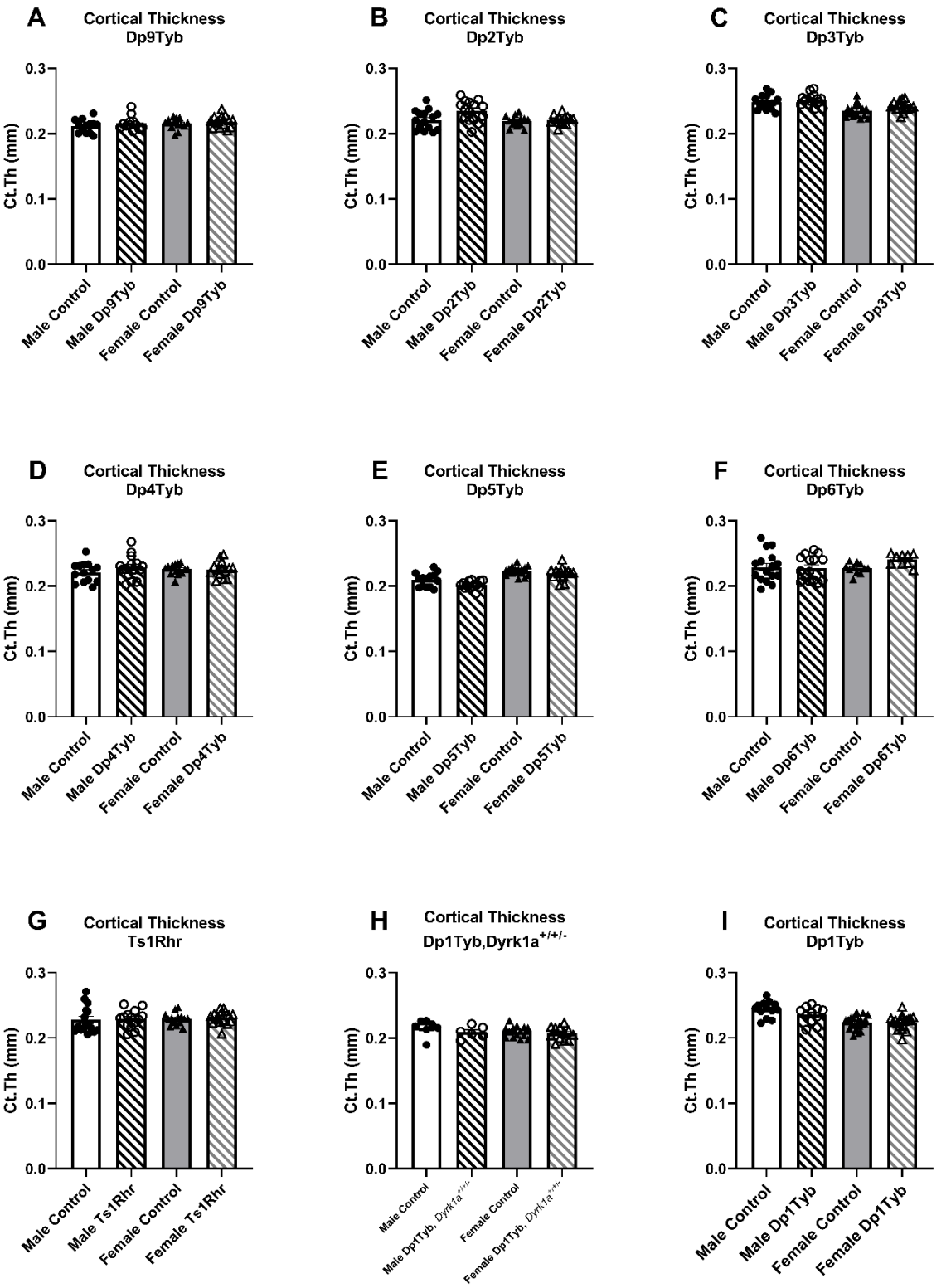

Fig. S7. Cortical thickness measurements in triplicated (Dp) models and control mice. Animal numbers in Tables 2. Data are mean ± SEM. Dp1Tyb data from Thomas et al. (2020).

