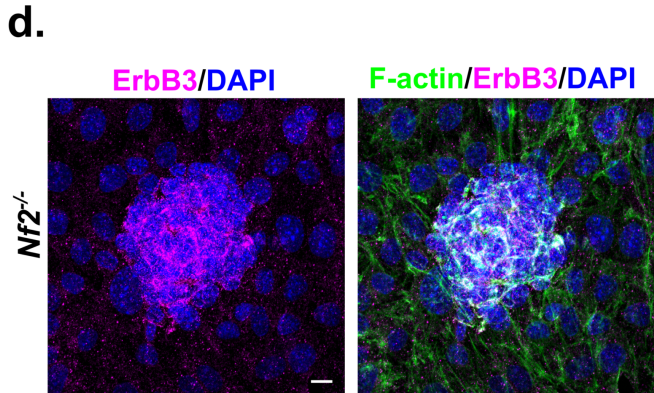
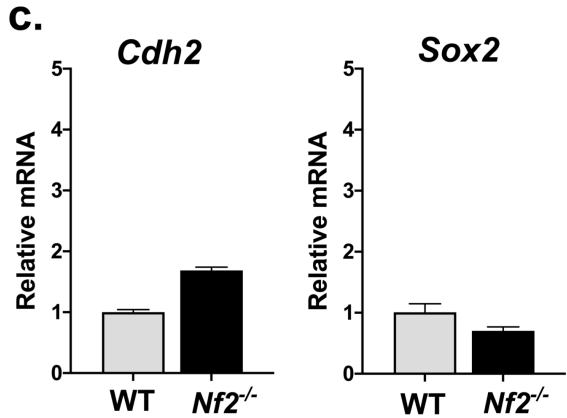
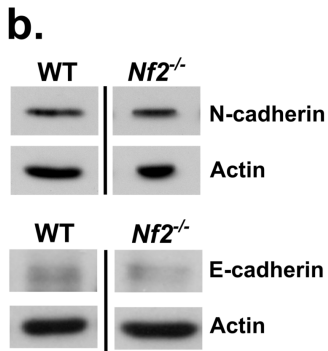
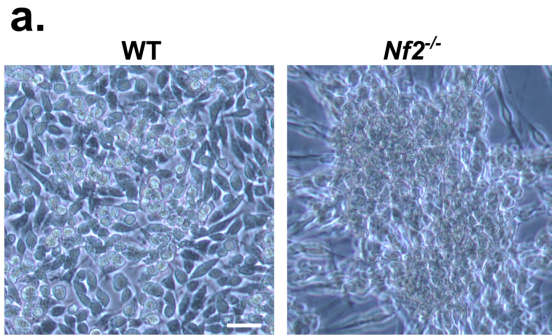
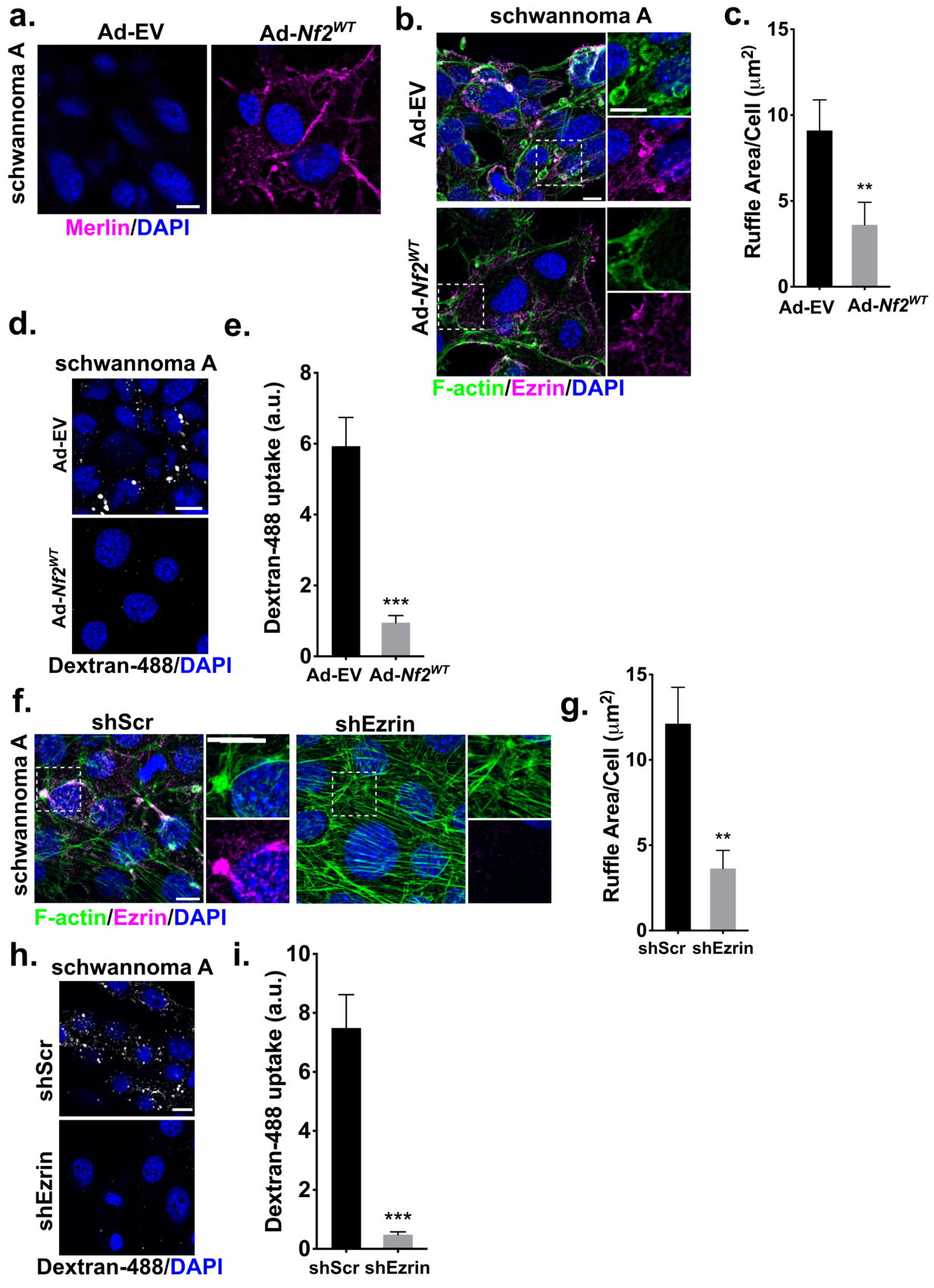


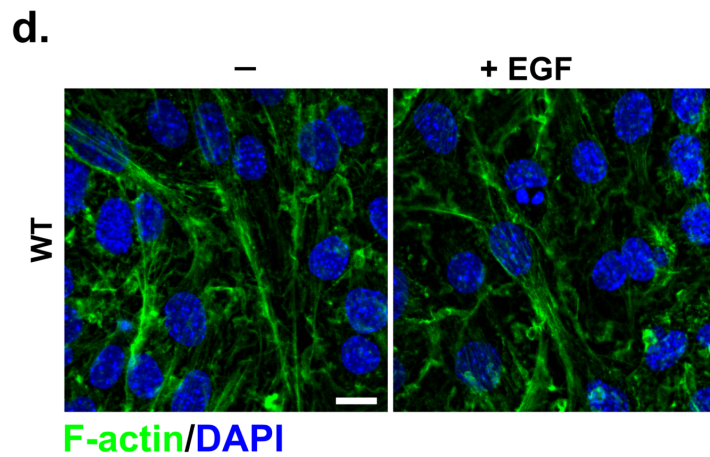
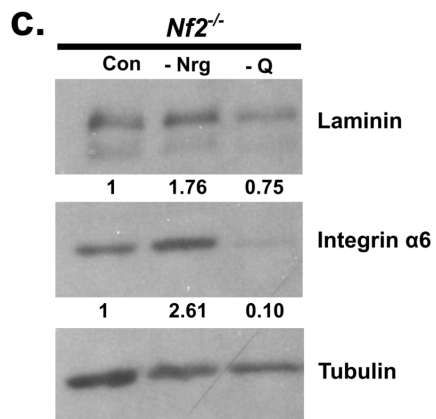
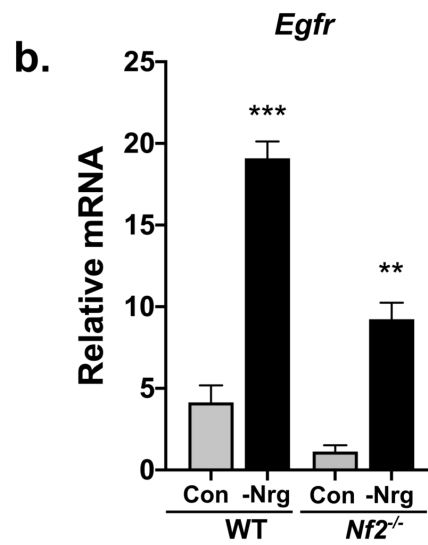
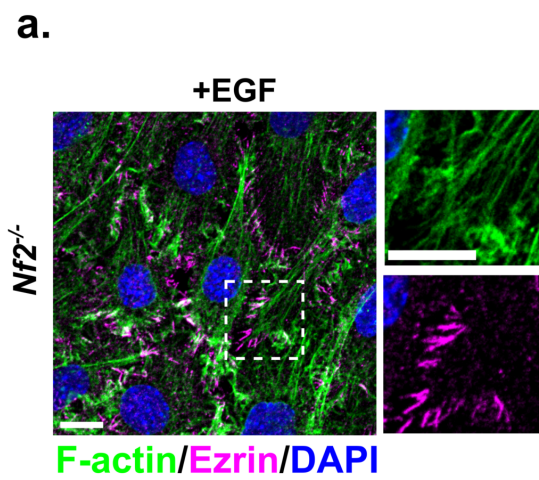
Supplemental Figure 1. A. Representative immunoblot showing protein levels of merlin and the SC marker p75 in *Nf2^{flox/flox}* (WT) and *Nf2^{-/-}* SCs. **B.** Quantitation of polarity in WT and *Nf2^{-/-}* SCs as determined by the aspect ratio (long to short axis). Bars represent mean +/- SEM in $n \geq 50$ cells per condition. N=3 independent experiments. **C.** Confocal images depicting enhanced Nrg1-induced cortical ruffling in late confluent *Nf2^{-/-}* but not control SCs. Images were generated by overlaying MIP of cortical actin (magenta) and basal actin (green) from 3D zstack images. **D.** Representative immunoblot showing protein levels of ErbB3 and activation of pAKT S473 and pERK1/2 in response to stimulation of WT and *Nf2^{-/-}* SCs with Nrg. Total levels of AKT and ERK1/2 served as loading controls. The line between lanes 2 and 3 indicates the removal of unrelated lanes from the image of the blot. **E.