SUPPLEMENTAL FIGURE LEGENDS

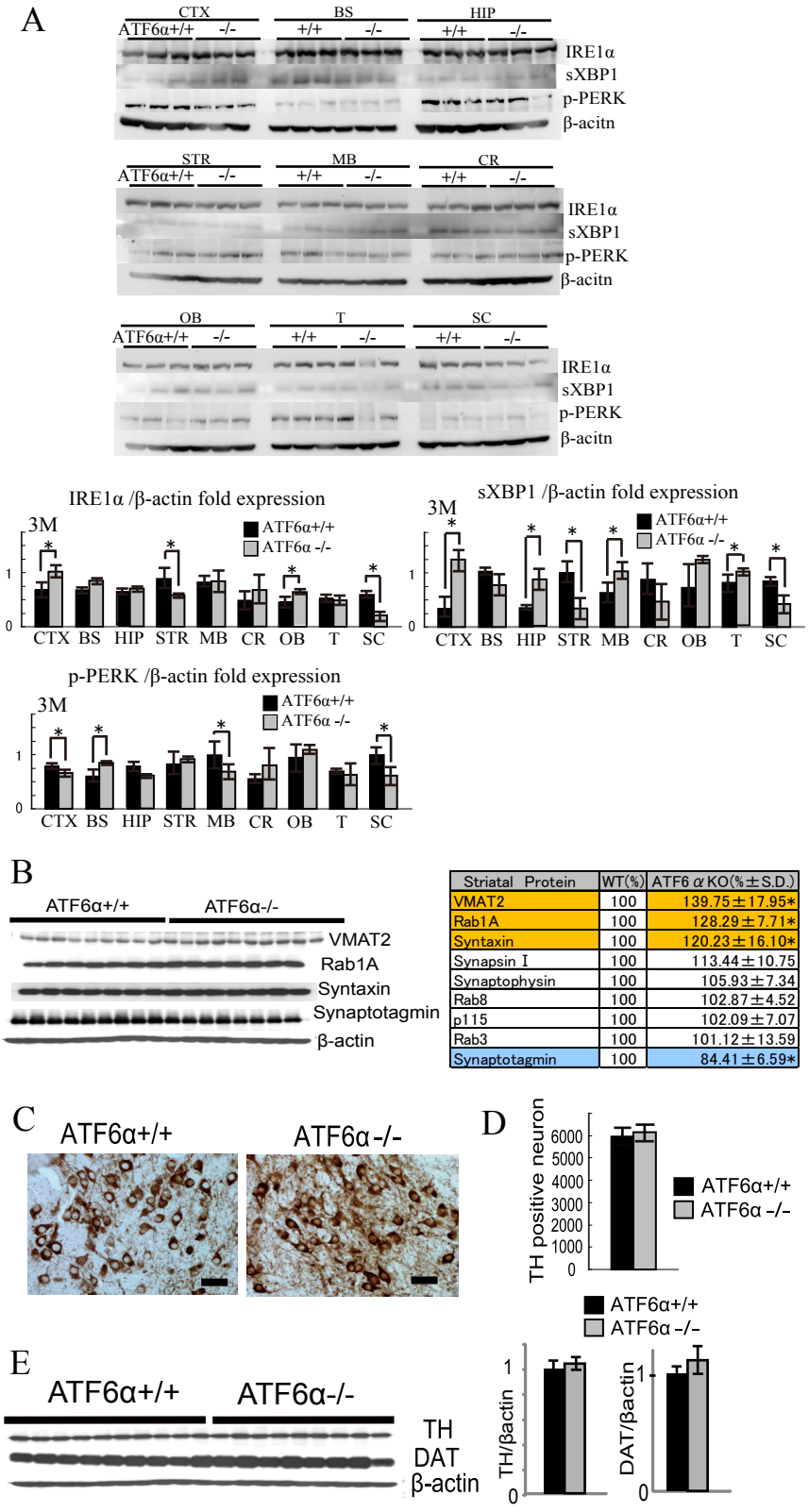
Figure S1. (A) ER stress sensors, IRE1α, sXBP1 and p-PERK are not different in various brain regions of ATF6α KO mice under physiological conditions *in vivo*. The tissue lysates of 3 month-aged ATF6α KO mice and ATF6α WT littermate were subjected to western blot analysis for detection of IRE1α, sXBP1, p-PERK and β-actin (n= 5). Each protein level was quantified using optical density and estimated relative to β-actin protein level. Abbreviation: CTX, cerebral cortex; BS, brainstem; HIP, hippocampus; STR, striatum; MB, midbrain; CR, cerebellum; OB, olfactory bulb; T, thalamus; SC, spinal cord; 3M, 3 months aged group. Asterisk indicates statistical significance (*p<0.05, **p<0.01). Each bar denotes the mean ± S.D. **(B)** Comparative analysis of levels of protein involved in synaptic secretion and vesicular transport between ATF6 α WT (+/+) an d KO (-/-) mice. Protein levels of VMAT2, Rab1A and Syntaxin were significantly increased in ATF6α KO mice as compared with those of WT mice. Protein levels in the striatum of 12 month-aged ATF6α WT and KO mice were measured by quantitative immunoblotting using image-J densitometry and the values relative to β-actin were compared with those of WT mice. (Each group, n=7-10) Abbreviation: VMAT2, Vesicular Monoamine Transporter 2. **(C-E)** ATF6α is not essential for the development and the survival of dopaminergic neurons. 12 month-o ld male ATF6 α KO (-/-) mice and ATF6α WT (+/+) littermates were used for comparative analysis. Each bar denotes the mean ± S.D. **(C)** Representative TH staining of coronal midbrain sections of ATF6α KO and ATF6α WT mice. Scale bar indicates 50μm. **(D)** The number of TH-positive neurons in the SNc of ATF6α KO and ATF6α WT mice (n= 5 for each group). **(E)** Immunoblot analysis of the striatum tissue lysates of ATF6α KO and ATF6α WT mice for detection of TH and DAT (n= 9-10). Each protein level was quantified using optical density. Abbreviation: TH, Tyrosine hydroxylase; DAT, dopamine transporter.