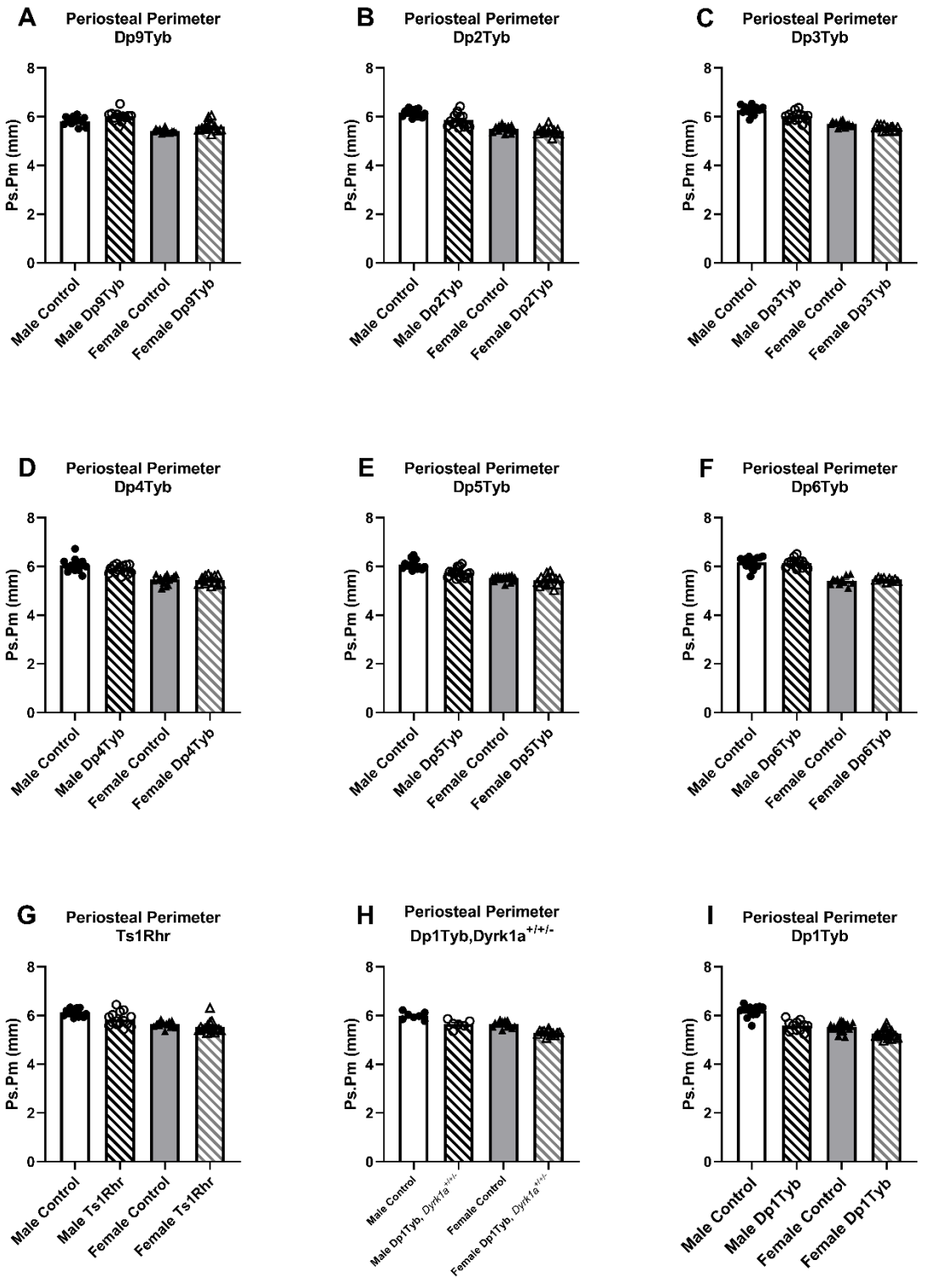

Fig. S8. Periosteal perimeter measurements in triplicated (Dp) mouse models and control mice. Animal numbers are as listed in Tables 1 and 2. Data are mean ± SEM. Dp1Tyb data comes from Thomas et al. (2020).

