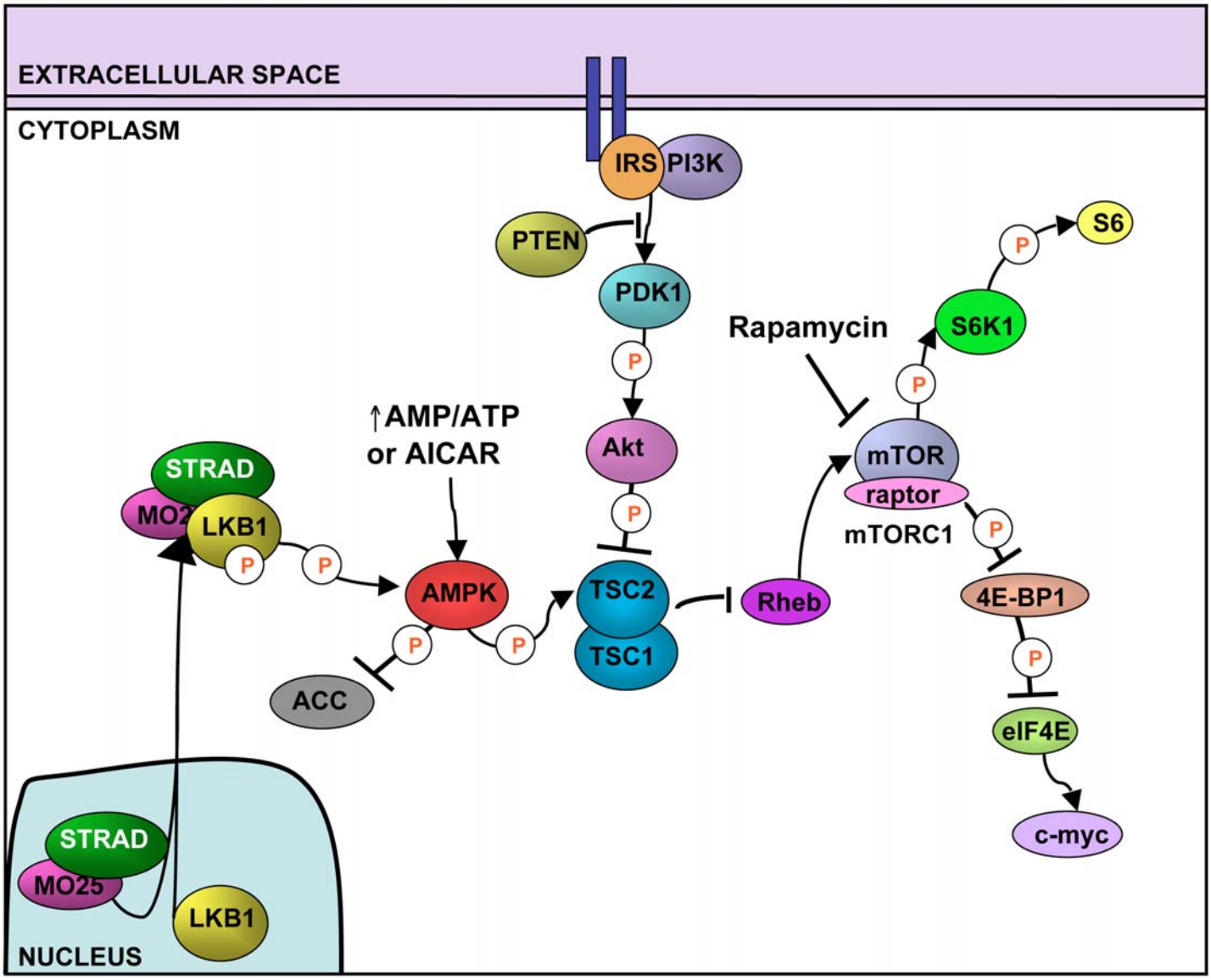