Figure S2. (A) Hydrogen peroxide (H_2O_2)–induced oxidative stress induced phosphorylation of p38MAPK and cleavage of pATF6α (P) to produce pATF6α(N). Immunoblot of cell lysates from ATF6α WT (+/+) and ATF6α KO (-/-) mice embryonic fibroblasts (MEFs) treated with 50 μM H_2O_2 for 60, 120, 240 mins using antibodies against ATF6α, p38MAPK, phosphorylated p38MAPK (p-p38MAPK) and β-actin. 5 μM SB203585 was added into the medium prior to H_2O_2 treatment as indicated. **(B)** There was no aggregate stained with 1% Thioflavin T (dye for amyloid) and no accumulated material immunostained with anti-α-synuclein antibody or anti-phosphorylated α-synuclein (P-α-synuclein) antibody. **(C)** Representative images of primary co-cultured dopaminergic neurons derived from the midbrain and the striatum of the embryonic day 15 ATF6α WT/KO mice. Primary cultured cells were immunostained with DAPI, anti-Tuj1 (neuronal marker) antibody and anti-TH antibody. Scale bars indicate 100μm. Abbreviation: BF, bright-field image; TH, Tyrosine hydroxylase.

Figure S3. (A-C) MPP^+ induces release of N-terminal ATF6α fragment with subsequent translocation into the nucleus and colocalization with phosphorylated p38MAPK. SH-SY5Y cells were transfected with p38MAPK and pGFP-ATF6α (P) for 24 hours and then immunostained with anti-p38MAPK antibody **(A, red)** and DAPI **(A, blue)**. After transfection SH-SY5Y cells were treated with 1mM MPP^+ for 24 hours, fixed and stained with anti-p38MAPK antibody **(B, red)** or anti-phosphorylated p38MAPK (p-p38MAPK) antibody **(C, red)** and DAPI (blue). Scale bars indicate 10 μm. **(D-G)** Hydrogen peroxide (H_2O_2) induces release of N-terminal ATF6α fragment with subsequent translocation into the nucleus and colocalization with phosphorylated p38MAPK. HEK293T cells were transfected with p38MAPK and pGFP-ATF6α (P) for 24 hours and then immunostained with anti-p38MAPK antibody **(D, red)** or anti-p-p38MAPK antibody **(E, red)**. After transfection HEK293T cells were treated with 50 μM H_2O_2 for 60 mins, fixed and stained with anti-p38MAPK antibody **(F, red)** or anti-p-p38MAPK antibody **(G, red)**. Scale bars indicate 10 μm. **(H)** H_2O_2 treatment