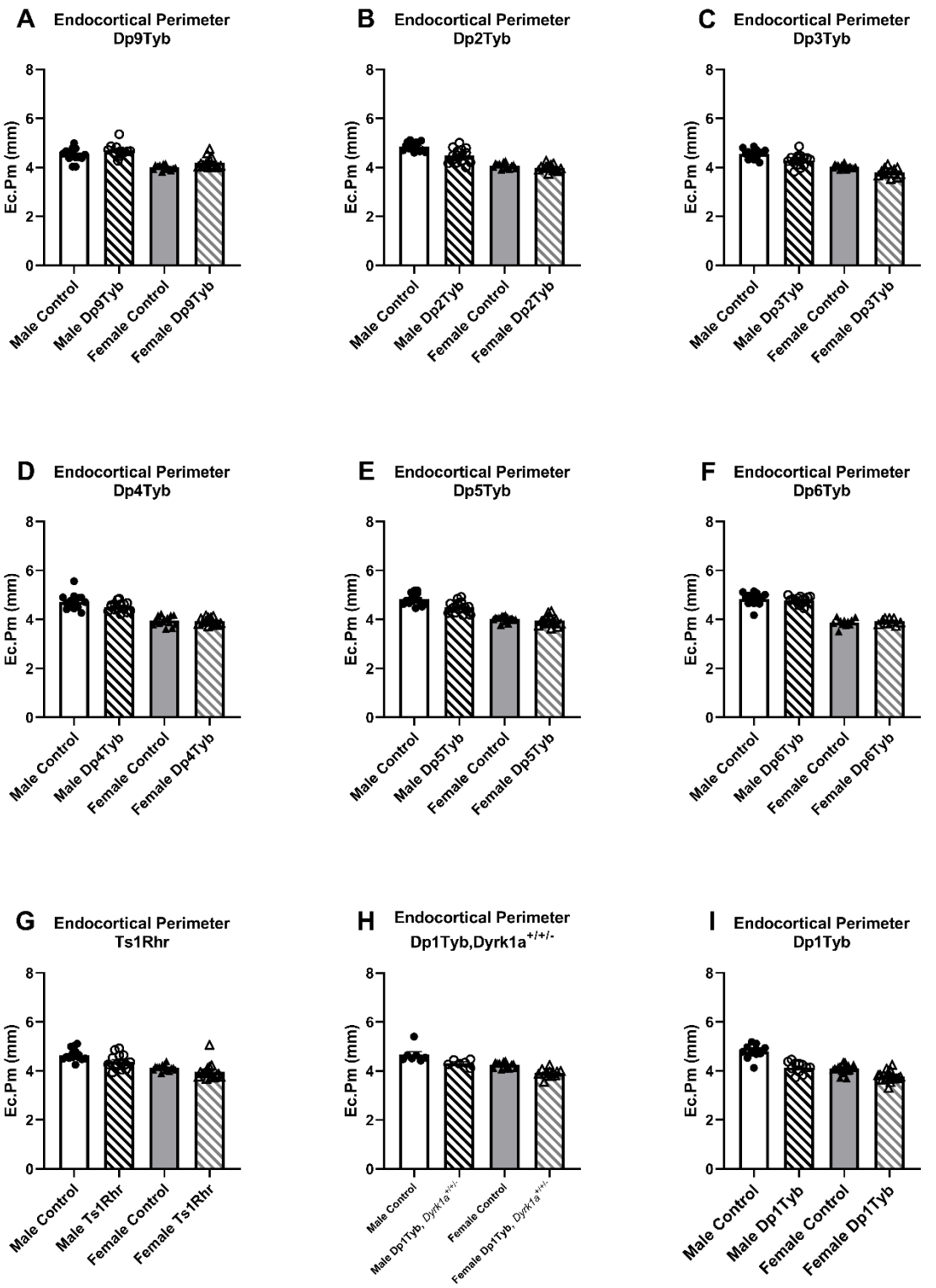

Fig. S9. Endocortical perimeter measurements in triplicated (Dp) mouse models and control mice. Animal numbers are as listed in Tables 1 and 2. Data are mean ± SEM. Dp1Tyb data comes from Thomas et al. (2020).

