Supplemental Materials

Mutation of neuron-specific chromatin remodeling subunit BAF53b: Rescue of plasticity and memory by manipulating actin remodeling.

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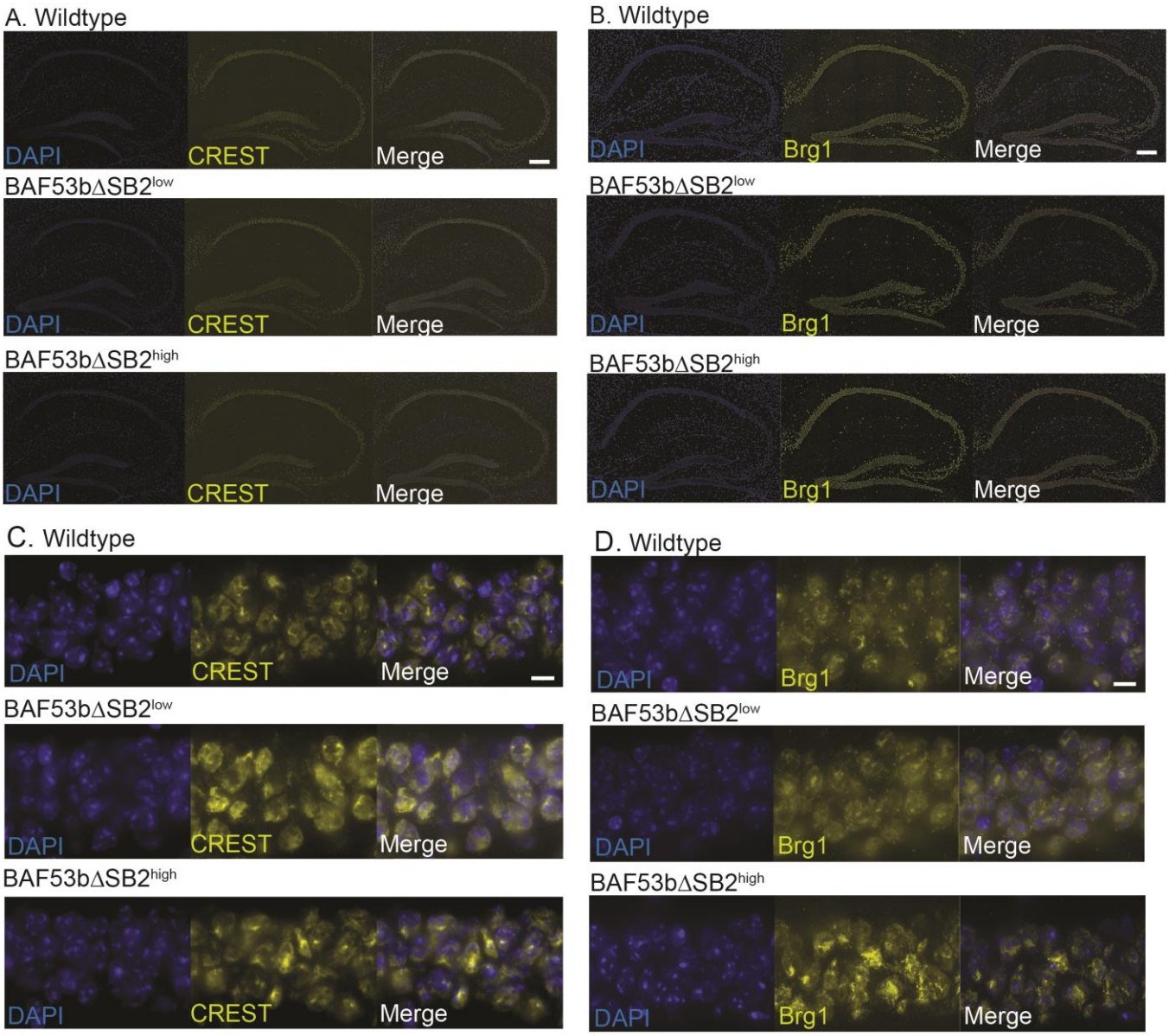

Figure S1. nBAF subunit expression in dorsal hippocampus in wildtype, BAF53bΔSB2^{low}, and BAF53bΔSB2^{high} mice.

