

## Supplemental Tables

Supplemental Table 1. Average and standard error of the mean (SEM) of  $\mu$ CT parameters for temporal reduction of *Dyrk1a* copy number in maleTs65Dn mice at P30.

	<b>BMD</b>	<b>BV/TV</b>	<b>Tb.Th</b>	<b>Tb.Sp</b>	<b>Tb.N</b>				
<b><i>Euploid</i></b>	0.203 ± 0.016	26.98 ± 3.03	0.069 ± 0.004	0.166 ± 0.010	3.83 ± 0.232				
<b><i>Eu,Dyrk1a<sup>+/+</sup>/dox-cre</i></b>	0.211 ± 0.012	28.79 ± 2.23	0.063 ± 0.002	0.142 ± 0.005	4.53 ± 0.234				
<b><i>Ts65Dn</i></b>	0.152 ± 0.010	18.27 ± 1.70	0.060 ± 0.001	0.212 ± 0.014	3.02 ± 0.242				
<b><i>Ts,Dyrk1a<sup>+/+</sup>/dox-cre</i></b>	0.132 ± 0.013	14.73 ± 1.79	0.058 ± 0.002	0.213 ± 0.011	2.52 ± 0.272				
	<b>Tt.Ar</b>	<b>Ma.Ar</b>	<b>Ct.Ar</b>	<b>Ct.Th</b>	<b>Ps.Pm</b>	<b>Ec.Pm</b>	<b>I<sub>max</sub></b>	<b>I<sub>min</sub></b>	<b>Ct.TMD</b>
<b><i>Euploid</i></b>	1.46 ± 0.075	0.812 ± 0.047	0.646 ± 0.031	0.173 ± 0.005	5.10 ± 0.122	3.90 ± 0.104	0.155 ± 0.016	0.092 ± 0.009	1.02 0.007
<b><i>Eu,Dyrk1a<sup>+/+</sup>/dox-cre</i></b>	1.42 ± 0.033	0.801 ± 0.011	0.620 ± 0.026	0.168 ± 0.006	5.01 ± 0.057	3.86 ± 0.025	0.141 ± 0.009	0.086 ± 0.005	1.04 ± 0.005
<b><i>Ts65Dn</i></b>	1.09 ± 0.039	0.636 ± 0.023	0.458 ± 0.019	0.140 ± 0.004	4.46 ± 0.078	3.45 ± 0.062	0.082 ± 0.007	0.050 ± 0.003	0.980 ± 0.006
<b><i>Ts,Dyrk1a<sup>+/+</sup>/dox-cre</i></b>	1.08 ± 0.056	0.646 ± 0.015	0.440 ± 0.042	0.134 ± 0.011	4.44 ± 0.125	3.47 ± 0.047	0.076 ± 0.011	0.049 ± 0.006	0.985 ± 0.012

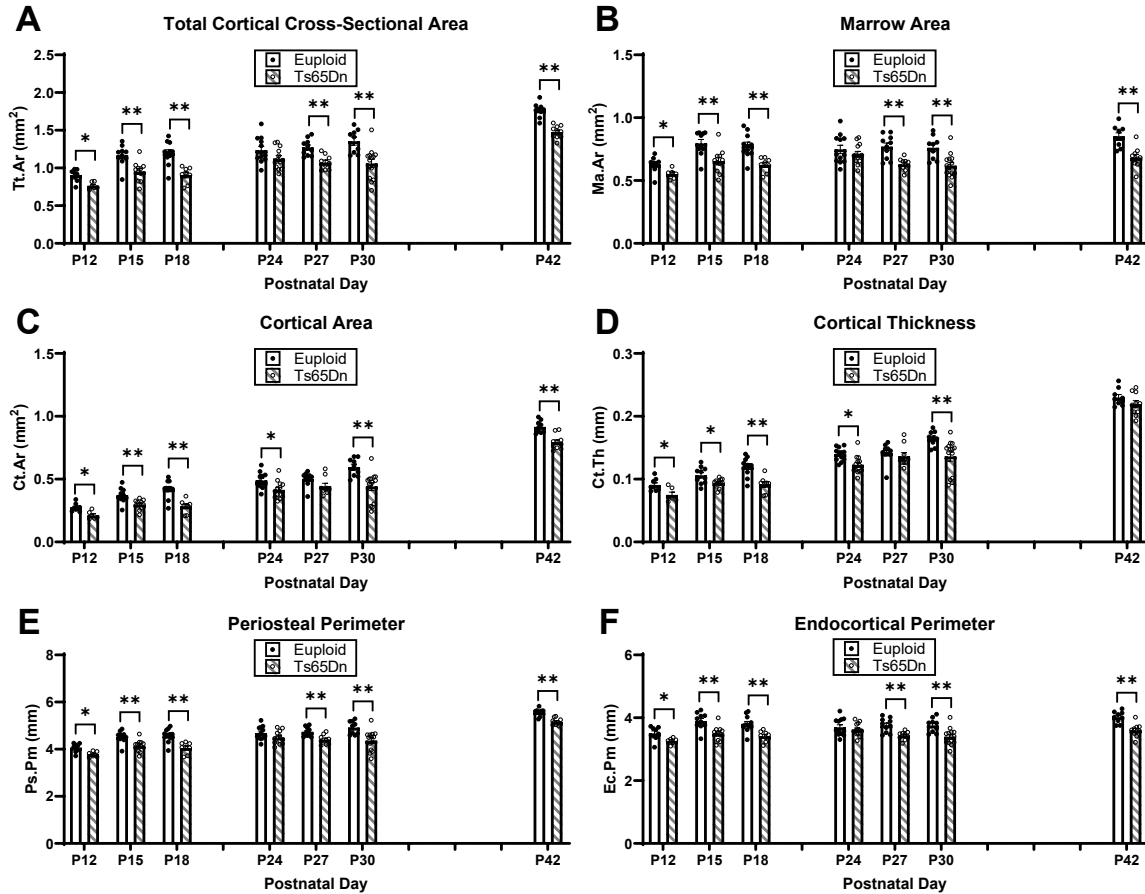
Supplemental Table 2. Comparison of P30 vehicle (10%DMSO:90%PBS)-treated and untreated euploid and Ts65Dn mice. Data are average ± SEM.

