

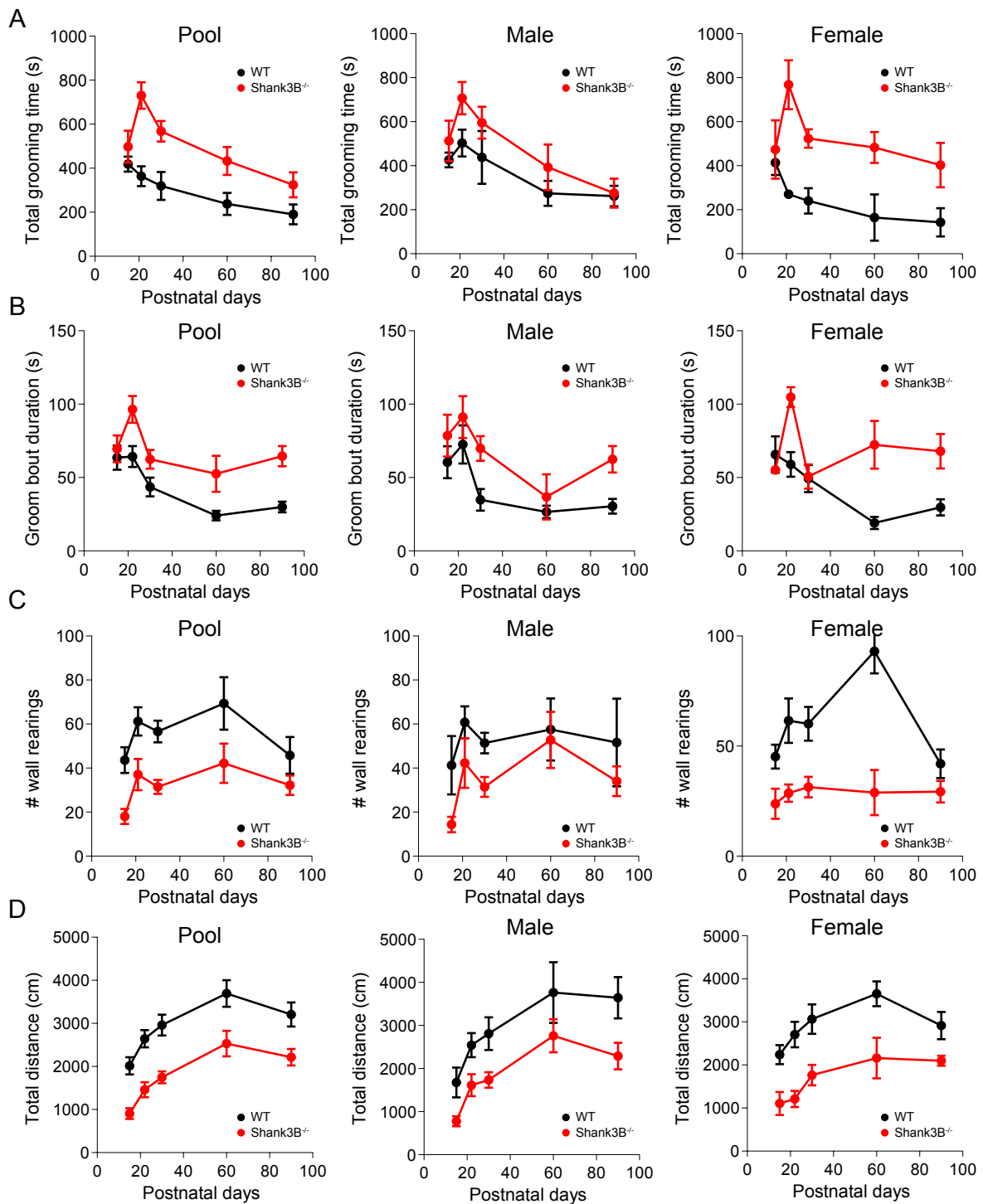
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Supplemental Information

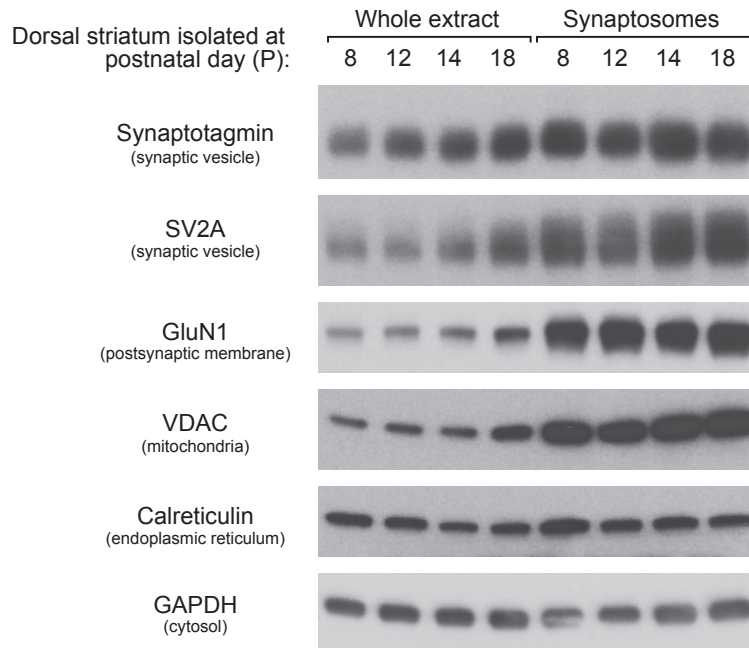
Abnormal Striatal Development Underlies the Early Onset of Behavioral Deficits in *Shank3B*^{-/-} Mice

Rui Tiago Peixoto, Lynne Chantranupong, Richard Hakim, James Levasseur, Wengang Wang, Tasha Merchant, Kelly Gorman, Bogdan Budnik, and Bernardo Luis Sabatini

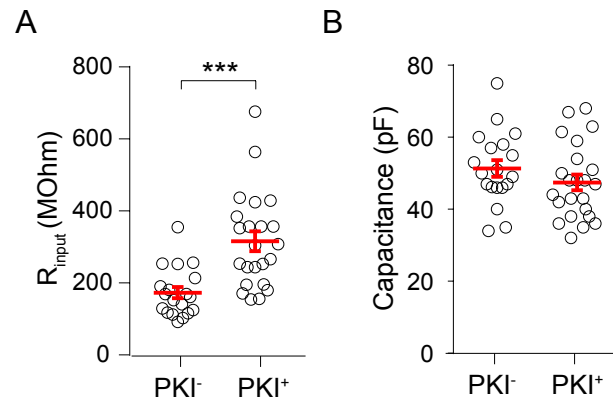
Supplemental Figures



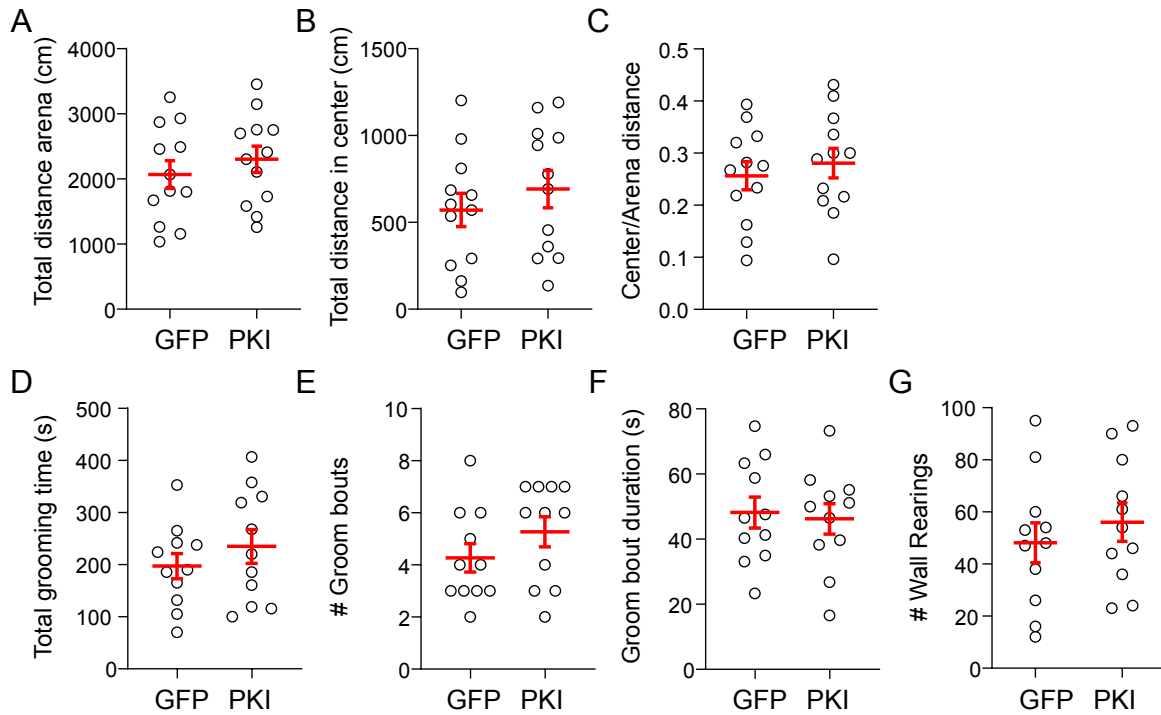
Supplemental Figure 1 – Related to Figure 1. No sexual dimorphism observed in developing Shank3B^{-/-} mice in the open field test. (A) Mean ± SEM of total grooming time by P15-90 WT (black) and Shank3B^{-/-} (red) mice during 30 min in open field arena. Left panel - total pool; Center panel – males; Right panel – females. WT: 