(A) Brg1 is expressed throughout dorsal hippocampus in wildtype, BAF53bΔSB2^{low}, and BAF53bΔSB2^{high} mice. Sagittal sections (20um) were taken from animals from each genotype, stained for Brg1 and DAPI (nuclear marker) as described in the methods section. 20x scans were taken of dorsal hippocampus. Scale bar is 200um. (B) CREST is expressed throughout dorsal hippocampus in wildtype, BAF53bΔSB2^{low}, and BAF53bΔSB2^{high} mice. Images acquired as in (A). Scale bar is 200um. (C) Brg1 nuclear expression colocalizes with nuclear marker DAPI in CA1 of wildtype, BAF53bΔSB2^{low}, and BAF53bΔSB2^{high} mice. Sagittal sections (20um) were taken from animals from each genotype, stained for Brg1 and DAPI (nuclear marker. 63x confocal images stacks acquired in CA1 were max intensity projected using Image J. Scale bar is 10um. (D) CREST expression colocalizes with nuclei marker DAPI in CA1 of wildtype, BAF53bΔSB2^{low}, and BAF53bΔSB2^{high} mice. Images were prepared as in (C). Scale bar is 10um.

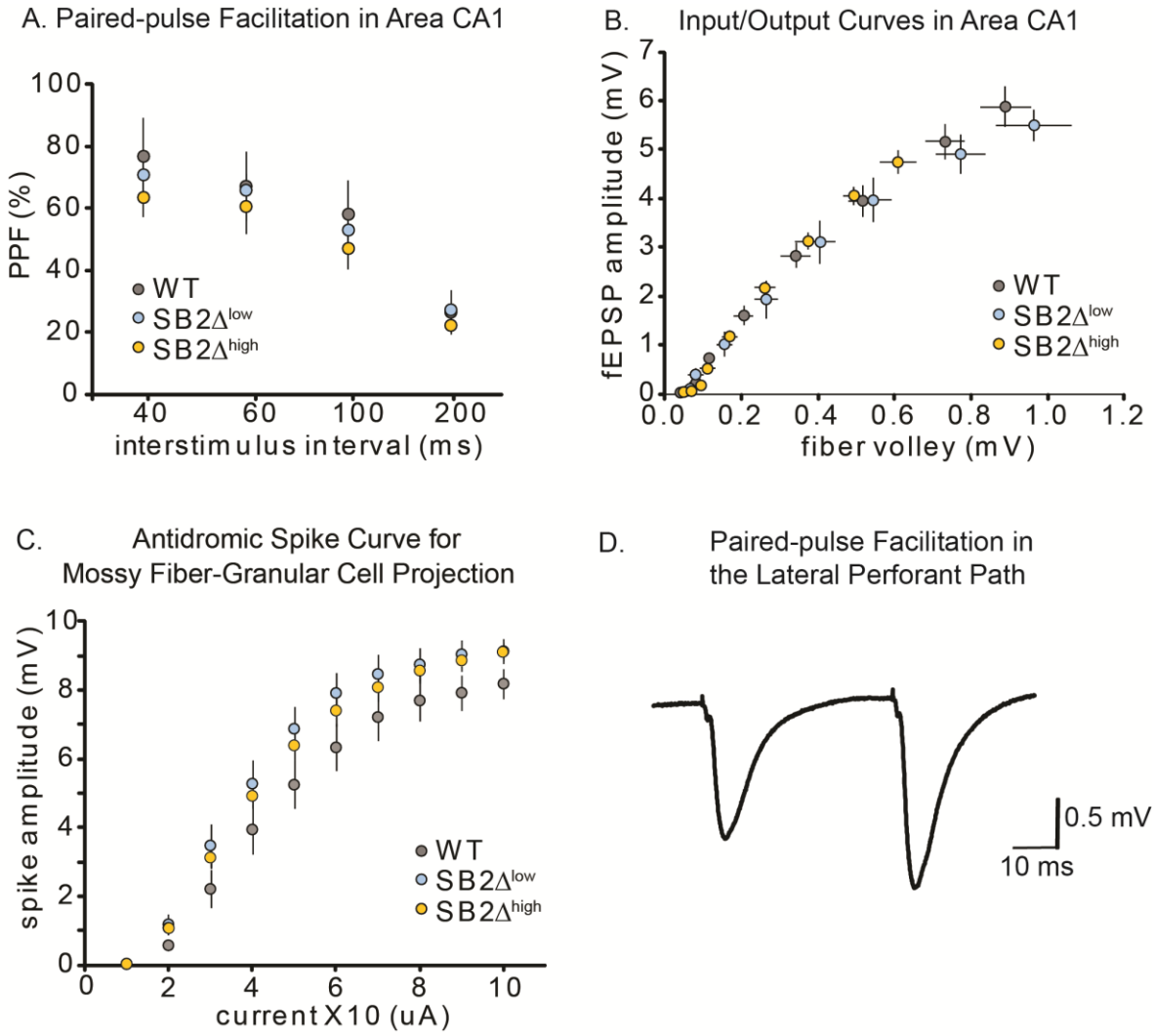

Figure S2. Baseline electrophysiology in slices from BAF53bΔSB2^{low} and BAF53bΔSB2^{high} mice. (A) Paired-pulse facilitation of the initial slope of the synaptic response in hippocampal CA1 (40, 60, 100, and 200 ms inter-pulse intervals) was not significantly difference between groups in slices from