	<b>BMD</b> (g/cm <sup>3</sup> )	<b>BV/TV</b> (%)	<b>Tb.Th</b> (mm)	<b>Tb.Sp</b> (mm)	<b>Tb.N</b> (1/mm)	<b>Body Weight</b> (g)
<b><i>P30 untreated euploid</i></b>	0.181 ± 0.012	23.94 ± 2.44	0.065 ± 0.001	0.171 ± 0.014	3.65 ± 0.320	19.63 ± 0.99
<b><i>P30 vehicle-treated euploid</i></b>	0.199 ± 0.010	26.07 ± 2.07	0.069 ± 0.001	0.160 ± 0.010	3.78 ± 0.274	18.58 ± 0.58

<b>P30 untreated Ts65Dn</b>	0.132 ± 0.013	15.32 ± 2.26	0.062 ± 0.002	0.245 ± 0.022	2.36 ± 0.312		12.74 ± 1.16		
<b>P30 vehicle- treated Ts65Dn</b>	0.181 ± 0.008	23.05 ± 1.41	0.069 ± 0.001	0.187 ± 0.010	3.30 ± 0.183		15.72 ± 0.77		
	<b>Tt.Ar (mm<sup>2</sup>)</b>	<b>Ma.Ar (mm<sup>2</sup>)</b>	<b>Ct.Ar (mm<sup>2</sup>)</b>	<b>Ct.Th (mm)</b>	<b>Ps.Pm (mm)</b>	<b>Ec.Pm (mm)</b>	<b>I<sub>max</sub> (mm<sup>4</sup>)</b>	<b>I<sub>min</sub> (mm<sup>4</sup>)</b>	<b>Ct.TMD (g/cm<sup>3</sup>)</b>
<b>P30 untreated euploid</b>	1.36 ± 0.053	0.761 ± 0.031	0.595 ± 0.024	0.165 ± 0.004	4.92 ± 0.094	3.76 ± 0.077	0.131 ± 0.011	0.078 ± 0.006	1.01 ± 0.004
<b>P30 vehicle- treated euploid</b>	1.39 ± 0.040	0.772 ± 0.021	0.618 ± 0.022	0.170 ± 0.004	4.94 ± 0.064	3.78 ± 0.048	0.135 ± 0.008	0.085 ± 0.005	1.01 ± 0.008
<b>P30 untreated Ts65Dn</b>	1.06 ± 0.055	0.618 ± 0.025	0.442 ± 0.032	0.136 ± 0.007	4.37 ± 0.114	3.40 ± 0.071	0.079 ± 0.010	0.060 ± 0.005	0.964 ± 0.012
<b>P30 vehicle- treated Ts65Dn</b>	1.20 ± 0.049	0.686 ± 0.026	0.516 ± 0.025	0.151 ± 0.005	4.64 ± 0.096	3.57 ± 0.069	0.102 ± 0.009	0.062 ± 0.004	0.974 ± 0.008

## Supplemental Figures

Supplemental Figure 1. Cortical analysis of male Ts65Dn femurs from postnatal day (P)12-42. Remaining cortical parameters from  $\mu$ CT analysis. Data are mean  $\pm$  SEM. Significance determined through two-tail t-test with FDR adjustment. (\*) indicates  $p \leq 0.05$ , (\*\*) indicates  $p \leq 0.01$ .



Supplemental Figure 2. Osteogenic gene expression at P24, P27, and P30

