Supplemental Fig 1. Akt binds SRPK2 in vitro and in vivo. *A.* Akt kinase activity is necessary for its binding to SRPK2. Myc-SRPK2 was cotransfected into HEK293 cells with various Akt constructs. SRPK2 was immunoprecipitated with anti-Myc antibody, and the associated proteins were analyzed by immunoblotting with anti-HA antibody. Wild-type and CA Akt (T308DS473D) strongly bound to SRPK2, whereas kinase-dead Akt KD (K179A) and KD* (T308DS473DK179A) weakly associated with SRPK2 (top panel). The transfected constructs were verified (middle and bottom panels). *B.* The N-terminal PH and C-terminal regulatory domains of Akt implicate in binding to SRPK2. Myc-SRPK2 was cotransfected into HEK293 cells with various GST-Akt fragments. Akt was pulled down with glutathione beads and the coprecipitated proteins were monitored by immunoblotting (top panel). *C.* Akt phosphorylation of SRPK2 is required for its association with Akt. Cortical neurons were pretreated with various inhibitors for 30 min, followed by EGF for 10 min. Endogenous SRPK2 was immunoprecipitated and the coprecipitated Akt was monitored by immunoblotting analysis. *D.* SRPK2 phosphorylation is indispensable for its interaction with Akt. Various Myc-SRPK2 constructs were cotransfected into HEK293 cells with HA-Akt. Transfected SRPK2 was immunoprecipitated and the coprecipitated Akt was monitored by immunoblotting analysis. T492D strongly bound to Akt, while T492A failed (top panel). The cotransfected constructs was verified by immunoblotting (middle and bottom panels).

Supplemental Fig 2. Active Akt provokes endogenous SRPK2 nuclear translocation. HEK293 cells were transfected with various Akt contructs or treated with EGF in the presence or absence of wortmannin. Endogenous SRPK2 and its phosphorylation was monitored by Immunofluorescent staining. Akt-CA strongly provoked endogenous SRPK2 nuclear translocation (A). EGF-stimulated SRPK2 nuclear translocation was blocked by wortmannin pretreatment (B). *C,* SRPK2 phosphorylation mimetic mutant T492D resides in the nucleus. Wild-type SRPK2 mainly localized in the cytoplasm, and a portion of it also distributed in the nucleus, whereas KD and T492A mutants resided in the cytoplasm. T492D mutant predominantly mainly localized in the nucleus.

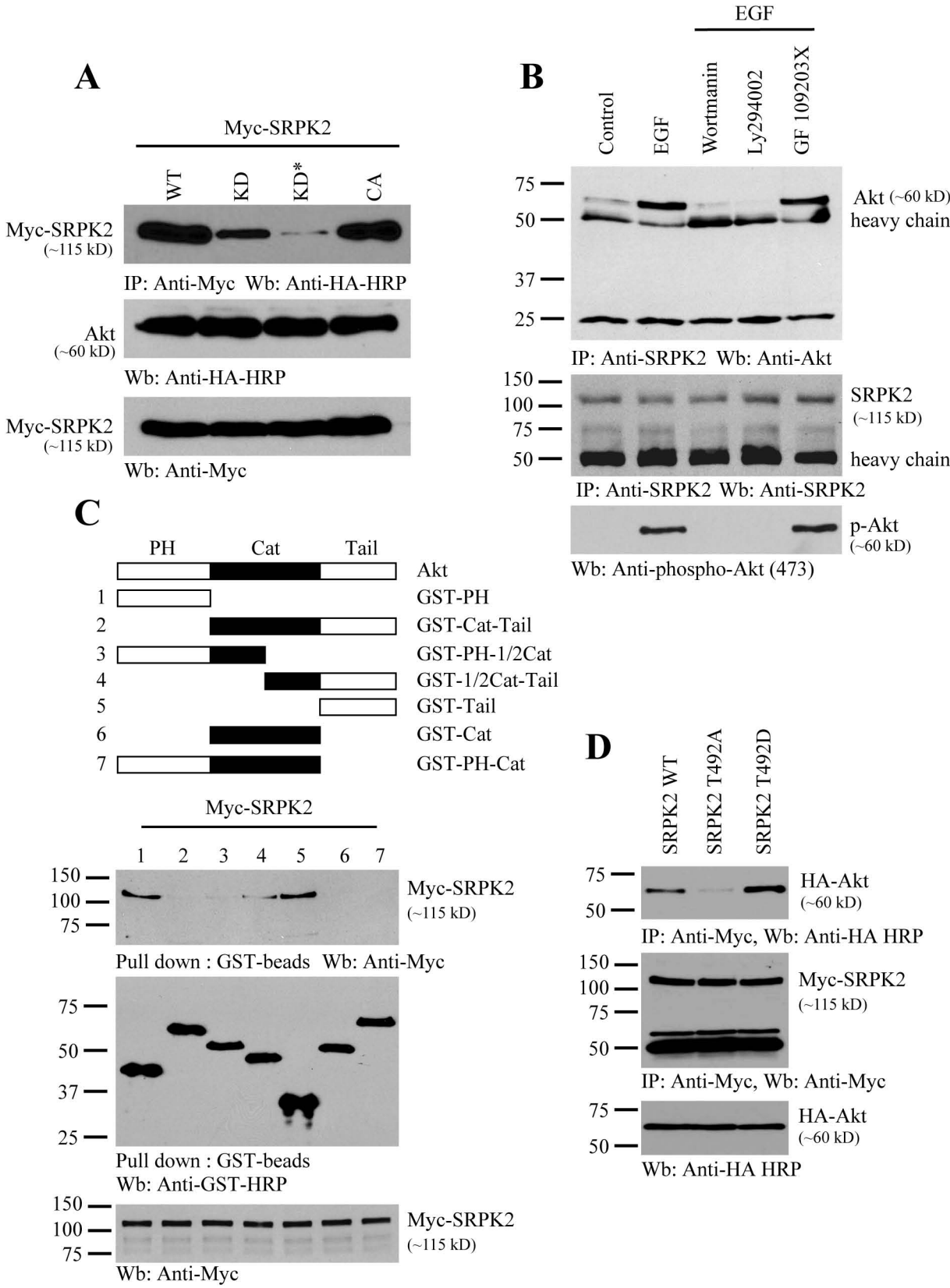
Supplemental Fig 3. SRPK2 mediates cyclin D1 nuclear location in cortical neurons. Cortical neurons were infected with various SRPK2 constructs, respectively. After 4 day, neurons were fixed with 3.7% paraformaldehyde and stained with anti-cyclin D1 and anti-MAP2 antibodies. SRPK2 wild-type and T492D mutant strongly elevated cyclin D1 nuclear location. The nuclear localized cyclin D1 is indicated with white arrows (lower panel).