4 males, 6 females; Shank3B^{-/-}: 8 males, 5 females. (B) Mean ± SEM of grooming bout duration P15-90 WT (black) and Shank3B^{-/-} (red) mice during 30 min in open field arena. Left panel - total pool; Center panel – males; Right panel – females. WT: 4 males, 6 females; Shank3B^{-/-}: 8 males, 5 females. (C) Mean ± SEM of number of wall rearings by P15-90 WT (black) and Shank3B^{-/-} (red) mice during 30 min in open field arena. Left panel - total pool; Center panel – males; Right panel – females. WT: 4 males, 6 females; Shank3B^{-/-}: 8 males, 5 females. (D) Mean ± SEM of total distance traveled by P15-90 WT (black) and Shank3B^{-/-} (red) mice during 30 min in open field arena. Left panel - total pool; Center panel – males; Right panel – females. WT: 4 males, 6 females; Shank3B^{-/-}: 8 males, 5 females.



Supplemental Figure 2 – Related to Figure 2. Immunoblot profiling of striatal synaptosomes across development. Immunoblots against Synaptotagmin, Synaptic vesicle glycoprotein 2A, NR1 (GluN1), Voltage dependent anion channel (VDAC), Calreticulin and Glyceraldehyde 3-phosphate dehydrogenase, performed in whole extracts or synaptosomal fractions collected from mice across the P8-P18 developmental time period.



Supplemental Figure 3 – Related to Figure 4. Expression of PKI α in SPNs during P8-P15 increases membrane resistance. (A) Mean \pm SEM of input resistance and (B) capacitance of SPNs recorded by whole-cell recordings in coronal brain slices of P15 mice infected with AA8-Syn-PKI α -IRES-mRuby2 in DMS at P8. PKI⁺ group represents SPNs expressing PKI α and PKI⁻ group corresponds to neighboring uninfected controls. N=19,23 neurons from 5 mice, unpaired Mann-Whitney test, ***p<0.001.