BAF53bΔSB2^{low}, BAF53bΔSB2^{high} and WT mice (2-way RM-ANOVA, no main effect of genotype $F_{2,48}$=0.32, p=0.73, a significant main effect of inter-pulse interval $F_{3,48}$=135.5, p<0.0001, but no significant interaction $F_{6,48}$=0.58, p=0.75). n=7 slices from >4 animals per genotype. (B) Input/Output curves compare amplitudes of the presynaptic fiber volley to the fEPSP amplitude across a range of stimulation currents in hippocampal CA1. Input/output curves were not measurable different between BAF53bΔSB2^{low}, BAF53bΔSB2^{high} and WT mice (1-way ANOVA on slope of curve, F_2=1.50, p=0.25). n=7-8 slices from >4 animals per genotype. (C) Input/output curve measuring the amplitude of the cell spike in the granular cell layer generated by antidromic stimulation of mossy fiber projections across a range of currents showed no significant difference between BAF53bΔSB2^{low}, BAF53bΔSB2^{high} and WT mice (2-way RM-ANOVA no main effect of genotype $F_{2,288}$=2.09, p=0.14, a main effect of stimulation $F_{9,288}$=357.7, p<0.0001, no significant interaction $F_{18,288}$=0.74, p=0.77). n=11-12 slices from 3-4 animals per genotype. (D) Representative trace of characteristic paired-pulse facilitation recorded in the lateral perforant path of a wildtype slice during the delivery of a pair of stimuli (40 ms interval) near the hippocampal fissure.