Supplemental Fig 4. *A,* Cdk4 inhibitor has no effect on cyclin D1/Cdk4 expression, but it blocks its kinase activity and prevents apoptosis. Cortical neurons were infected with various SRPK2 proteins and treated with Cdk4 inhibitor (76 nM). The lysates were assessed by western blotting with antibodies against indicated proteins. DNA fragmentation was also conducted to verify apoptosis (bottom panel). *B.* The control cdk2 inhibitor has no effect on cyclin D1/cdk4 expression and fails to block apoptosis. Cortical neurons were infected with various SRPK2 proteins and treated with Cdk2 inhibitor (60 nM). The lysates were assessed by western blotting using antibodies against indicated proteins. DNA fragmentation was also conducted to verify apoptosis (bottom panel).

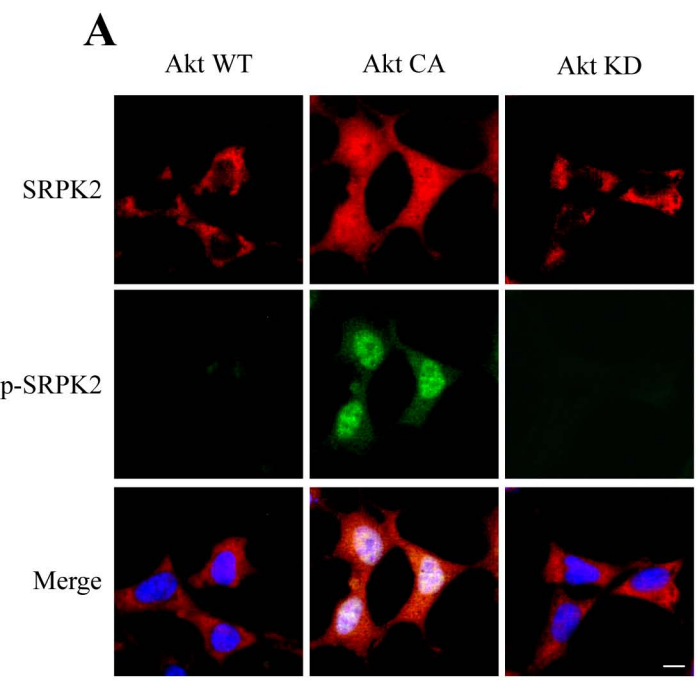
Supplemental Fig 5. Akt regulates SRPK2/cyclin D1 expression in MEF cells. Akt is required for SRPK2 and cyclin D1/Cdk4 expression. Wild-type, Akt 1 knockout, Akt 2 knockout, and Akt1/2 double knockout MEF cells were analyzed by western blotting. Compared to wild-type MEF cells, SRPK2 expression was decreased in Akt1 or Akt2 depleted cells, and it was almost not detectable in Akt1 and 2 double knockout cells (top panel). Cyclin D1 was dramatically attenuated in both Akt 1 and Akt2 null cells, and it was completely repressed in double knockout cells (4^{th} panel). Cdk4 was demonstrable in wild-type MEF cells, but it was not detectable in any of Akt null cells (bottom panel). Although Akt 1 and Akt 2 exhibited a slightly different effect on cyclin B1 expression, Cyclin B1 was completely abolished in double knockout cells (5^{th} panel).