Supplemental Figure 4 - Related to Figure 5. Postnatal expression of PKI in DMS does not change behavior of WT mice in the open field test. (A) Mean \pm SEM of total distance traveled for 20 min in the open field test by P21 WT mice injected with AAV-EGFP or AAV-PKI medial striatum at P8. (B) Mean \pm SEM of total distance traveled in the center of arena. (C) Mean \pm SEM of the ratio of distance traveled in the center of the arena over total distance traveled. (D) Mean \pm SEM total grooming time of P21 WT mice expressing GFP or PKI in the open-field. (E) Mean \pm SEM number of and (F) duration of grooming bouts per session. (F) Mean \pm SEM Number of wall rearing bouts per session.

Supplemental Table 1- Related to Figures 2D and 2E. Abundance levels of proteins with significant expression changes P8-P18 ($p < 0.0013$). Developmental expression index is Log₂ of abundance values normalized to P8.

Gene name	Developmental expression Index (Log ₂)	P8 – abundance	P12 – abundance	P14 – abundance	P18 – abundance
Shank3	1.001422974	1.56E+07	2.09E+07	2.81E+07	3.13E+07
Dync1h1	-0.471813639	2.89E+08	2.43E+08	2.12E+08	2.09E+08
Map1b	-1.654911085	7.44E+08	3.05E+08	2.60E+08	2.36E+08
Golgb1	-0.560994839	1.40E+07	1.51E+07	1.43E+07	9.48E+06
Sptbn2	0.345359316	3.21E+07	3.84E+07	4.08E+07	3.91E+07
Fasn	-1.141840815	2.02E+08	1.45E+08	1.09E+08	9.14E+07
Rrbp1	-0.592640033	3.51E+07	3.93E+07	2.80E+07	2.33E+07
Mycbp2	-0.955232055	2.09E+07	1.43E+07	1.20E+07	1.08E+07
Map2	-0.877343301	6.48E+07	4.11E+07	3.53E+07	4.01E+07
Lrp1	-1.325891641	7.63E+07	5.13E+07	4.21E+07	3.04E+07
Myo5a	-0.516578781	1.35E+08	1.13E+08	1.08E+08	9.46E+07
Pclo	0.247594378	9.99E+07	1.04E+08	1.19E+08	1.17E+08
Gprin1	-0.790803702	6.64E+07	5.53E+07	4.42E+07	3.84E+07
Clip2	-0.971303718	3.59E+07	2.49E+07	2.26E+07	1.83E+07
Mapk8ip3	-0.793195254	3.05E+07	2.71E+07	2.29E+07	1.76E+07
Snd1	-0.975069033	2.06E+07	1.39E+07	1.37E+07	1.05E+07
Cntn1	-0.477420425	2.04E+08	1.90E+08	1.75E+08	1.46E+08
Map1a	-0.226884197	8.63E+07	8.55E+07	8.83E+07	7.38E+07
Trio	-0.788461955	2.87E+07	2.06E+07	1.91E+07	1.66E+07
Bsn	0.836166321	7.95E+07	1.08E+08	1.42E+08	1.28E+08
Dctn1	-0.133341457	3.35E+07	3.57E+07	3.18E+07	3.06E+07
Tenm4	-0.555460767	7.84E+06	6.68E+06	6.61E+06	5.33E+06