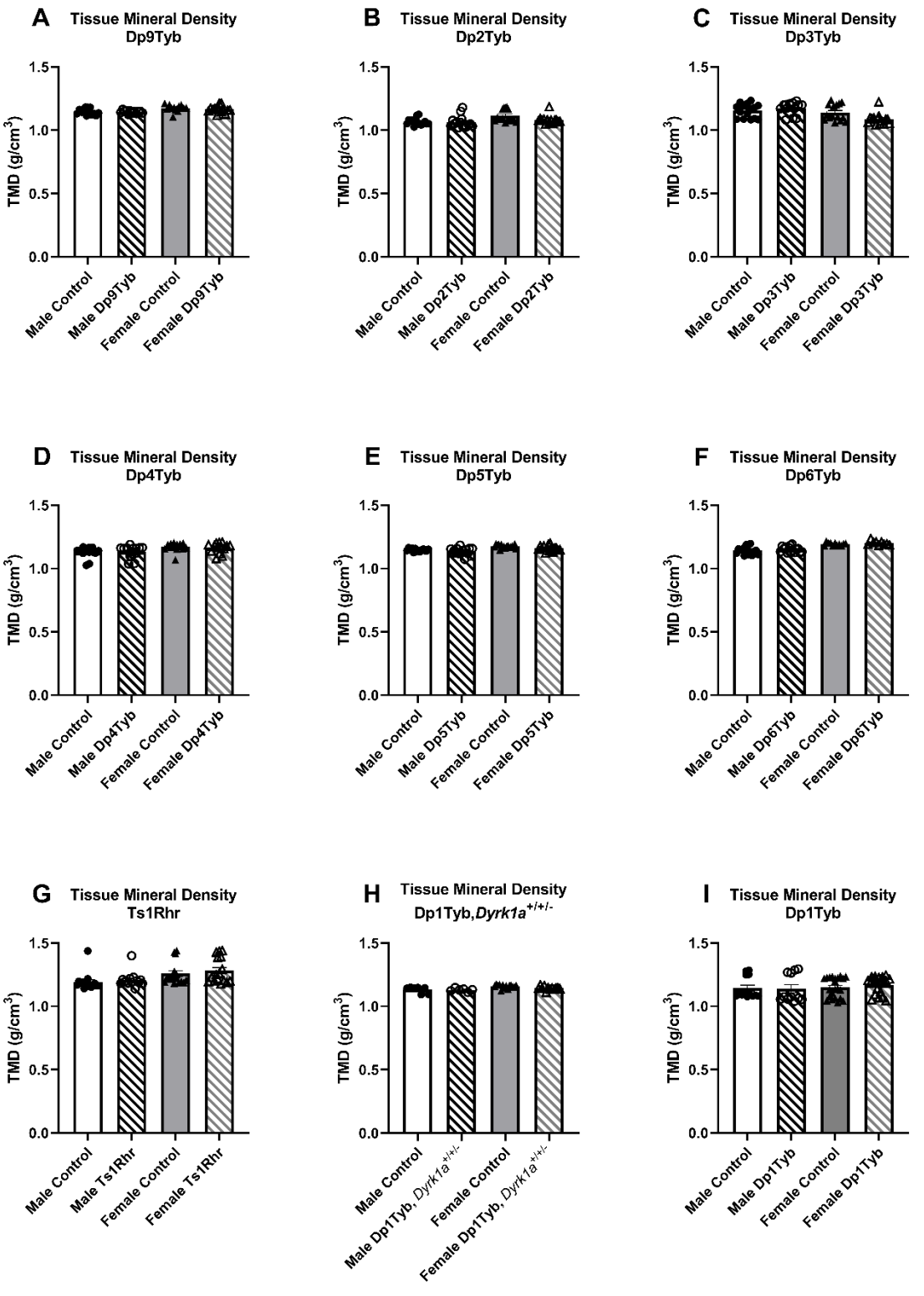

Fig. S10. Tissue mineral density measurements in triplicated (Dp) mouse models and control mice. Animal numbers are as listed in Tables 1 and 2. Data are mean ± SEM. Dp1Tyb data comes from Thomas et al. (2020).