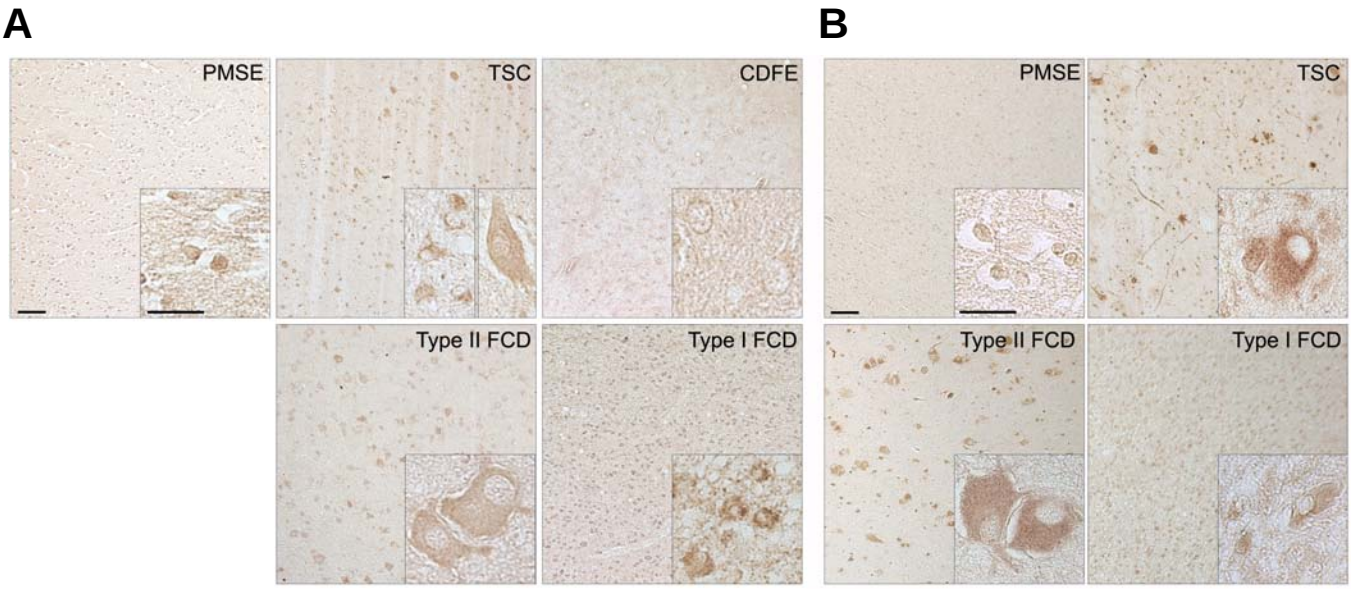
Supplemental Information