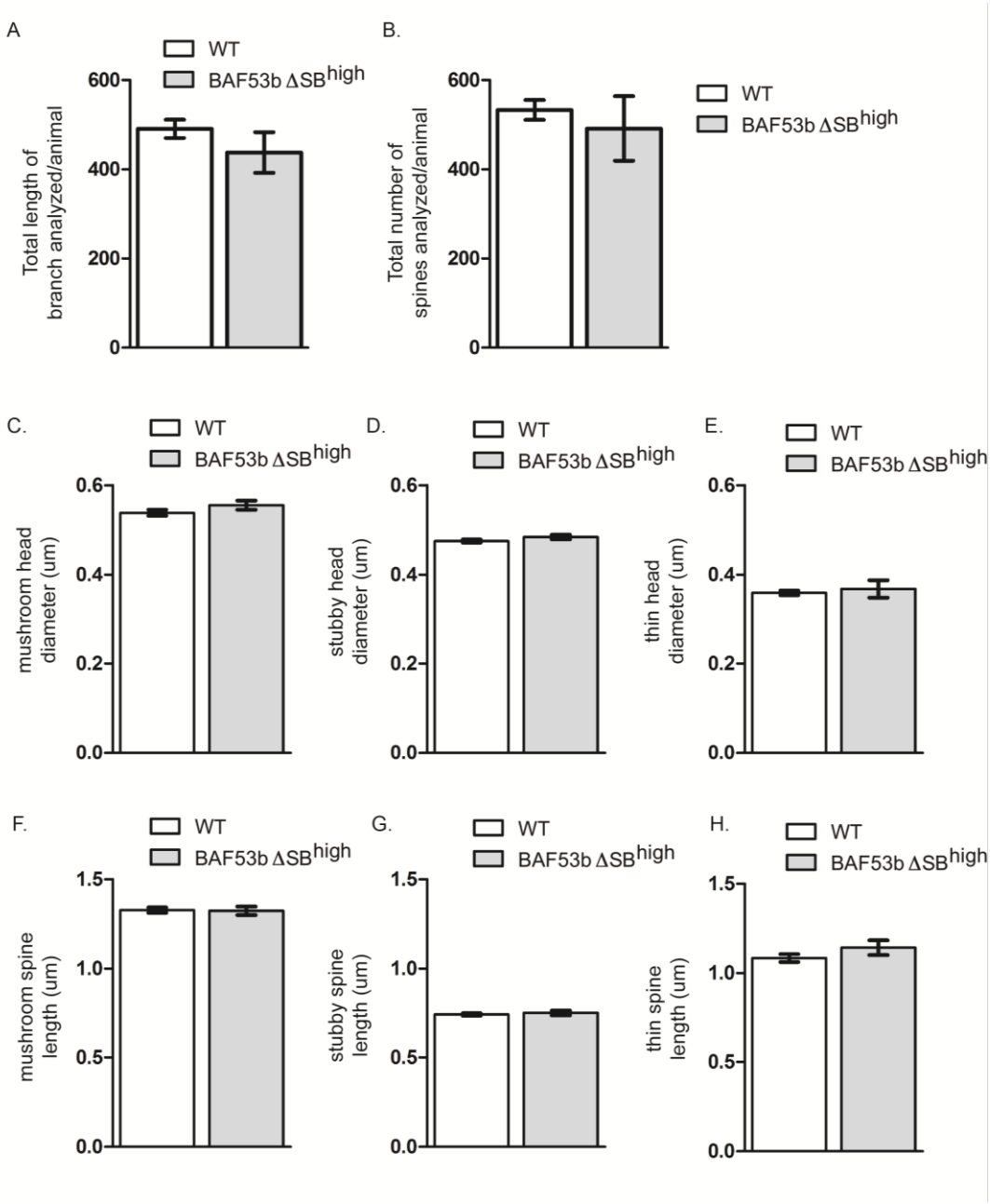

Figure S3. Dendritic Spine measures in hippocampal CA1 are similar in wildtype and BAF53bΔSB2^{high} mice

(A) Total length of dendritic branches analyzed (n=7 animals per genotype, 9-11 branches per animal) in wildtype and BAF53bΔSB2^{high} mice is equivalent $t(12)=1.06$, $p=0.31$. (B) The total number of spines analyzed per animal for each genotype is also equivalent (Mann-Whitney U (12)=16.50, p=0.34). (C) Head diameter (microns) of spines categorized as mushroom was equivalent between the two genotypes (Mann-Whitney U (12)=15.00, p=0.26). (D) Head diameter (microns) of spines categorized as stubby was equivalent between the two genotypes (Mann-Whitney U (12)=16.00, p=0.32). (E) Head diameter (microns) of spines categorized as thin was equivalent between the two genotypes (Mann-Whitney U (12)=22.00, p=0.80). (F) Spine length (from dendritic branch to tip of spine head in microns) of spines categorized as mushroom was equivalent between the two genotypes (Mann-Whitney U (12)=21.00, p=0.71). (G) Spine length (from dendritic branch to tip of spine head in microns) of spines categorized as stubby was equivalent between the two genotypes (Mann-Whitney U (12)=20.00, p=0.62). (H) Spine length (from dendritic branch to tip of spine head in microns) of spines categorized as thin was equivalent between the two genotypes (Mann-Whitney U (12)=16.00, p=0.32). All graphs mean +/- SEM.

