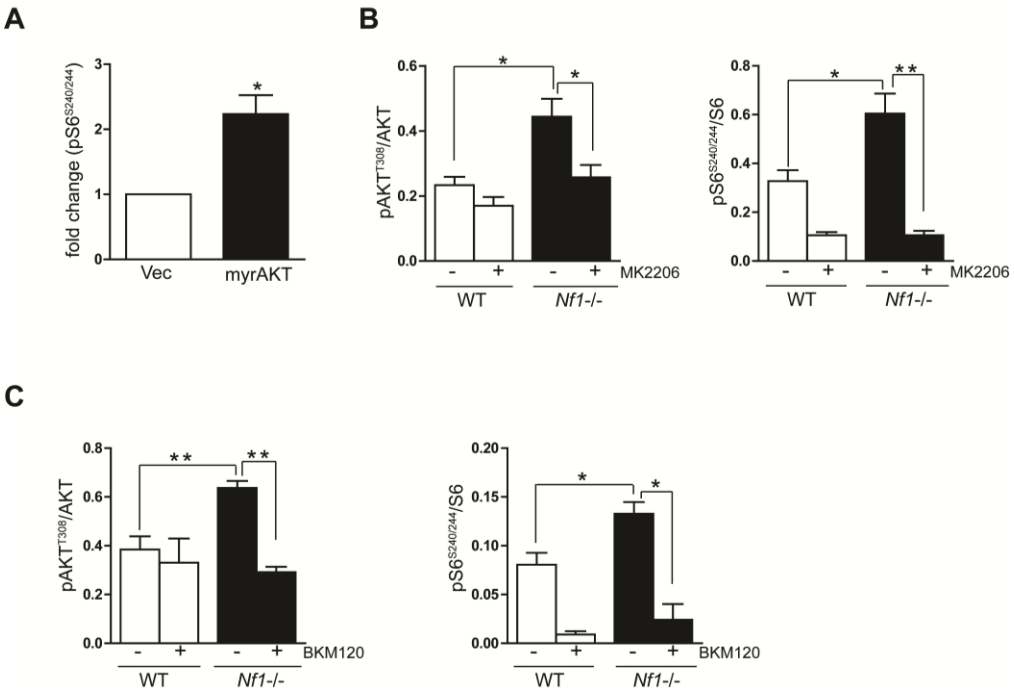
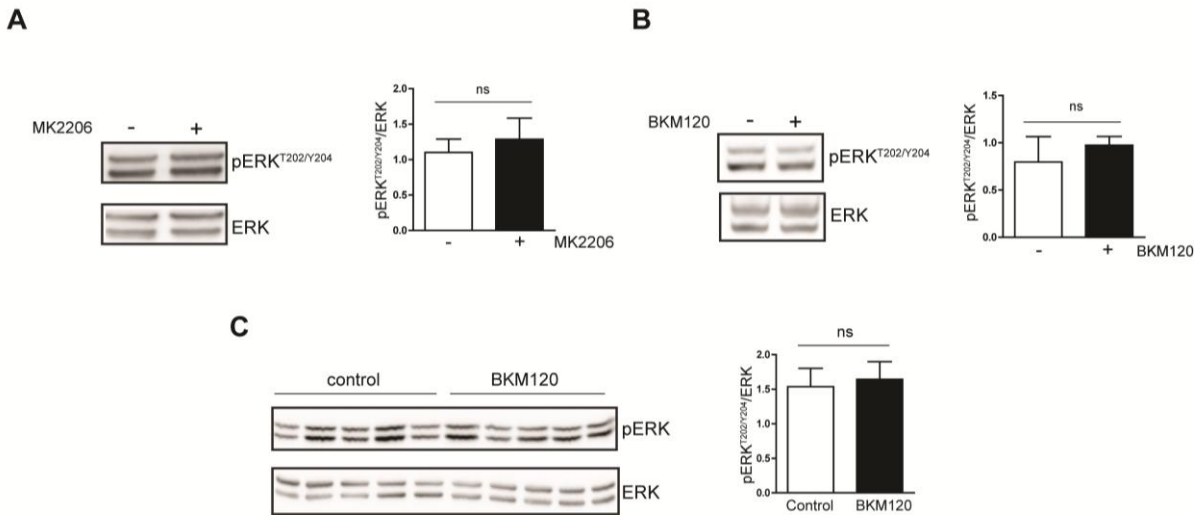
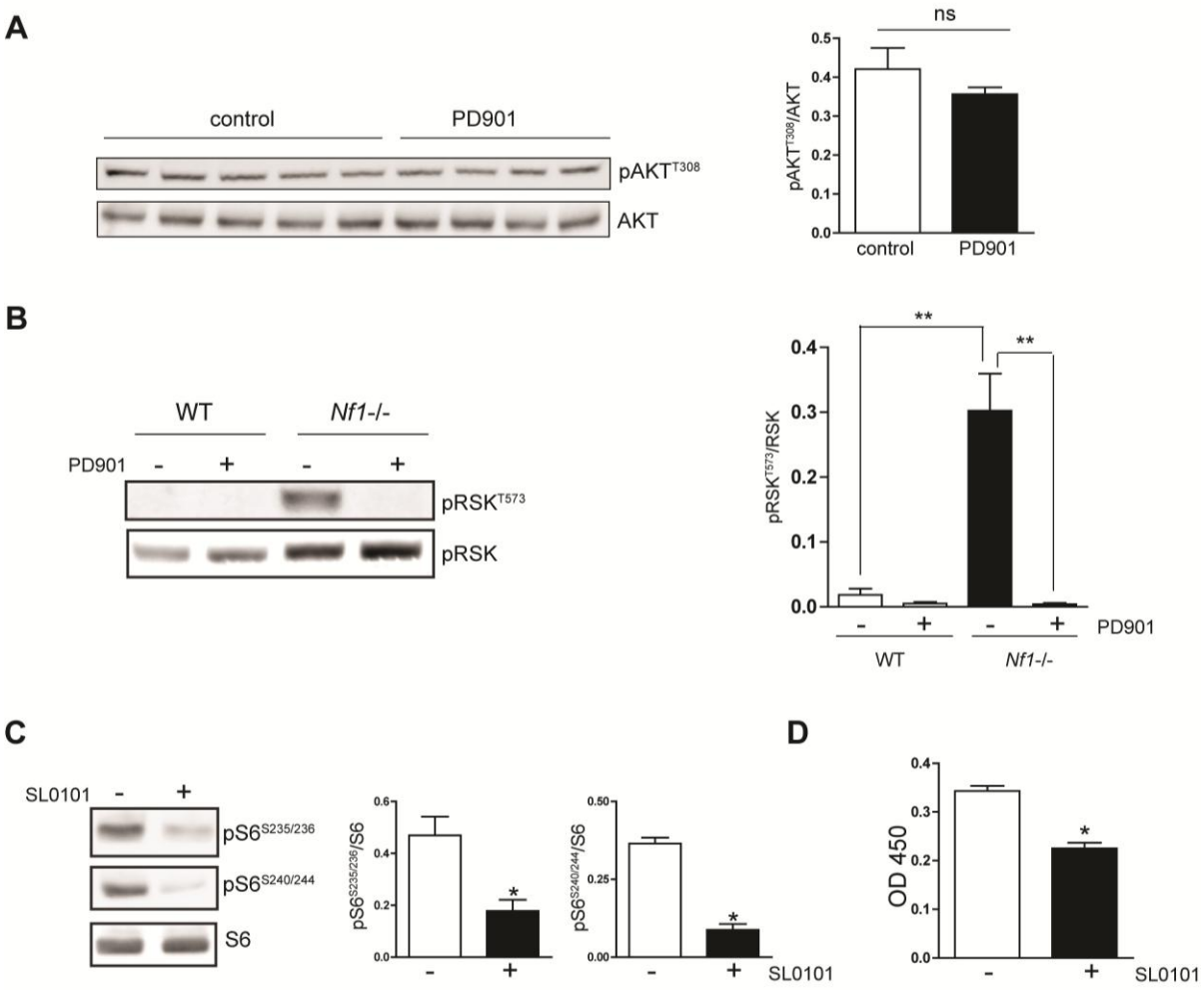


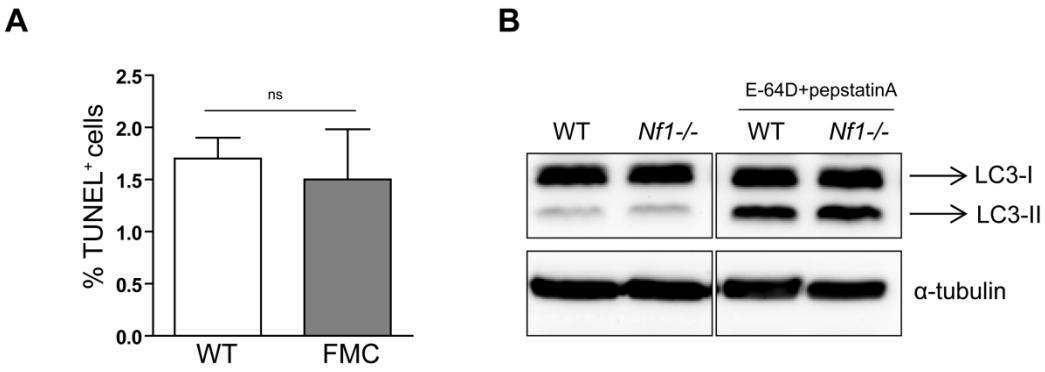
Supplementary Fig. 1. Western blot quantification from at least three independent replicates (Figure 2) demonstrates (**A**) increased S6 (S240/244) phosphorylation following myrAKT expression, (**B**) reduced AKT (T308) and S6 (S240/244) phosphorylation following MK2206 treatment of *Nf1*-deficient astrocytes, and (**C**) reduced AKT (T308) and S6 (S240/244) phosphorylation following BKM120 treatment of *Nf1*-deficient astrocytes. Bar graph denotes mean ± SEM, (*) $p<0.05$, (**) $p<0.01$.



