Table S1. Target sequences for generation of *atg5* or *atg7* siRNAs

siRNA construct	Target sequences (5′–3′)
atg5	
Construct 1	CAACGTGCTTTACTCTCTA
Construct 2	TGAGATAACTGAACGAGAA
Construct 3	ATCTGAGCTATCCAGACAA
Scrambled	GTCCCGGATACCTAATAAA
atg7	
Construct 1	ACTACAATGGTGACTCTGC
Construct 2	CTCAAGCTGATGTGCTGGC
Construct 3	TACTGTTATTGCAGCCAGC
Scrambled	GGATCGCTGGCGCTATCTA

Figure Legends

Figure S1. Quantification of survival of mature cortical neurons expressing the FTD3-associated mutant protein CHMP2B^{Intron5} with or without 10 μM Wortmannin, another inhibitor of PI3 kinases. The values are mean ± SEM from three or four independent experiments. *** $P < 0.001$ as determined by ANOVA with Newman-Keuls multiple test.

Figure S2. 3-MA prevents the increase in endogenous LC3-II levels as a result of reduced mSnf7-2 function in mature cortical neurons, indicating an inhibition of autophagosome formation.

Figure S3. Atg5 knockdown by siRNA delayed dysfunctional ESCRT-III-induced neuronal cell loss. (A) Testing *atg5* siRNA efficiency. #3 was used for the following experiments. (B) An image of cultured rat cortical neurons 3 days after transfection with scrambled siRNA. (C) Mature cortical neurons 3 days after transfection with *mSnf7-2* siRNA show extensive neuronal cell loss. (D) Knockdown of Atg5 activity by siRNA increases the survival of cortical neurons with reduced mSnf7-2 activity. (E) Expression of CHMP2B^{Intron5} led to extensive neuronal cell loss in cultured wildtype rat cortical neurons. (F) Knockdown of Atg5 activity by siRNA increases the survival of cortical neurons expressing CHMP2B^{Intron5}. (G) Quantification of survival of mature cortical neurons expressing the FTD3-associated mutant protein CHMP2B^{Intron5} or lacking mSnf7-2 activity with or without the transfection of *atg5* siRNA. The values are mean ± SEM from three independent experiments. * $P < 0.05$, *** $P < 0.001$ as determined by ANOVA with Newman-Keuls multiple test. Bar for B–F, 50 μm.

Figure S4. Loss of Atg5 activity blocks the formation of autophagosomes in response to starvation. (A) Autophagosome accumulation in starved mouse cortical neurons as indicated by the GFP-LC3 marker. (B) EM analysis shows the accumulation of autophagosomes in starved mouse cortical neurons. To starve mature neurons, neurons were incubated in Earle's balanced salt solution which doesn't have any growth factors or glucose for 24 h. (C) *atg5* knockout neurons failed to show the accumulation of GFP-LC3-positive autophagosomes in response to starvation. (D) EM analysis shows the absence of autophagosomes in *atg5* knockout neurons under the starvation condition. Bars in A and C, 10 μm. Bars in B and D, 1μm.