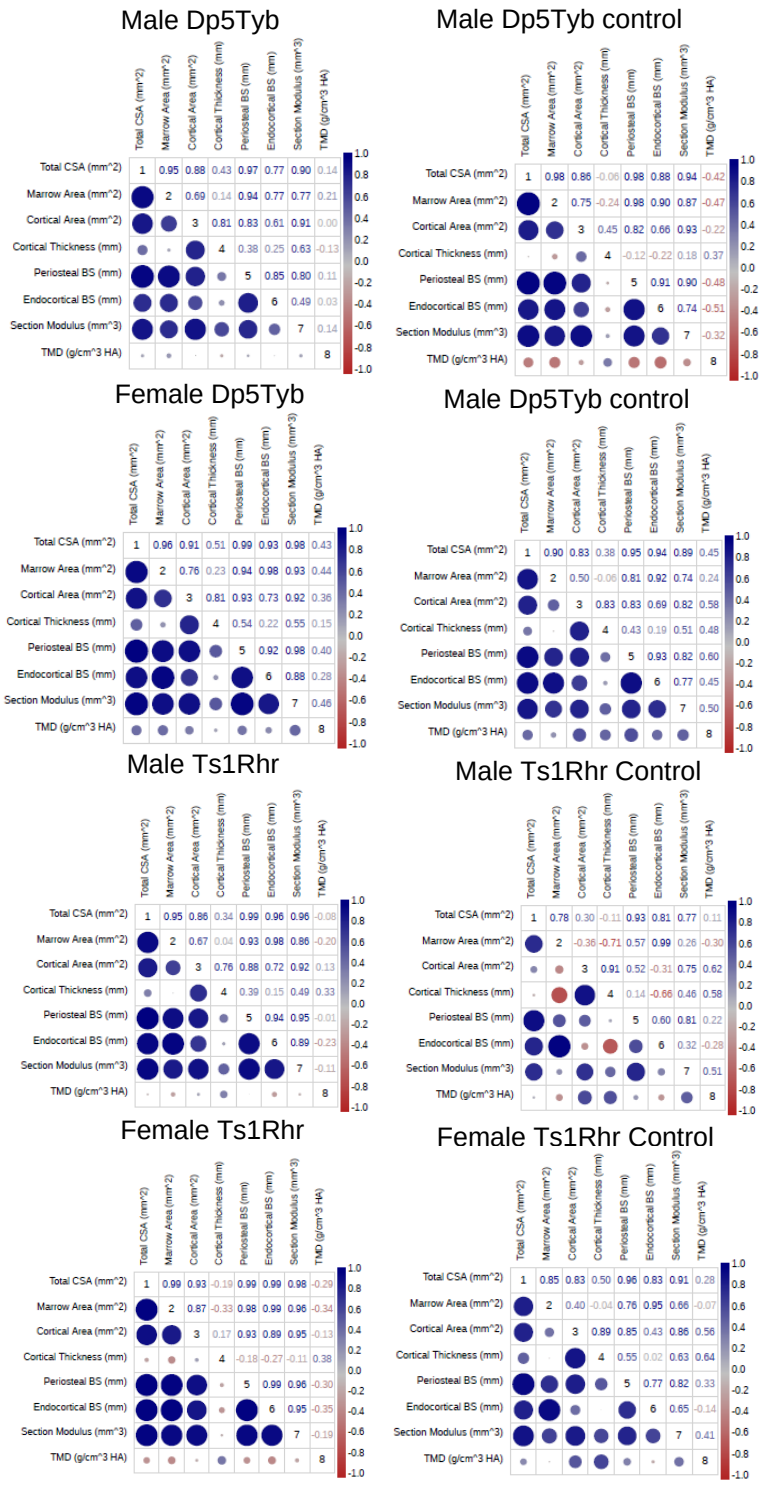

Fig. S11. Correlation between bone parameters of Dp5Tyb and Ts1Rhr male and female mice. Scale of correlation is at the right, with blue as a positive and red as a negative correlation. The larger the circle, the greater the correlation.

Table S1. Results of Tukey's post hoc analysis (multiple comparisons) for two-way ANOVAs. This was only performed if there was a significant (adjusted p value < 0.05) interaction on the two-way ANOVA. [a] logarithmic transformation of data. [b] significant Levene's test (unequal variances) and subsequent analysis indicated no significant difference. M = male, F = female, WT = control/ wildtype, Dp = triplicated Dp/Ts strain

	Dp2Tyb					
	Tt.Ar	***Ma.Ar***	***Ec.Pm***	***Yield Stress***	***Ultimate Stress***	***Resilience***
M WT vs M Dp	0.0003	<0.0001	<0.0001	0.0006	0.0016	0.0158
M WT vs F WT	<0.0001	<0.0001	<0.0001	<0.0001	0.0010	<0.0001
M WT vs F Dp	<0.0001	<0.0001	<0.0001	<0.0001	0.0002	<0.0001
M Dp vs F WT	0.0002	0.0073	<0.0001	0.0185	0.9673	0.0728
M Dp vs F Dp	<0.0001	0.0001	<0.0001	0.0010	0.8413	0.0804
F WT vs F Dp	0.6889	0.5669	0.6048	0.8560	0.9886	0.9988
	Dp3Tyb					
	TMD					
M WT vs M Dp	0.7818					
M WT vs F WT	0.8954					
M WT vs F Dp	0.0093					
M Dp vs F WT	0.3618					
M Dp vs F Dp	0.0005					
F WT vs F Dp	0.0565					
	Dp5Tyb						
	BMD	***BV/TV***	***Tt.Ar***	***Ma.Ar[a]***	***Ct.Ar***	***Ps.Pm***	***Ec.Pm***
M WT vs M Dp	0.0137	0.0283[b]	<0.0001	<0.0001	<0.0001	<0.0001	0.0002
M WT vs F WT	<0.0001	<0.0001	<0.0001	<0.0001	0.0346	<0.0001	<0.0001
M WT vs F Dp	<0.0001	<0.0001	<0.0001	<0.0001	0.0002	<0.0001	<0.0001
M Dp vs F WT	<0.0001	<0.0001	0.0654	<0.0001	0.1077	0.0039	<0.0001
M Dp vs F Dp	<0.0001	<0.0001	0.0011	<0.0001	0.9847	<0.0001	<0.0001
F WT vs F Dp	0.5883	0.8185	0.4037	0.4407	0.2208	0.4387	0.6417
	Dp6Tyb				
	BMD	***BV/TV***	***Tb.Th***	***Tb.N***	***Modulus***
M WT vs M Dp	0.0685	0.0684	0.9995	0.029[b]	0.9836
M WT vs F WT	<0.0001	<0.0001	<0.0001	<0.0001	0.0292
M WT vs F Dp	<0.0001	<0.0001	0.4481	<0.0001	<0.0001
M Dp vs F WT	<0.0001	<0.0001	<0.0001	<0.0001	0.0684
M Dp vs F Dp	<0.0001	<0.0001	0.5147	<0.0001	<0.0001
F WT vs F Dp	0.4520	0.2257	0.0215	0.5337	0.002