** Representative immunoblot showing protein levels of ezrin in *Nf2^{-/-}* SCs infected with shSCR- or shEzrin-expressing lentiviruses. Actin served as a loading control. **F.** Confocal images showing ezrin (magenta) and F-actin (green) localization in *Nf2^{-/-}* SCs infected with shSCR or shEzr-expressing lentiviruses. **G.** Quantitation of cortical ruffling area in *Nf2^{-/-}* SCs infected with shSCR or shEzr-expressing lentiviruses. Data are presented as mean +/- SEM of $n \geq 10$ cells per condition, N=2 independent experiments. P values were calculated with unpaired two-tailed Student's t-test. *** $p < 0.001$, ** $p < 0.01$. Scale bars=10 μm .



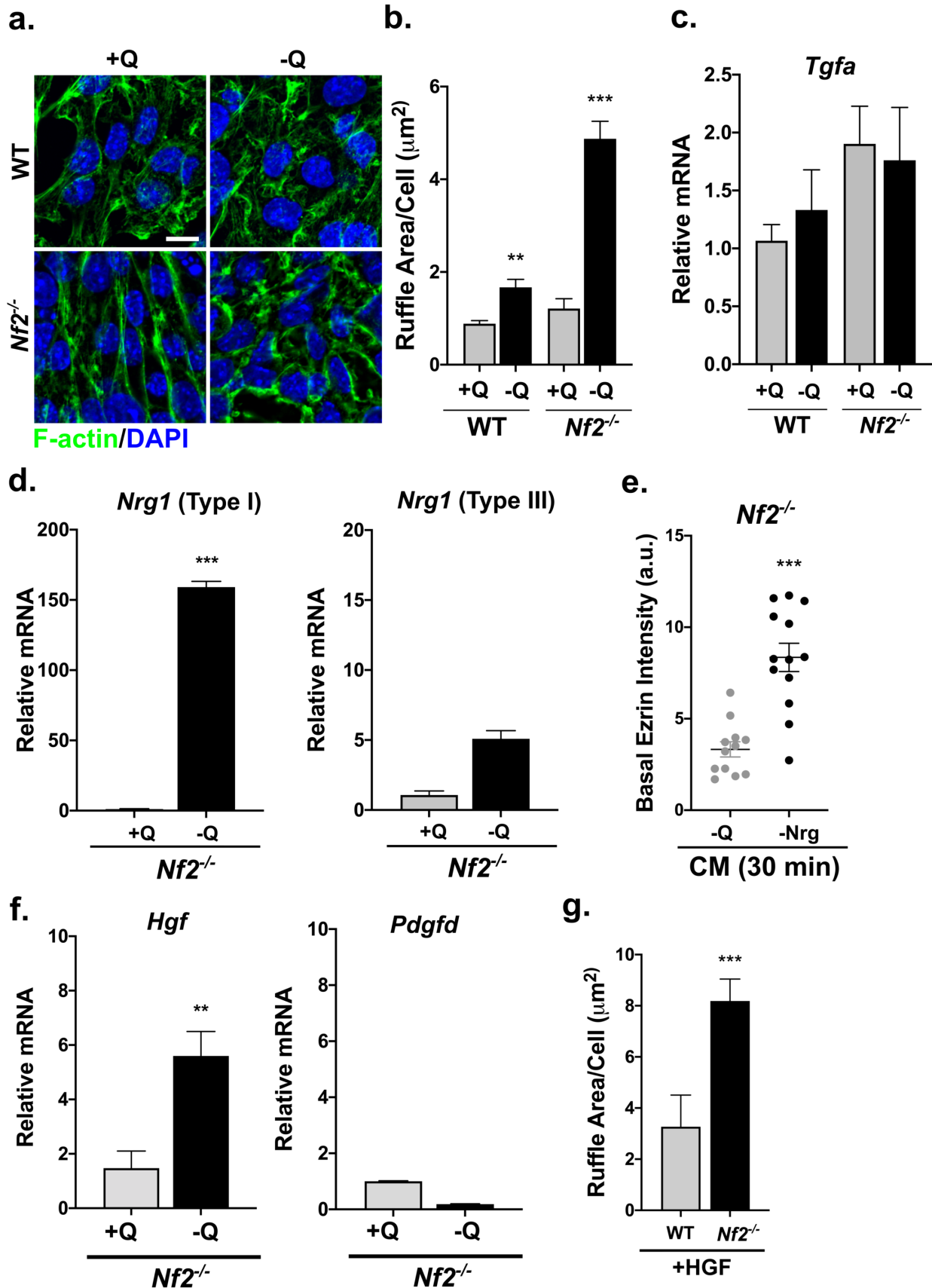
Supplemental Figure 2. A. Phase contrast images of late confluent WT and *Nf2^{-/-}* SCs. **B.** Immunoblot showing protein levels of N-cadherin and E-cadherin in WT and *Nf2^{-/-}* SCs. Actin served as a loading control. The line between lanes indicates the removal of unrelated lanes from the image of the blot. **C.** mRNA expression of *Sox2* and *Ncad* in WT and *Nf2^{-/-}* SCs. Data is presented as mean +/- SEM relative to WT mRNA levels, N=3. **D.** MIP from Fig.2F showing membrane recruitment and colocalization of ErbB3 (magenta) and F-actin (green) in late confluent *Nf2^{-/-}* SCs. Scale bars=10 μ m.