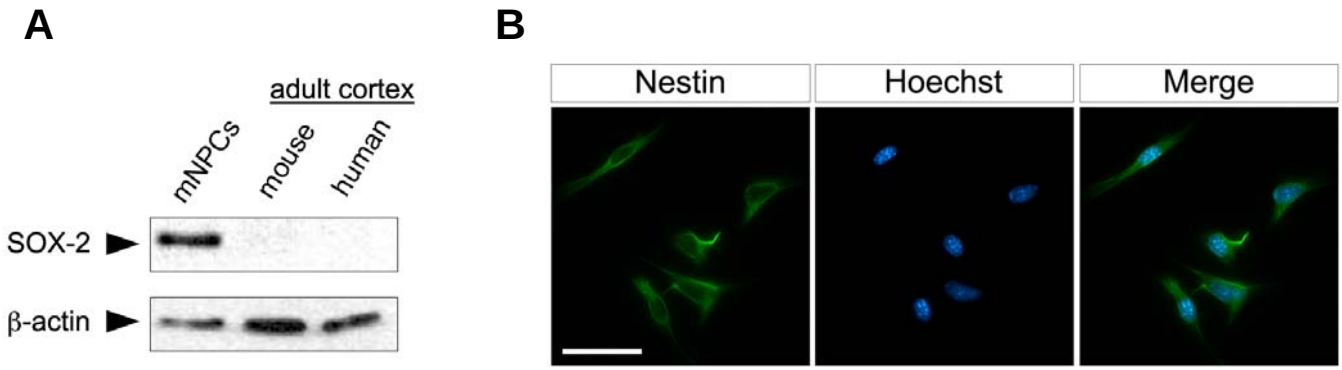
Supplementary Figures



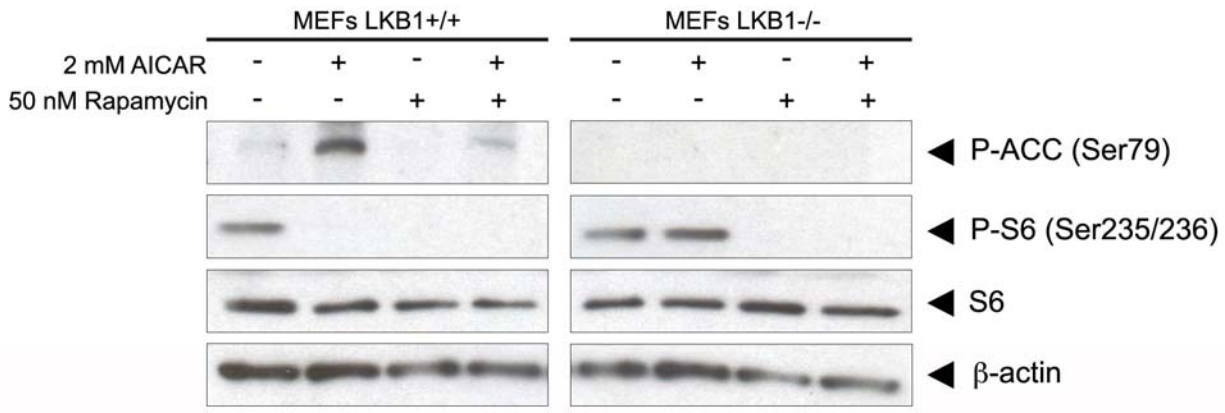
Supplemental Figure 1. LKB1:STRADα and mTORC1 signaling



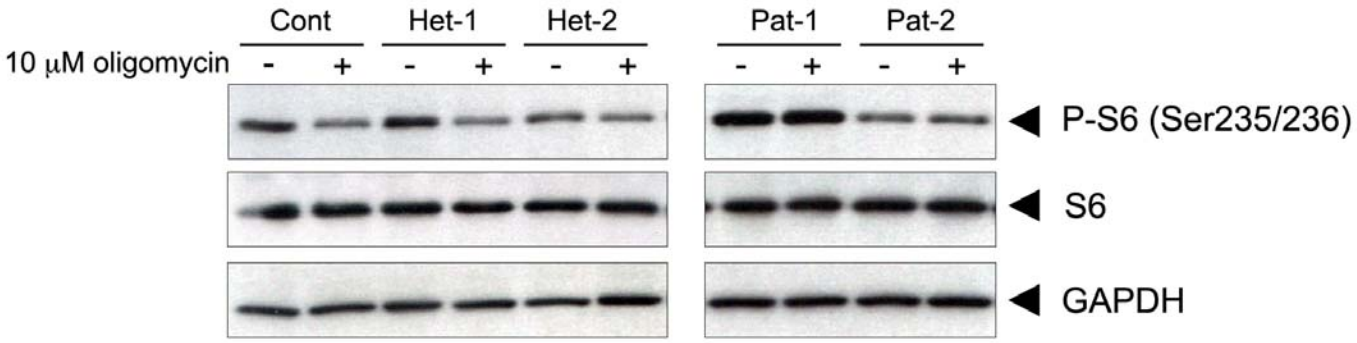
Supplemental Figure 2. Cortical neurons in PMSE exhibit exclusively nuclear LKB1 (**A**) Immunostaining for LKB1 using rabbit antiserum to LKB1 (Novus) in cortical specimens from PMSE, Tuberous Sclerosis Complex (TSC), Cortical Dysplasia Focal Epilepsy syndrome (CDFE), sporadic Type II Focal Cortical Dysplasia (Type II FCD), and sporadic Type I Focal Cortical Dysplasia (Type I FCD). (**B**) Immunostaining for LKB1 using rabbit antiserum to LKB1 (Santa Cruz) in cortical specimens from PMSE, Tuberous Sclerosis Complex (TSC), sporadic Type II Focal Cortical Dysplasia (Type II FCD), and sporadic Type I Focal Cortical Dysplasia (Type I FCD). Scale bars in **A** and **B** represent 100 μm, inset: 25 μm.