Birc6	-1.200026146	8.80E+06	6.53E+06	5.02E+06	3.83E+06
Tubb3	-1.425857463	2.96E+08	1.98E+08	1.50E+08	1.10E+08
Cspg4	-1.119271421	1.04E+07	9.27E+06	8.15E+06	4.81E+06
Nav1	-1.23219087	1.69E+07	1.36E+07	1.03E+07	7.18E+06
Plcb1	0.35532532	8.90E+07	1.14E+08	1.07E+08	8.91E+07
Kif21b	-1.627549694	4.13E+07	3.50E+07	1.79E+07	1.34E+07
Kidins220	-0.888611119	6.39E+06	4.56E+06	4.21E+06	3.45E+06
Vcp	-0.364353809	6.68E+07	5.74E+07	5.19E+07	5.20E+07
Srgap2	-1.109706268	2.16E+07	1.51E+07	1.21E+07	1.00E+07
Pi4ka	0.496942717	1.13E+07	1.52E+07	1.52E+07	1.60E+07
Camsap1	-1.044826875	2.09E+07	1.58E+07	1.34E+07	1.01E+07
Hspa8	0.270495593	4.00E+08	3.65E+08	4.35E+08	4.82E+08
Syne1	0.175561144	2.89E+07	3.03E+07	3.26E+07	2.94E+07
Vps13d	-0.345767074	5.56E+06	6.06E+06	5.49E+06	4.37E+06
Atp1a1	0.812063113	9.93E+07	1.50E+08	1.74E+08	1.74E+08
Rab3c	1.364851955	3.79E+06	6.86E+06	7.83E+06	9.76E+06
Dbn1	-1.776520668	5.13E+07	2.79E+07	2.15E+07	1.50E+07
Tnik	-0.241910063	1.12E+07	1.13E+07	1.02E+07	9.50E+06
Cltc	0.85025068	2.28E+08	3.33E+08	3.58E+08	4.12E+08
Vwa8	-0.11388885	2.13E+07	2.01E+07	2.10E+07	1.96E+07
Ywhaz	0.348601074	2.31E+08	2.56E+08	2.52E+08	2.94E+08
Tjp2	-0.505424112	4.19E+06	3.82E+06	3.77E+06	2.95E+06
Kpnb1	-1.648047026	4.28E+07	1.86E+07	2.32E+07	1.37E+07
Psmd1	-0.874396026	2.60E+07	2.29E+07	2.02E+07	1.42E+07
Srgap3	-1.37205892	3.13E+07	2.18E+07	1.93E+07	1.21E+07
Lppr4	-0.366664661	1.79E+07	2.34E+07	1.85E+07	1.39E+07
Hsph1	0.35747565	4.16E+07	5.33E+07	4.30E+07	3.76E+07
Plxnb2	-0.519235914	6.68E+06	6.26E+06	5.73E+06	4.66E+06
Igsf3	-1.85314073	1.23E+07	6.55E+06	4.27E+06	3.40E+06
Hdlbp	-1.052422656	1.70E+07	1.22E+07	1.19E+07	8.20E+06
Ppp1r21	-0.930192155	1.43E+07	1.23E+07	1.19E+07	7.51E+06
Taok1	-0.921719076	1.34E+07	9.91E+06	9.47E+06	7.08E+06

Csnk2a2	0.434721145	2.67E+06	3.05E+06	3.27E+06	3.61E+06
Eif3a	-0.326866524	4.13E+06	4.36E+06	3.93E+06	3.29E+06
Syn1	1.182704702	1.14E+08	1.81E+08	2.23E+08	2.59E+08
Plxnd1	-0.393204593	1.00E+07	9.51E+06	7.96E+06	7.64E+06
Ahi1	0.262244765	4.03E+05	3.51E+05	4.34E+05	4.83E+05
Aars2	-0.099811608	2.50E+06	2.36E+06	2.40E+06	2.33E+06
Kif5b	-0.813504025	4.18E+07	4.33E+07	3.19E+07	2.38E+07
Ruvbl2	-0.94283616	3.77E+06	1.96E+06	2.12E+06	2.27E+06
Rabep1	-0.904507475	3.95E+07	3.71E+07	3.29E+07	2.11E+07