Table S2. Percent differences in trabecular skeletal values of male and female triplicated and control littermate mice. Percent change ([([mean of Dp-mean of Control]/mean of Control)*100]) reported in tables. Red indicates significant deficit; blue indicates significant improvement compared to same-sex control littermates (adjusted $p < 0.05$ via two-tail t test). Adjusted p values reported in Table S4.

	MALE								
	Dp1Tyb	**Dp1Tyb, *Dyrk1a*$^{+/+/-}$**	**Dp9Tyb**	**Dp2Tyb**	**Dp3Tyb**	**Ts1Rhr**	**Dp4Tyb**	**Dp5Tyb**	**Dp6Tyb**
BMD	-15.78%	-0.11%	17.03%	6.85%	-0.82%	-5.27%	1.21%	-10.35%	-8.03%
BV/TV	-15.83%	1.30%	29.48%	13.17%	-3.29%	-7.82%	2.71%	-11.63%	-8.72%
Tb.Th	-6.71%	-2.60%	3.64%	0.52%	0.88%	-1.21%	-2.33%	-5.68%	-0.19%
Tb.Sp	3.76%	-0.46%	-11.25%	-9.35%	0.67%	2.94%	-2.87%	2.27%	4.96%
Tb.N	-10.29%	4.16%	25.04%	12.88%	-4.12%	-6.64%	5.14%	-6.36%	-8.35%

	FEMALE								
	Dp1Tyb	**Dp1Tyb, *Dyrk1a*$^{+/+/-}$**	**Dp9Tyb**	**Dp2Tyb**	**Dp3Tyb**	**Ts1Rhr**	**Dp4Tyb**	**Dp5Tyb**	**Dp6Tyb**
BMD	10.84%	10.55%	19.26%	-1.31%	4.99%	-21.00%	2.17%	6.59%	10.09%
BV/TV	11.12%	22.32%	37.26%	6.27%	2.84%	11.34%	6.35%	6.60%	17.36%
Tb.Th	0.73%	1.57%	5.61%	-1.22%	1.02%	-0.13%	2.49%	-2.57%	7.41%
Tb.Sp	-4.37%	-4.14%	-6.29%	-4.00%	-0.004%	-3.80%	0.09%	-2.46%	-2.50%
Tb.N	9.97%	20.15%	29.24%	8.78%	2.01%	11.48%	4.33%	9.32%	9.19%

Table S3. Percent differences in cortical skeletal values of male and female triplicated and control littermate mice. Percent change ([([mean of Dp-mean of Control]/mean of Control)*100]) reported in tables. Red indicates significant deficit; blue indicates significant improvement compared to same-sex control littermates (adjusted $p < 0.05$ via two-tail t test). Adjusted p values reported in Table S4.

	MALE								
	Dp1Tyb	**Dp1Tyb, *Dyrk1a*$^{+/+/-}$**	**Dp9Tyb**	**Dp2Tyb**	**Dp3Tyb**	**Ts1Rhr**	**Dp4Tyb**	**Dp5Tyb**	**Dp6Tyb**
Tt.Ar	-22.64%	-11.99%	7.81%	-10.19%	-9.12%	-10.22%	-6.23%	-12.88%	-1.95%
Ma.Ar	-28.91%	-14.16%	8.80%	-17.78%	-14.11%	-14.39%	-10.57%	-14.72%	-2.26%
Ct.Ar	-16.18%	-9.44%	6.65%	-1.08%	-4.28%	-5.59%	-1.24%	-10.55%	-1.61%
Ct.Th	-3.48%	-3.14%	2.12%	6.32%	1.60%	0.65%	3.39%	-3.72%	-0.59%
Ps.Pm	-9.89%	-5.71%	3.50%	-4.87%	-4.13%	-4.54%	-2.60%	-5.36%	-0.44%
Ec.Pm	-13.55%	-7.34%	4.17%	-7.85%	-5.68%	-5.88%	-4.33%	-6.91%	-1.35%