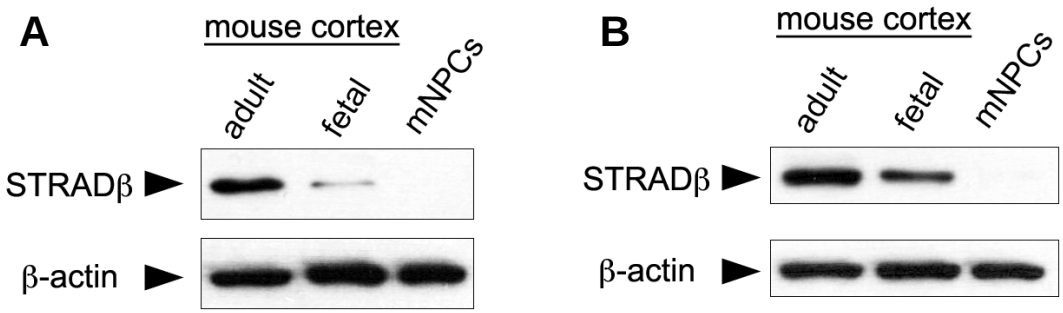
Supplemental Figure 3. Characterization of mouse neural progenitor cells (mNPCs). (**A**) Immunoblotting of mNPCs lysates, adult mouse cortex, and adult human cortex for SOX-2 expression. The blot was reprobed for β-actin to assess equal loading. (**B**) Immunostaining of mNPCs for nestin (green). Cells were counterstained with Hoechst to visualize the nuclei (blue). Scale bar represents 50 μm.



Supplemental Figure 4. LKB1-null mouse embryonic fibroblasts (MEFs) fail to activate AMPK or suppress phosphorylation of S6 following AICAR treatment in a rapamycin-dependent manner. Wild-type and LKB1-null MEFs were serum starved and treated with either AICAR, rapamycin, or AICAR followed by rapamycin. Western blot analysis for phospho-acetyl-CoA carboxylase (P-ACC, Ser79) shows that LKB1-null MEFs fail to activate AMPK following AICAR treatment, in contrast to wild-type MEFs. Immunoblotting for P-S6 (Ser235/236) reveals that unlike wild-type MEFs, LKB1-null MEFs cannot attenuate P-S6 levels following AICAR treatment. Rapamycin application following AICAR addition results in decreased P-S6 levels in LKB1-null MEFs, consistent with an mTORC1-dependent mechanism. Immunoblotting for total S6 protein reveals stable S6 expression in all cell types and treatment conditions. Blots were reprobed for β-actin to assess equal loading.



Supplemental Figure 5. Lymphoblastoid cell lines (LCLs) from PMSE patients fail to attenuate P-S6 levels following oligomycin treatment. LCLs established from controls (Cont), heterozygous parents (Het-1, Het-2), and PMSE patients (Pat-1, Pat-2) were treated with oligomycin for 3 hours and the phosphorylation status of S6 (Ser235/236) was assessed by immunoblotting. LCLs from PMSE patients fail to attenuate P-S6 levels following oligomycin treatment, in contrast to controls and heterozygotes. Immunoblotting for total S6 protein reveals stable S6 expression in all cell types and treatment conditions. Blots were reprobed with GAPDH to assess equal loading. All LCLs were first pre-treated with an CaMKK inhibitor STO-609 in order to evaluate LKB1-dependent AMPK activation and subsequent inhibition of mTORC1.



Supplemental Figure 6. STRADβ is expressed in mouse adult and fetal cortex, but not in mouse neural progenitor cells (mNPCs). Immunoblotting for STRADβ with two different antibodies, **(A)** AnaSpec and **(B)** Abcam, reveals STRADβ expression in mouse adult and fetal cortex, but not in mNPC. Blots were reprobed with β-actin to assess equal loading.