Cat	-0.970097959	1.50E+07	1.42E+07	9.64E+06	7.66E+06
Stip1	-0.544978809	3.70E+07	4.30E+07	3.17E+07	2.53E+07
Hyou1	-0.237788772	2.29E+07	2.53E+07	1.94E+07	1.96E+07
Tln2	-0.089365585	4.34E+07	4.57E+07	4.40E+07	4.08E+07
ldh3a	0.543781337	3.08E+08	3.24E+08	3.93E+08	4.49E+08
Ralgapa1	-0.941314876	3.55E+06	3.06E+06	2.64E+06	1.85E+06
Nedd4	-0.562162773	1.15E+07	1.08E+07	9.73E+06	7.76E+06
Nbea	-0.692597913	2.81E+07	2.57E+07	2.25E+07	1.74E+07
Pcdha9	-0.617110757	9.19E+05	7.98E+05	7.87E+05	5.99E+05
Akap12	-1.723031147	1.58E+07	9.07E+06	6.68E+06	4.79E+06
2010300C02Rik	0.443967445	5.38E+06	6.08E+06	7.32E+06	5.16E+06
Rab11fip5	-1.080911643	5.56E+06	3.92E+06	3.97E+06	2.63E+06
Cep170	-1.694769951	3.31E+07	1.91E+07	1.57E+07	1.02E+07
Ppfia3	-0.275575071	2.02E+07	1.75E+07	1.67E+07	1.96E+07
KIAA1109	-0.450782946	1.29E+07	1.23E+07	1.16E+07	9.41E+06
Aco2	1.21655633	8.16E+07	1.33E+08	1.42E+08	1.90E+08
Ccdc88c	-1.615961057	4.02E+06	2.76E+06	2.30E+06	1.31E+06
Gnao1	0.653146394	3.40E+08	4.68E+08	4.77E+08	5.34E+08
Tenm1	-0.706313937	7.90E+06	6.99E+06	5.50E+06	4.84E+06
Ppfia2	-0.58367777	1.35E+07	1.23E+07	1.09E+07	9.01E+06
Itsn1	-0.47969752	2.48E+07	2.15E+07	2.01E+07	1.78E+07
Wdfy3	-0.478377444	2.32E+07	2.33E+07	2.21E+07	1.67E+07
Uba1	-0.823367674	7.44E+07	6.28E+07	5.17E+07	4.20E+07
Pitrm1	0.171130925	3.53E+07	3.97E+07	3.79E+07	3.42E+07
Dpysl2	-0.281931485	5.15E+08	5.03E+08	4.38E+08	4.23E+08
Ptk2	-0.346553218	3.89E+06	4.27E+06	3.71E+06	3.06E+06
Camsap2	-1.038028349	1.05E+07	9.26E+06	6.93E+06	5.10E+06
Hsp90b1	-0.838538577	4.52E+07	4.04E+07	3.05E+07	2.53E+07
Myo9a	-0.798123774	2.68E+06	2.16E+06	1.79E+06	1.54E+06
Ildr2	0.338969901	2.30E+06	2.59E+06	2.90E+06	2.19E+06
Tkt	-0.712609064	1.49E+08	1.22E+08	1.02E+08	9.12E+07
Dpp3	-0.520462478	4.99E+06	4.56E+06	3.81E+06	3.48E+06
Lmtk2	-0.640687067	2.75E+06	2.53E+06	2.52E+06	1.76E+06
Eif4g3	-0.208579646	1.00E+07	9.77E+06	9.23E+06	8.68E+06
Trim2	-0.5439055	1.44E+07	1.23E+07	1.08E+07	9.89E+06
Ctnna2	-0.318202524	2.58E+07	2.20E+07	2.09E+07	2.07E+07
Ctnnd2	-0.478352062	3.19E+07	2.86E+07	2.97E+07	2.29E+07
Mrps22	0.0753752	1.25E+07	1.31E+07	1.26E+07	1.20E+07
Tenm2	-0.905496021	1.55E+07	1.01E+07	9.23E+06	8.25E+06
Maoa	-0.327848929	1.68E+07	1.34E+07	1.35E+07	1.52E+07