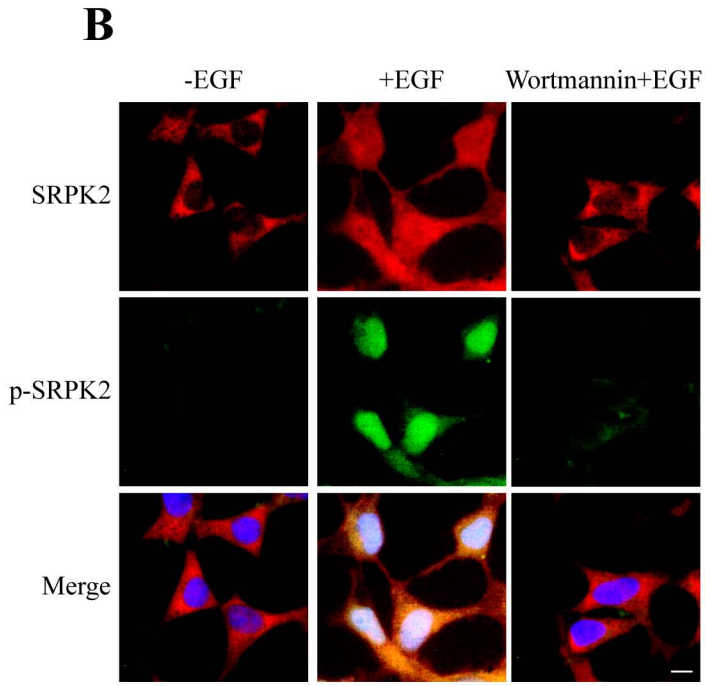
Supplemental Fig 6. Acinus does not regulate cyclin D1 expression in neurons. Primary cortical neuronal cultures were infected with various SRPK2 and acinus lentivirus. In 24 h, the cell lysates were analyzed by immunoblotting with various antibodies. Wild-type SRPK2 and T492D but not T492A provoked cyclin D1 expression, whereas wild-type acinus, S422D (SRPK2 phosphorylation mimetic mutant) or S422A (unphosphorylable mutant) proteins failed to trigger cyclin D1 expression (3rd panel). Cyclin B1 and Cdk4 were also strongly induced by T492D but not by any acinus proteins (4th and 5th panels). Infected SRPK2 and acinus proteins were verified (top and 2nd panels).