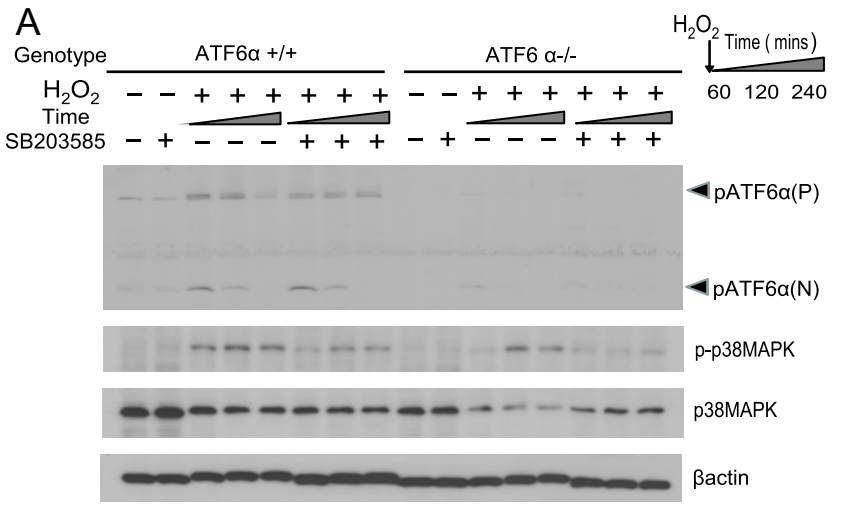
enhances the binding of N-terminal fragment of ATF6α with p-p38MAPK. HEK293T cells were transfected with 2 μg flag-p38MAPK vector and 2 μg N-terminal fragment of ATF6α (1-373) vector; they were then cultured with or without 50 μM H_2O_2 in the presence or absence of 5 μM SB203585 for 60 mins. Each lysates were immunoprecipitated with anti-flag antibody **(Upper panel)** or anti-p-p38MAPK antibody **(Middle panel)** and immunoblotted with an anti-ATF6α antibody. Western blot analysis of 10 % input lysates were performed with anti-ATF6α, p-p38MAPK, p38MAPK and β-actin antibodies **(Lower panels)**. Abbreviation: IP, immunoprecipitation; IB, immunoblotting; SB, SB203585; N-ATF6α, N-terminal fragment of ATF6α (1-373). **(I and J)** p38MAPK phosphorylation enhances the transcriptional activity of ATF6α. **(I)** Vectors(1 μg ERSE reporter carrying BiP promoter-Luciferase vector, 100ng pRL-SV40 vector and 1 μg control vector or p38MAPK vector) were mixed with 1 μg Mock(pcDNA-3.1(+)) or N-terminal fragment (1-373)(N-ATF6α) or dominant-negative form (171-373)(ATF6α-DN) of ATF6α vector for transfection of HEK293T cells in a 6-well dish for 48 h. HEK293T cells were challenged with or without 50 μM H_2O_2 for 1 h and lysed for analysis of BiP reporter expression. Each bar denotes the mean ± S.D. **(J)** Vectors (1 μg 5×UPRE reporter vector, 100ng pRL-SV40 vector and 1 μg control vector or p38MAPK vector) were mixed with 1 μg Mock (pcDNA-3.1(+)) or N-ATF6α or ATF6α-DN vector for transfection of HEK293T cells in a 6-well dish for 48 h. 293T cells were challenged with or without 50 μM H_2O_2 for 1 h and lysed for analysis of UPRE reporter expression.