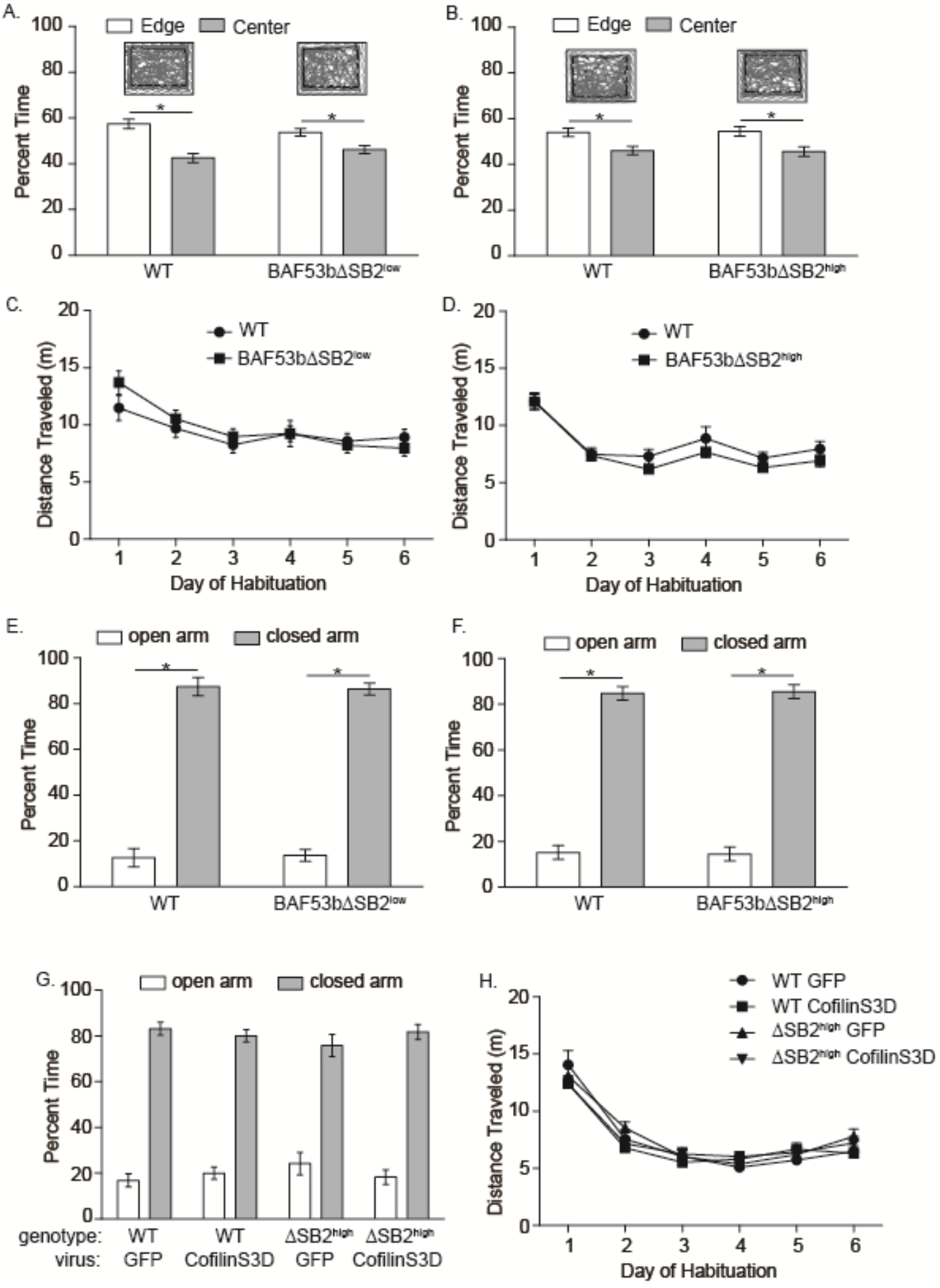
A.
Edge
Center
Percent Time
100
80
60
40
20
0
*
*
WT
BAF53bΔSB2low
B.
Edge
Center
Percent Time
*
*
WT
BAF53bΔSB2high
C.
WT
BAF53bΔSB2low
Distance Traveled (m)
20
15
10
5
0
1
2
3
4
5
6
Day of Habituation
D.
WT
BAF53bΔSB2high
Distance Traveled (m)
Day of Habituation
E.
open arm
closed arm
Percent Time
*
*
WT
BAF53bΔSB2low
F.
open arm
closed arm
Percent Time
*
*
WT
BAF53bΔSB2high
G.
open arm
closed arm
Percent Time
genotype:
virus:
WT
GFP
WT
CofilinS3D
ΔSB2high
GFP
ΔSB2high
CofilinS3D
H.
WT GFP
WT CofilinS3D
ΔSB2high GFP
ΔSB2high CofilinS3D
Distance Traveled (m)
Day of Habituation