	FEMALE								
	Dp1Tyb	**Dp1Tyb, *Dyrk1a*$^{+/+/-}$**	**Dp9Tyb**	**Dp2Tyb**	**Dp3Tyb**	**Ts1Rhr**	**Dp4Tyb**	**Dp5Tyb**	**Dp6Tyb**
Tt.Ar	-11.54%	-13.12%	6.44%	-3.32%	-6.49%	-4.49%	-0.67%	-4.32%	2.29%
Ma.Ar	-16.09%	-16.78%	7.82%	-5.22%	-11.19%	-6.88%	-0.84%	-4.41%	-1.77%
Ct.Ar	-7.13%	-9.04%	5.07%	-1.42%	-2.34%	-2.23%	-0.52%	-4.23%	5.96%
Ct.Th	-0.01%	-1.31%	1.39%	0.79%	2.51%	1.00%	-0.12%	-1.82%	5.89%
Ps.Pm	-4.94%	-6.26%	3.06%	-1.68%	-2.87%	-2.11%	-0.36%	-1.75%	0.89%
Ec.Pm	-7.77%	-8.13%	4.66%	-2.23%	-5.39%	-3.88%	-0.38%	-2.06%	0.98%

Table S4. Results (adjusted p values) of two-tail t tests for trabecular and cortical parameters. Significance was declared with an adjusted p value < 0.05). M = male, F = female, WT = control/wildtype, Dp = triplicated Dp/Ts strain

		Dp1Tyb	Dp1Tyb, *Dyrk1a*$^{+/+/-}$	Dp9Tyb	Dp2Tyb	Dp3Tyb	Ts1Rhr	Dp4Tyb	Dp5Tyb	Dp6Tyb
BMD	M WT vs M Dp	0.014	0.986	0.003	0.249	1.000	0.562	0.836	0.024	0.089
	F WT vs F Dp	0.444	0.135	0.063	0.822	1.000	0.330	0.851	0.394	0.188
BV/TV	M WT vs M Dp	0.015	1.000	0.002	0.073	1.000	0.609	0.837	0.034	0.054
	F WT vs F Dp	0.178	0.077	0.059	0.834	1.000	0.391	0.973	0.371	0.050
Tb.Th	M WT vs M Dp	0.014	1.000	0.068	0.861	1.000	0.478	1.000	0.019	0.920
	F WT vs F Dp	0.689	0.471	0.097	0.791	1.000	0.937	1.000	0.368	0.113
Tb.Sp	M WT vs. M Dp	0.304	1.000	0.018	0.007	0.974	0.578	0.764	0.482	0.100
	F WT vs F Dp	0.189	0.299	0.180	0.748	0.999	0.295	0.976	0.301	0.341
Tb.N	M WT vs M Dp	0.059	1.000	0.004	0.015	0.829	0.316	1.000	0.211	0.045
	F WT vs F Dp	0.272	0.129	0.068	1.000	0.938	0.538	0.854	0.556	0.113
Tt.Ar	M WT vs M Dp	<0.001	0.007	0.068	0.001	0.002	0.009	0.105	<0.001	1.000
	F WT vs F Dp	<0.001	<0.001	0.043	0.226	<0.001	0.191	1.000	0.217	0.746
Ma.Ar	M WT vs M Dp	<0.001	0.004	0.085	<0.001	0.002	0.008	0.030	<0.001	0.986
	F WT vs F Dp	<0.001	<0.001	0.035	0.236	<0.001	0.239	1.000	0.178	0.588
Ct.Ar	M WT vs M Dp	<0.001	0.052	0.046	0.723	0.058	0.101	0.734	<0.001	0.986
	F WT vs F Dp	0.001	<0.001	0.068	0.651	0.178	0.351	0.997	0.305	0.082
Ct.Th	M WT vs M Dp	0.108	0.297	0.288	0.024	0.284	0.822	0.277	0.019	0.860
	F WT vs F Dp	0.997	0.466	0.393	0.556	0.122	0.510	0.943	0.165	0.0158
Ps.Pm	M WT vs M Dp	<0.001	0.007	0.101	0.001	0.001	0.006	0.107	<0.001	0.860
	F WT vs F Dp	<0.001	<0.001	0.080	0.231	<0.001	0.343	1.000	0.242	0.667
Ec.Pm	M WT vs M Dp	<0.001	0.048	0.113	<0.001	0.004	0.016	0.131	<0.001	1.000
	F WT vs F Dp	<0.001	<0.001	0.043	0.211	<0.001	0.567	1.000	0.221	0.698

