

**Supplemental Table 1: Summary of phenotypes found in the mouse models for SMS and dup (17)(p11.2p11.2) syndromes.**

Phenotypes observed in mouse models for SMS and dup (17)(p11.2p11.2) syndromes are listed in the table. *Df(11)17/+*: mice containing a deletion of the SMS syntenic region. *Rai1+/-*: mice carrying a null allele of *Rai1*. *Dp(11)17/+*: mice containing a duplication of the SMS syntenic region. Locomotor activity was measured in the open field assay. Anxiety levels were determined in the open field test or in the light-dark test. The learning and memory phenotypes were studied with the fear conditioned paradigm. ND: not determined.

<b>Genotype Phenotype</b>	<i>Df(11)17/+</i>	<i>Dp(11)17/+</i>	<i>Dp(11)17/Df(11)17</i>	<i>Rai1+/-</i>	<i>Dp(11)17/Rai1-</i>
<b>Physical features</b>					
Craniofacial anomalies	yes (100%)	no	no	yes (~18%)	no
Body weight	obesity	underweight	normal	obesity	normal
Reduced male fertility	yes (genetic background dependent)	no	no	no	no
<b>Neurobehavioral abnormalities</b>					
Overt seizures	yes (20%)	no	no	yes (2%)	no
Abnormal EEG	yes	no	yes	ND	ND
Abnormal circadian rhythm	yes	no	ND	ND	ND
Locomotor activity	hypoactive	hyperactive	hyperactive	hypoactive	hyperactive
Anxiety	normal	elevated	normal	ND	normal
Learning and memory	normal	impaired	normal	normal	normal
Citation	21, 22	21, 22	21, present work	23	present work

**Supplemental Table 2. Restoring genomic balance corrects several abnormal behaviors and learning deficits observed in chromosome engineered animal models.**

		<b>Wild type</b>	<i>Dp(11)17/+</i>	<i>Df(11)17/+</i>	<i>Dp(11)17/ Df(11)17</i>
<b>Open Field</b>	N	12	21	7	10
	Total Distance (cm)	4523 +/- 551	6378 +/- 327	4716 +/- 498	6629 +/- 390
	Vertical Activity (number)	499 +/- 60	305 +/- 22	590 +/- 41	641 +/- 42
	Center/Total Distance	0.33 +/- 0.04	0.26+/-0.01	0.33+/-0.01	0.33+/- 0.02
<b>Fear Conditioned</b>	% Freezing to context	36.0 +/- 6.5	12.6 +/- 2.5	32.8 +/- 8.5	36.6 +/- 5.0
	% Freezing to sound	51.0 +/- 8	60.2 +/- 3.5	46.0 +/- 11	59.4 +/- 4.5

Average values for the different parameters measured in the open field test and the conditioned fear test are presented in the table.

**Supplemental Table 3. Normalizing *Rai1* gene dosage rescues several abnormal behaviors and learning and memory deficits of *Dp(11)17/+* mice.**

		<b>Wild type</b>	<b><i>Dp(11)17/+</i></b>	<b><i>Rai1</i><sup>+/-</sup></b>	<b><i>Dp(11)17/Rai1</i><sup>-</sup></b>
<b>Open Field</b>	N	21	18	17	21
	Total Distance (cm)	3022 +/- 259	3945 +/- 260	2270 +/- 175	3752 +/- 234
	Vertical Activity (number)	282 +/- 24	195 +/- 27	374 +/- 40	286 +/- 39
	Center/Total Distance	0.22 +/- 0.02	0.14 +/- 0.02	0.26 +/- 0.02	0.19 +/- 0.02
<b>Fear Conditioned</b>	% Freezing to context	53.6 +/- 5.5	25.7 +/- 4.5	55.7 +/- 5.4	40.9 +/- 5.2
	% Freezing to sound	60.3 +/- 4.5	72.8 +/- 3.9	48.4 +/- 5.2	73.3 +/- 4.0

Average values for the different parameters measured in the open field test and the conditioned fear test are presented in the table.