Figure S4. BAF53bΔSB2 transgenic mice have normal anxiety and locomotion.
(A) BAF53bΔSB2^{low} (n=14) mice have normal exploration in open field (5min) as compared to wildtype littermates (n=11) (RM-ANOVA, main effect of location $F_{1,23}$=24.58, p<0.0001, genotype $F_{1,23}$=32.86, p<0.001, and no interaction $F_{1,23}$=1.29, p=0.27; bonferroni corrected t-test edge vs. center for WT t(11)=4.07, p<0.001; and BAF53bΔSB2^{low} t(13)=2.88, p<0.05). (B) BAF53bΔSB2^{high} (n=9) mice have normal exploration in open field (5min) as compared to wildtype littermates (n=13) (RM-ANOVA, main effect of location $F_{1,40}$=18.33, p<0.0001, no effect of genotype $F_{1,40}$=0.00, p=1.00, and no interaction $F_{1,40}$=0.06, p=0.81; bonferroni corrected t-test edge vs. center for WT t(12)=3.16, p<0.01; and BAF53bΔSB2^{high} t(8)=2.94, p<0.05). (C) BAF53bΔSB2^{low} (n=9) mice have normal habituation performance as assessed by total distance traveled across days of exposure to an environment (5min/day) as compared to wildtype littermates (n=12) (RM-ANOVA, main effect of day $F_{5,95}$=8.64, p<0.0001 but no effect of genotype $F_{1,19}$=0.46, p=0.51 or interaction $F_{5,95}$=1.02, p=0.41). (D) BAF53bΔSB2^{high} (n=22) mice have normal habituation performance as assessed by total distance traveled across days of exposure to an environment (5min/day) as compared to wildtype littermates (n=23) (RM-ANOVA, main effect of day $F_{5,215}$=34.62, p<0.0001 but no effect of genotype $F_{1,43}$=1.69, p=0.20 or interaction $F_{5,215}$=0.57, p=0.72). (E) BAF53bΔSB2^{low} (n=15) mice exhibit normal levels of anxiety as assessed by the percentage of time spent in the open arm of the elevated plus maze compared to wildtype littermates (n=10) (RM-ANOVA, main effect of arm $F_{1,23}$=264.8, p<0.0001 but no effect of genotype $F_{1,23}$=-5.58, p=1.00 or interaction $F_{1,23}$=0.05, p=0.83) with both genotypes showing a significant preference for the open compared to closed arm (bonferroni corrected t-test t(9)=10.65, p<0.001 and t(14)=12.69, p<0.001 wildtype and mutant respectively). (F) BAF53bΔSB2^{high} (n=9) mice exhibit normal levels of anxiety as assessed by the percentage of time spent in the open arm of the elevated plus maze compared to wildtype littermates (n=9) (RM-ANOVA, main effect of arm $F_{1,16}$=268.0, p<0.0001 but no effect of genotype $F_{1,16}$=2.64, p=0.12 or interaction $F_{1,16}$=0.03, p=0.87) with both genotypes showing a significant preference for the open compared to closed arm (bonferroni corrected t-test t(8)=11.46, p<0.001 and t(8)=11.69, p<0.001 wildtype and mutant respectively). (G) Viral over-expression in adult hippocampus in BAF53bΔSB2^{high} mice (ΔSB2^{high} GFP, n=13 or ΔSB2^{high} cofilinS3D, n=18) produces similar behavior on the elevated plus maze as wildtype littermates with either AAV-GFP (WT GFP, n=14) or AAV-cofilinS3D (WT cofilinS3D, n=16) expression in dorsal hippocampus. Two-way RM-ANOVA, main effect of arm $F_{1,57}$=306.43, p<0.0001 but no effect of genotype/virus $F_{3,57}$=0.00, p=1.00 or interaction $F_{3,57}$=0.77, p=0.52 with all genotype/virus combinations showing a significant preference for the open compared to closed arm. Bonferroni corrected t-test: WT GFP t(13)=9.29, p<0.001; WT cofilinS3D t(15)=8.99, p<0.001; ΔSB2^{high} GFP t(12)=6.97, p<0.001; and ΔSB2^{high} cofilinS3D t(17)=10.06, p<0.001. (H) Viral over-expression in adult hippocampus in BAF53bΔSB2^{high} mice (ΔSB2^{high} GFP, n=13 or ΔSB2^{high} cofilinS3D, n=18) produces similar habituation across days of exposure to a context as in wildtype littermates with either AAV-GFP (WT GFP, n=14) or AAV-cofilinS3D (WT cofilinS3D, n=16) expression in dorsal hippocampus. Two-way RM-ANOVA, main effect of day $F_{5,285}$=102.36, p<0.0001 but no effect of genotype/virus $F_{3,57}$=0.31, p=0.82 or interaction $F_{15,285}$=1.14, p=0.32. Mean +/- SEM.