Table S5. qPCR probes utilized by Transnetyx (Cordova, TN, USA) for genotyping

	Probe 1				Probe 2				Probe 3				Probe 4			
	Name	*Forward Primer*	*Reporter*	*Reverse Primer*	*Name*	*Forward Primer*	*Reporter*	*Reverse Primer*	*Name*	*Forward Primer*	*Reporter*	*Reverse Primer*	*Name*	*Forward Primer*	*Reporter*	*Reverse Primer*
Dp1Tyb	3'i17	CGGGCC TCTTCG CTATTA CG	CTGCAA ACTCTA AAAGAT CCGGC	CTCTCT CCCTGA GTGCAT TCTC	5'i16	CCCTAA GTCCTT GTCCCT CACA	CAGTGC AGATCC GGCGCG	GCAGTT GTTTAA ACTTCT AGAGAA TGAGTT C								
Dp9Tyb	3'i17	CGGGCC TCTTCG CTATTA CG	CTGCAA ACTCTA AAAGAT CCGGC	CTCTCT CCCTGA GTGCAT TCTC	5'h04	CTTCTC TGGACC AAAGGG TTCTTG ACA	CTAGTG GATCTC GAGCC	CTATGG CTTCTG AGGCGG AAAGAA CCA								
Dp2Tyb	3'h04	CGGTGC GGGCCT CTT	ATTACG CCAGGG CGCG	CCCCAC CCAATG TCCAAA GAC	5'i02	GCCTTG ACTGAG GACGTT GA	CGCGCC GGATCG AT	GCAGTT GTTTAA ACTTCT AGAGAA TGAGTT C								
Dp3Tyb	3'i02	CGTTGG CCGATT CATTAA TGCA	CTTAAC CACACC CTTACT CG	GACACA CCACAT CACTGA AACAG	5'i16	CCCTAA GTCCTT GTCCCT CACA	CAGTGC AGATCC GGCGCG	GCAGTT GTTTAA ACTTCT AGAGAA TGAGTT C								
Dp4Tyb	3'i02	CGTTGG CCGATT CATTAA TGCA	CTTAAC CACACC CTTACT CG	GACACA CCACAT CACTGA AACAG	5'c09	GCGTTA CACACA GAGCAT GAAC	CCGGAT CACACT CATGTC G	GGCTTC TGAGGC GGAAAG A								
Dp5Tyb	3'c09	CGGGCC TCTTCG CTATTA CG	CACAGC TTTGAT CCGGCG CG	AGCCAG GCGGTG CTG	5'b18	CGAACA ACTCAA GGGAGG AAAGAT C	CGCGCC AAGCTT TA	AGAGCA GAATAG CAGTTG TTTAAA CTTCT								
Dp6Tyb	3'b18	CGTTGG CCGATT CATTAA TGCA	ATTTGA GCTTTG ATCCGG CGCG	CCTTCC TTCATA ACTGAG TGTCGT A	5'i16	CCCTAA GTCCTT GTCCCT CACA	CAGTGC AGATCC GGCGCG	GCAGTT GTTTAA ACTTCT AGAGAA TGAGTT C								
Ts1Rhr	Ts1Rhr Tg	CCTGAA GTCCCG	CACACC ATATCT	CATCAA TGTATC												
		GATGCC A	GCATCA	TTATCA TGTCTT TTCCGG GCT												
Dp1Tyb, *Dyrk1a*$^{+/+/-}$	3'i17	CGGGCC TCTTCG CTATTA CG	CTGCAA ACTCTA AAAGAT CCGGC	CTCTCT CCCTGA GTGCAT TCTC	5'i16	CCCTAA GTCCTT GTCCCT CACA	CAGTGC AGATCC GGCGCG	GCAGTT GTTTAA ACTTCT AGAGAA TGAGTT C	Dyrk1a-1-KO	GGAAGA CAATAG CAGGCA TGCT	CTATGG GTCTAG AGCTCA TG	GTACTT CATTTC AGTGTC GTGTTT GTT	Dyrk1a-1-WT	GCGTTT CTGAAT CAAGCC CAGATA	AAGTGC GGCTGC TTGAGC T	TCATTT CAGTGT CGTGTT TGTTCA TG

Table S6. Results of significant Levene's test and subsequent Welch's F statistic and Games-Howell test. M = male, F = female, WT = control/wildtype, Dp = triplicated Dp/Ts strain. Highlighted cells indicate significance was lost with the alternative analysis.

Click here to download Table S6