Supplementary Fig. 2. PI3K/AKT inhibition does not inhibit ERK (T202/Y204) phosphorylation in vitro or in vivo. Western blots demonstrate no reduction of ERK (T202/Y204) phosphorylation in *Nf1*-/- astrocytes following treatment with (**A**) the AKT inhibitor MK2206 (50nM) or (**B**) the PI3K inhibitor BKM120 (5nM). (**C**) No change in ERK (T202/Y204) phosphorylation was observed in the brains of FMC mice treated with BKM120 (20mg/kg). Bar graph denotes mean ± SEM, ns, not significant.



Supplementary Fig. 3. MEK/ERK regulates mTOR activation through p90RSK signaling in *Nf1*-deficient astrocytes. (**A**) MEK inhibition (PD901) does not reduce AKT activation (T308) in in the brains of FMC mice in vivo. (**B**) *Nf1*-deficient astrocytes exhibit increased p90RSK phosphorylation (activation; T573), which is reduced to WT levels following MEK inhibition (PD901). Treatment with the p90RSK inhibitor SL0101 (100µM) inhibits (**C**) mTOR activation (S6 phosphorylation, S235/236 and S240/244) and (**D**) *Nf1*-deficient astrocyte proliferation. Bar graph denotes mean ± SEM, (*) $p<0.05$, (**) $p<0.01$. ns, not significant.



Supplementary Fig. 4. *Nf1* loss does not change apoptosis or autophagy. (A) The levels of apoptosis are similar between WT and FMC optic nerves in vivo, as measured by TUNEL staining. (B) Western blotting demonstrates no change in LC3II processing, a marker of autophagic activity, following *Nf1* gene inactivation in astrocytes in vitro. Autophagic flux was determined by assessing LC3-II expression in the presence and absence of lysosomal protease inhibitors (E-64D and pepstatin A at 10µg/ml).