PDB ID	Chain ID	Source Organism	Res.	BAF53a Cov	BAF53a Ident	BAF53a Pos	BAF53b Cov	BAF53b Ident	BAF53b Pos	ΔSB2 Cov	ΔSB2 Ident	ΔSB2 Pos
1C0F	**A**	*Dictyostelium Discoideum*	2.40	98%	36%	54%	98%	37%	54%	98%	39%	55%
4EFH	**A**	*Acanthamoeba Castellanii*	2.48	98%	37%	54%	98%	38%	55%	98%	38%	54%
3CHW	**A**	*Dictyostelium Discoideum*	2.30	98%	36%	54%	98%	38%	55%	98%	38%	54%
1NLV	**A**	*Dictyostelium Discoideum*	1.80	98%	36%	54%	98%	37%	55%	98%	38%	54%
3CI5	**A**	*Dictyostelium Discoideum*	1.70	98%	36%	54%	98%	37%	55%	98%	38%	54%
1C0G	**A**	*Dictyostelium Discoideum*	2.00	98%	36%	54%	98%	38%	55%	98%	38%	54%
1DEJ	**A**	*Dictyostelium Discoideum*	2.40	98%	36%	54%	98%	38%	55%	98%	38%	54%
3MN5	**A**	*Oryctolagus Cuniculus*	1.50	97%	35%	53%	97%	37%	54%	97%	39%	55%
1KXP	**A**	*Oryctolagus Cuniculus*	2.10	97%	36%	53%	97%	38%	54%	97%	38%	54%
3A5L	**C**	*Dictyostelium Discoideum*	2.40	98%	36%	54%	98%	37%	55%	98%	38%	54%
1IJJ	**A**	*Oryctolagus Cuniculus*	2.85	97%	36%	53%	97%	38%	54%	97%	38%	54%
4B1V	**A**	*Oryctolagus Cuniculus*	1.75	97%	36%	53%	97%	38%	54%	97%	38%	54%
3A5M	**C**	*Dictyostelium Discoideum*	2.40	98%	36%	54%	98%	37%	55%	98%	38%	54%
1QZ5	**A**	*Oryctolagus Cuniculus*	1.45	97%	36%	53%	97%	38%	54%	97%	38%	54%
1EQY	**A**	*Oryctolagus Cuniculus*	2.30	97%	36%	53%	97%	38%	54%	97%	38%	54%
1YVN	**A**	*Saccharomyces Cerevisiae*	2.10	97%	36%	54%	97%	37%	55%	97%	37%	54%
1D4X	**A**	*Caenorhabditis Elegans*	1.75	97%	36%	54%	97%	37%	54%	97%	38%	54%
4B1W	**B**	*Oryctolagus Cuniculus*	1.95	97%	35%	53%	97%	37%	54%	97%	38%	54%
2OAN	**A**	*Bos Taurus*	2.61	97%	35%	54%	97%	37%	54%	97%	37%	54%
3U4L	**A**	*Bos Taurus*	2.40	97%	35%	54%	97%	37%	54%	97%	37%	54%
1YAG	**A**	*Saccharomyces Cerevisiae*	1.90	97%	36%	54%	97%	37%	55%	97%	37%	54%
1T44	**A**	*Oryctolagus Cuniculus*	2.00	96%	36%	53%	96%	38%	54%	96%	38%	54%
2BTF	**A**	*Bos Taurus*	2.55	97%	35%	53%	97%	37%	54%	97%	37%	53%
1LCU	**A**	*Oryctolagus Cuniculus*	3.50	96%	36%	54%	96%	36%	54%	96%	38%	54%
2GWJ	**A**	*Oryctolagus Cuniculus*	1.90	96%	36%	53%	96%	38%	54%	96%	38%	54%