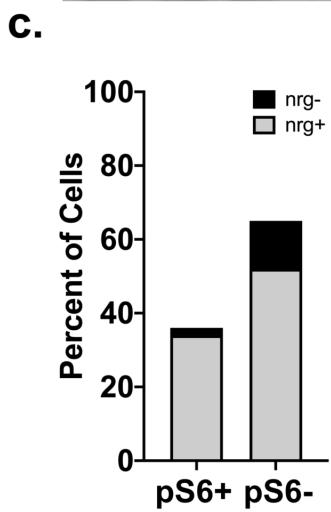
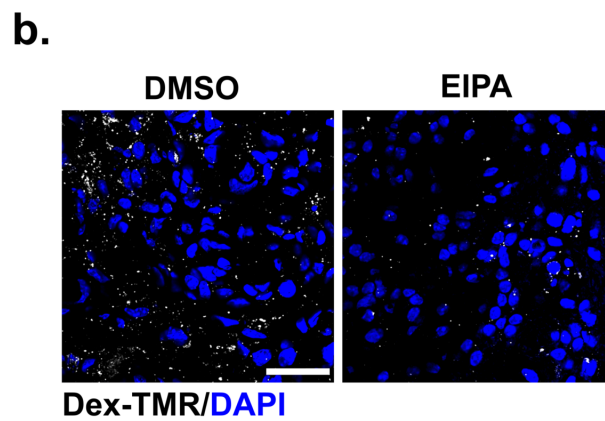
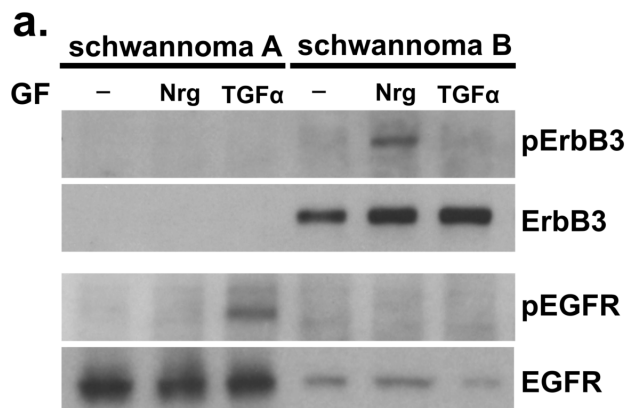
Supplemental Figure 3. **A.** Confocal images showing merlin (magenta) localization in *Nf2^{-/-}* schwannoma cells expressing EV or *Nf2^{WT}* via adenoviral infection. **B.** Confocal images of F-actin (green) and ezrin (magenta) localization in *Nf2^{-/-}* schwannoma cells expressing EV or *Nf2^{WT}* adenovirus. **C.** Quantitation of cortical ruffling in cells shown in (B). **D.** Dextran-488 uptake in *Nf2^{-/-}* schwannoma cells expressing EV or *Nf2^{WT}* adenovirus. **E.** Graph of (D). **F.** Confocal images of F-actin (green) and ezrin (magenta) localization in *Nf2^{-/-}* schwannoma cells infected with shSCR- or shEzrin-expressing lentivirus. **G.** Quantitation of cortical ruffling of cells in (F). **H.** Dextran-488 uptake in *Nf2^{-/-}* schwannoma cells expressing shSCR- or shEzrin lentivirus. **I.** Graph of (H). For all graphs, bars represent mean +/- SEM for n ≥ 10 cells per condition, N≥2 independent experiments. P values were calculated with unpaired two-tailed Student's t-test. ***p<0.001, **p<0.01. Scale bars=10 μm.