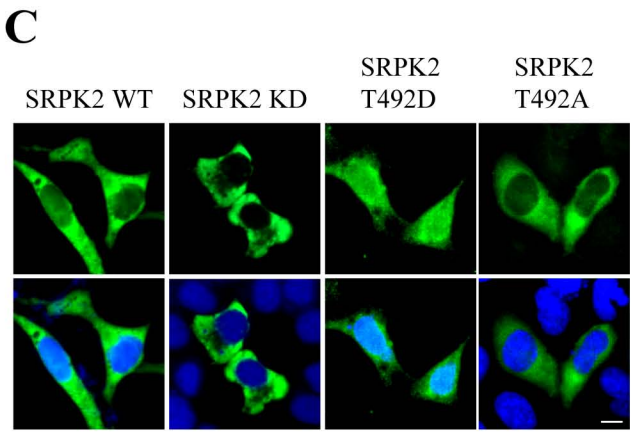
Supplemental Figure 1



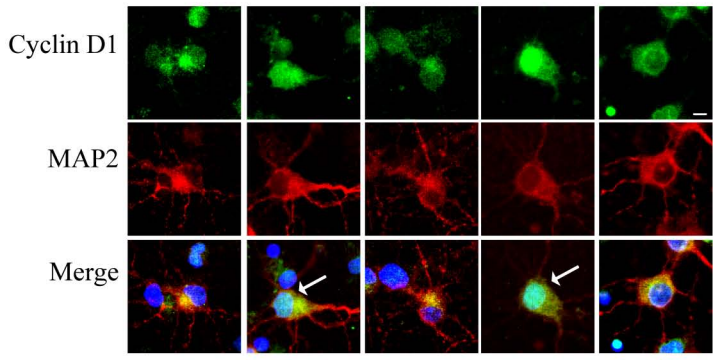
Supplemental Figure 2







Supplemental Figure 3



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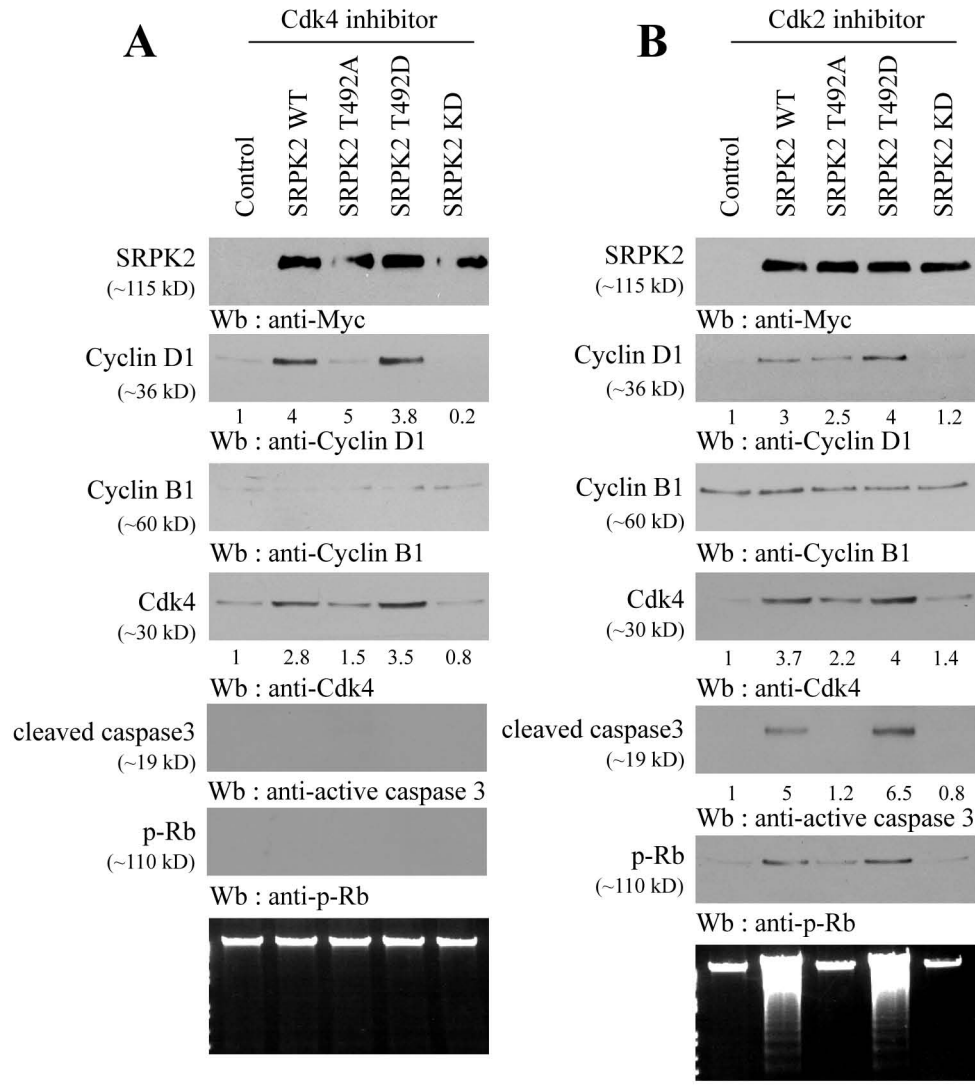
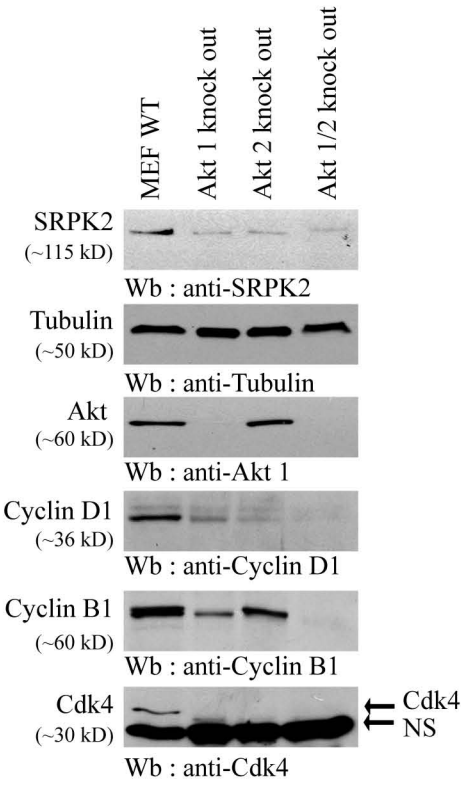


Supplemental Figure 5



Supplemental Figure 6