4CBU	**A**	*Plasmodium Falciparum*	1.30	99%	34%	54%	99%	34%	54%	99%	34%	53%
3W3D	**A**	*Gallus Gallus*	1.80	97%	35%	53%	97%	37%	54%	97%	37%	53%
4CBW	**A**	*Plasmodium Berghei*	2.50	98%	34%	54%	98%	35%	55%	98%	36%	54%
1ATN	**A**	*Oryctolagus Cuniculus*	2.80	97%	35%	53%	97%	37%	54%	97%	38%	53%
4JHD	**B**	*Drosophila Melanogaster*	2.91	97%	35%	53%	97%	37%	54%	97%	37%	53%
3M6G	**A**	*Oryctolagus Cuniculus*	2.00	96%	35%	53%	96%	37%	54%	96%	38%	54%
2HF3	**A**	*Drosophila Melanogaster*	1.80	97%	35%	53%	97%	36%	54%	97%	37%	53%
4JHD	**A**	*Drosophila Melanogaster*	2.91	97%	35%	53%	97%	36%	54%	97%	37%	53%
3EKS	**A**	*Drosophila Melanogaster*	1.80	97%	35%	53%	97%	36%	54%	97%	37%	53%
4M63	**C**	*Drosophila Melanogaster*	2.75	97%	35%	53%	97%	36%	53%	97%	37%	53%
4CBX	**A**	*Plasmodium Berghei*	2.20	97%	35%	53%	97%	35%	53%	97%	35%	54%

Table S1. **Description of the thirty-six Actin structures used as templates to predict BAF53a, BAF53b wildtype and BAF53bΔSB2 3D structures.**

The PDB entry identifier, the chain identifier, the source organism, and the X-ray crystallography resolution are reported in the left-most four columns respectively. The percentage of amino acids in the protein sequence covered by the alignment (Cov), the percentage of identical amino acids (Ident) and positive substitutions (Pos) between the aligned sequences are shown for the blast alignments between the Actin protein sequences and BAF53a, BAF53b and the BAF53bΔSB2 mutant construct protein sequences.