Supplemental Figure 4. A. Confocal images depicting the distribution of F-actin (green) and ezrin (magenta) in *Nf2^{-/-}* SCs starved of Nrg1 overnight and stimulated with 10 ng/ml EGF. **B.** mRNA expression *EGFR* in WT and *Nf2^{-/-}* SCs under steady state conditions or after 24 h Nrg1-deprivation. Data is presented as mean +/- SEM relative to WT mRNA levels, N=2. **C.** Immunoblot depicting the levels of the basal markers laminin and $\alpha 6$ integrin in *Nf2^{-/-}* SCs under steady-state, Nrg1-deprived and glutamine-deprived (-Q) conditions. Tubulin was used as a loading control. **D.** Confocal images of F-actin (green) localization in WT SCs starved of Nrg1 overnight and stimulated with EGF. P values were calculated with unpaired two-tailed Student's t-test. ***p<0.001, **p<0.01. Scale bars=10 μ m.



Supplemental Figure 5. A. Confocal images depicting F-actin (green) localization in WT and *Nf2^{-/-}* SCs grown in complete medium (+Q) or glutamine-deprived medium (-Q) for 24 h. **B.** Quantitation of cortical ruffling in cells shown in (A). Bars represent mean +/- SEM for n≥10 cells per condition. N=3 independent experiments. **C.