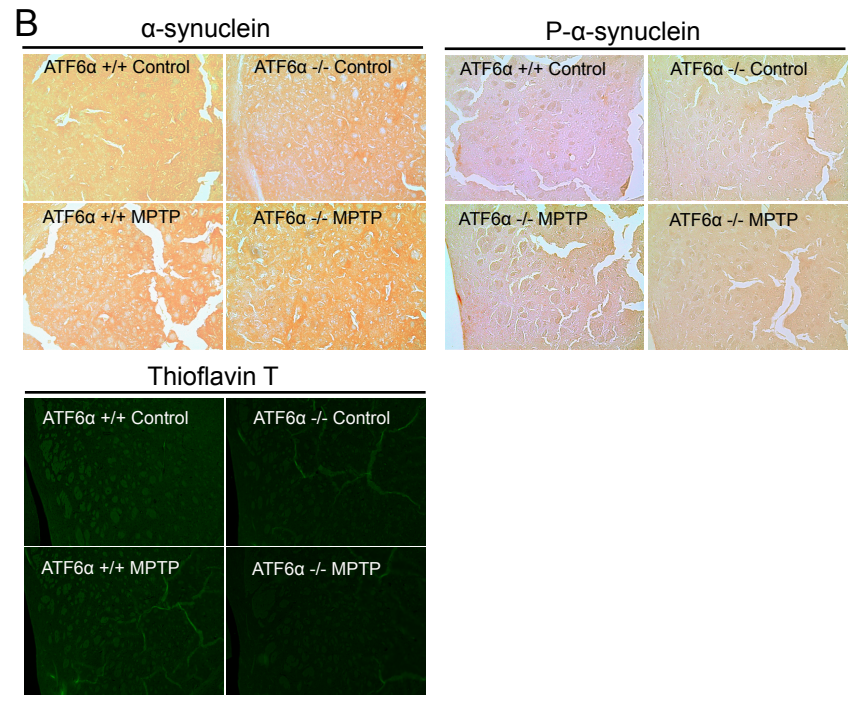
Supplemental Figure 1

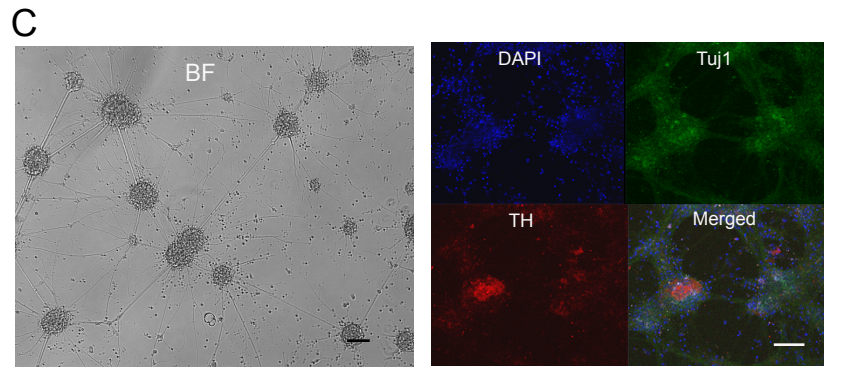


Striatal Protein	WT(%)	ATF6αKO(%±S.D.)
VMAT2	100	139.75±17.95*
Rab1A	100	128.29±7.71*
Syntaxin	100	120.23±16.10*
Synapsin I	100	113.44±10.75
Synaptophysin	100	105.93±7.34
Rab8	100	102.87±4.52
p115	100	102.09±7.07
Rab3	100	101.12±13.59
Synaptotagmin	100	84.41±6.59*