Shroom2	-0.611284038	4.49E+06	4.46E+06	3.47E+06	2.94E+06
Cct3	0.440224679	3.22E+07	3.38E+07	3.29E+07	4.37E+07
Pacs1	-0.113402687	9.49E+06	9.85E+06	9.66E+06	8.77E+06
Glud1	0.23413224	7.34E+07	8.43E+07	7.86E+07	8.63E+07
Taldo1	-0.211209467	7.17E+06	8.87E+06	6.67E+06	6.19E+06
Dip2b	-0.175634426	9.40E+06	1.02E+07	9.81E+06	8.32E+06
Tnc	-0.3501458	6.59E+06	9.17E+06	7.14E+06	5.17E+06
Strn3	-1.005389693	1.07E+06	6.94E+05	6.91E+05	5.32E+05
Iqsec1	-0.365957713	1.64E+07	1.27E+07	1.58E+07	1.41E+07
Gprin3	0.236745315	2.14E+07	2.47E+07	2.28E+07	2.53E+07
Dnajb1	-1.18977726	2.30E+06	1.62E+06	1.52E+06	1.01E+06
Ap3b2	-0.458225302	1.44E+07	1.17E+07	1.21E+07	1.05E+07
Ptpst	-0.701958837	3.95E+06	3.40E+06	2.93E+06	2.43E+06
Tax1bp1	-0.799618554	4.16E+06	3.48E+06	3.25E+06	2.39E+06

Mark1	-0.202690217	1.48E+07	1.29E+07	1.35E+07	1.43E+07
Epn2	-0.733515679	1.55E+07	1.26E+07	1.41E+07	9.32E+06
Exoc8	-1.044049777	2.34E+07	1.70E+07	1.50E+07	1.14E+07
P4hb	-0.559677519	5.68E+07	4.43E+07	3.90E+07	3.85E+07
Sirt2	1.627250289	1.39E+07	3.63E+07	3.94E+07	4.28E+07
Ipo5	-0.510386159	1.53E+07	1.07E+07	1.13E+07	1.21E+07
Phb2	0.155617366	1.43E+08	1.45E+08	1.56E+08	1.59E+08
Baiap2	0.829496395	3.07E+07	4.64E+07	5.43E+07	5.45E+07
Atp8a1	-1.993979354	6.07E+05	2.47E+05	1.57E+05	1.53E+05
Nav3	-1.034774628	1.34E+07	1.05E+07	8.63E+06	6.55E+06
Ppp6r2	-0.082375106	4.02E+06	4.63E+06	4.11E+06	3.80E+06
Ehd3	-0.238647953	1.08E+07	1.22E+07	1.18E+07	9.17E+06
Hip1	-0.764255908	1.68E+07	1.39E+07	1.13E+07	9.88E+06
Dlgap4	0.86210182	3.81E+04	5.64E+04	6.93E+04	4.15E+04
Pcx	-0.099179004	1.48E+06	1.50E+06	1.40E+06	1.38E+06
Immt	-0.117186848	5.27E+05	5.09E+05	5.56E+05	4.86E+05
Sept6	0.65522811	1.76E+07	2.77E+07	2.46E+07	2.31E+07
Mical3	-0.827140173	2.08E+07	1.64E+07	1.51E+07	1.17E+07
Wdr44	-0.275552617	7.01E+06	8.57E+06	7.44E+06	5.79E+06
Ddx1	-0.576502132	1.25E+07	1.17E+07	9.71E+06	8.37E+06
C530008M17Rik	-0.812550674	1.66E+06	1.30E+06	1.01E+06	9.46E+05
Nucb1	-0.258867824	3.11E+06	3.05E+06	2.60E+06	3.25E+06
Hspa4	-0.630915565	5.09E+07	4.09E+07	4.47E+07	3.29E+07
Itpr1	1.062369778	2.73E+07	5.07E+07	5.71E+07	5.11E+07
Gpd2	1.306858306	1.99E+07	2.36E+07	2.94E+07	4.92E+07
Epb41l2	0.63662181	1.55E+07	2.41E+07	2.41E+07	2.29E+07
Shank3	1.001422974	1.56E+07	2.09E+07	2.81E+07	3.13E+07