** mRNA expression of *Tgfa* in WT and *Nf2^{-/-}* SCs grown in complete (+Q) or glutamine-deprived (-Q) medium for 24 h. Data is presented as mean +/- SEM relative to WT, +Q mRNA levels, N=3. **D.** mRNA expression of soluble *Nrg1 Type I* and membrane-tethered *Nrg1 Type III* in *Nf2^{-/-}* SCs grown in complete or glutamine-deprived medium. Data is presented as mean +/- SEM relative to +Q mRNA levels, N=2. **E.** mRNA expression of *Hgf* and *Pdgfd* in *Nf2^{-/-}* SCs grown in complete or glutamine-deprived medium. Data is presented as mean +/- SEM relative to +Q mRNA levels, N=2. **F.** Quantitation of cortical ruffles in *Nf2^{-/-}* SCs with and without HGF stimulation. Bars represent mean +/- SEM for n ≥ 10 cells per condition. P values were calculated with unpaired two-tailed Student's t-test. ***p<0.001, **p<0.01. Scale bars=10 μm.



Supplemental Figure 6. A. Immunoblot showing protein levels of pErbB3, total ErbB3, pEGFR, and total EGFR in schwannoma A and schwannoma B cells upon stimulation with Nrg1 or TGF α for 10 min. **B.** Confocal images of *ex vivo* macropinocytic uptake of dextran-TMR in schwannoma tissue with and without EIPA treatment, as shown in Fig. 6H. Scale bar=30 μ m. **C.** Quantitation of percentages of cells staining positive or negative for pS6 and/or Nrg1 in tissue from early DRG lesions in *P0-Nf2⁴²⁻³* mice.