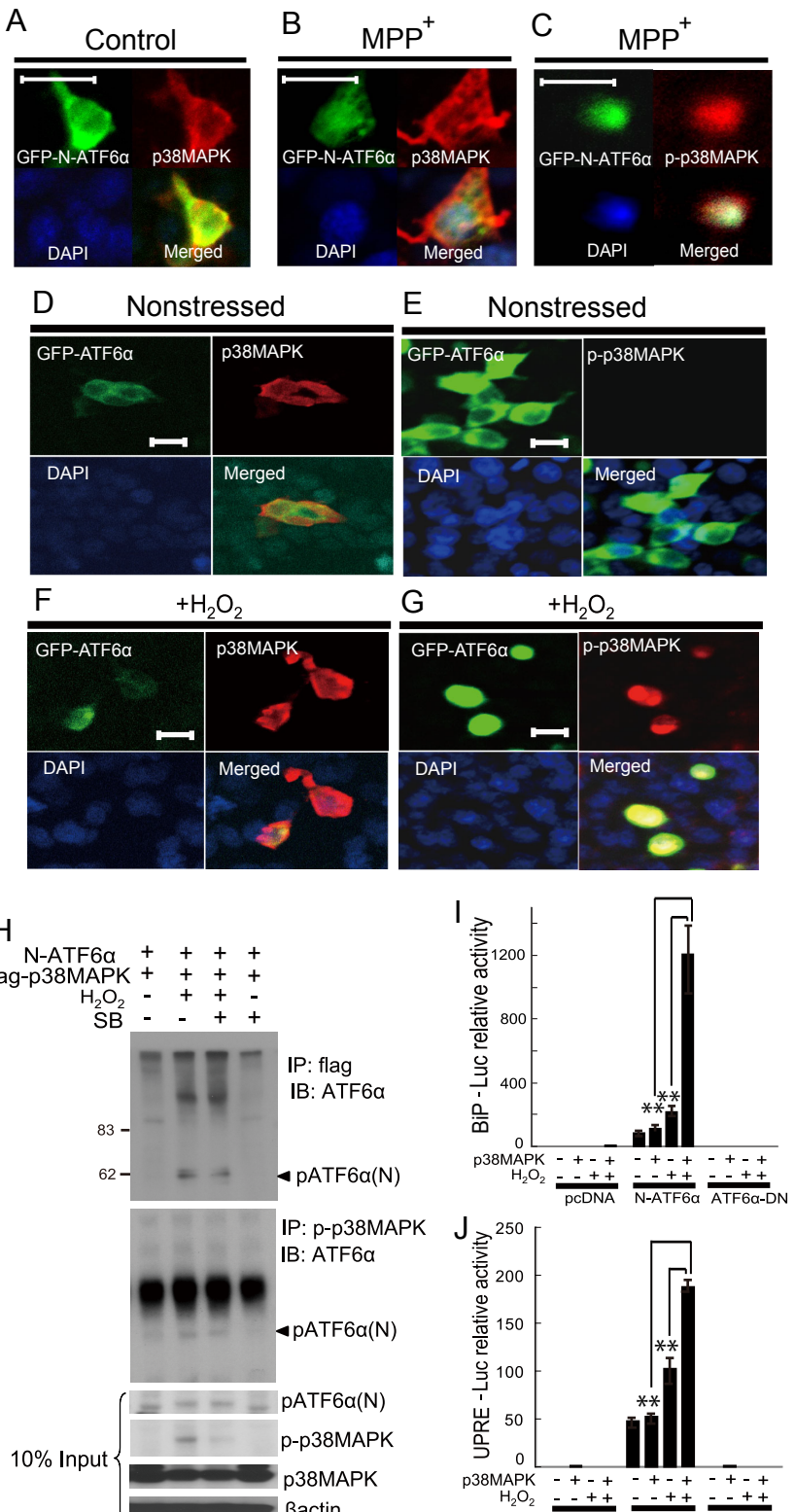
Supplemental Figure 2







Supplemental Figure 3



Supplemental Table 1

The List of the Primers and the Sequences

Primer for	Sequences
BiP forward	5’-ACTTGGAATGACCCTACGGTG-3’
BiP reverse	5’-TGCTTGTCGCTGGGCATC-3’
ATF6α forward	5’-TTATCAGCATACAGCCTGCG-3’
ATF6α reverse	5’- CTTGGGACTTTGAGCCTCTG-3’
GRP94 forward	5’- CTGGGTCAAGCAGAAAGGAG-3’
GRP94 reverse	5’-TGCCAGACCATCCATACTGA-3’
$p58^{IPK}$ forward	5’-GAAGCATCTTGAATTGGGGA-3’
$p58^{IPK}$ reverse	5’-CAAGCTTCCCTTGTTTGAGC-3’
Derlin-3 forward	5’-ATGCTGGAGGAGGGTTCTTT-3’
Derlin-3 reverse	5’-AGTGCTGTCAGAGTGGGCTT-3’
GAPDH forward	5’-CCCCACTAACATCAAATGGG-3’
GAPDH reverse	5’-CCATCCACAGTCTTCTGGGT-3’
endogenous human BiP promoter forward	5’-AGTGACGTTTATTGCGGAGG-3’
endogenous human BiP promoter reverse	5’-TTATATACCCTCCCCCAGCC-3’
endogenous human GAPDH forward	5’-CTTCGTATGACTGGGGGTGT-3’
endogenous human GAPDH reverse	5’-TTGAGGTCAATGAAGGGGTC-3’
endogenous human Ngn2 promoter forward	5’-CAGGACTGACAGGAGGAGGA-3’
endogenous human Ngn2 promoter reverse	5’- GTCTCGTGTGTTGTGGTGGT-3’