Supplemental Figure S1- GREB1 has a dose-dependent effect on proliferation in breast cancer cells. MCF7 (**A**) and ZR-75-1 (**B**) cells were transduced with GFP or increasing amounts of GREB1 adenovirus. The relative number of cells were measured on Day 0 and Day 5 my alamar blue assay. Data depicts 4 biological replicates with standard deviations. B. ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.00001$.

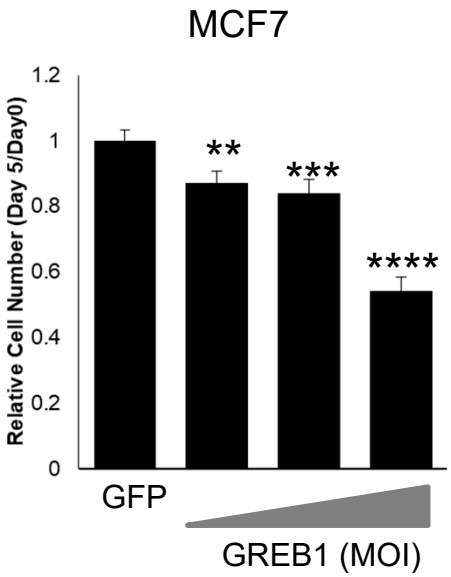
Supplemental Figure S2- Different mutations in the PI3K pathway have varying levels of Akt activity in breast cancer cell lines. A. MCF7, ZR-75-1, and T47D cells were serum starved for 16 hours before stimulation with 1 ng/mL of EGF for 1 hour. Cell lysates were harvested and analyzed by immunoblot for the indicated proteins. **B**. Quantification of the phosphor-GSK3β activity depicted in Figure 3B.

Supplemental Figure S3- GREB1 overexpression induces Akt hyperactivation at the plasma membrane. MCF7 cells were transduced with adenovirus expressing GFP or GREB1. The cells were then cultured in serum-free media for 16 hours before being stimulated with 1 ng/mL EGF for 0 or 5 minutes. Cells were fixed and stained for DAPI and **A)** Akt or **B)** p-Akt (Thr308). Immunofluorescence microscopy was used to visualize the activation and localization of Akt.

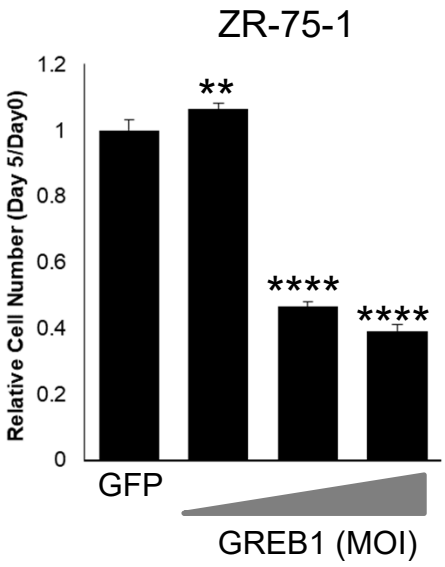
Supplemental Figure S4- Endogenous GREB1 re-localizes to the cytoplasm under growth-stimulatory conditions. A) MCF7 cells were serum starved for 4 hours and stimulated with 1 ng/mL EGF for 0, 5, or 15 minutes. Cells were fixed and stained for DAPI and endogenous GREB1. Immunofluorescence microscopy was used to visualize GREB1 localization. **B)** Cytoplasmic and nuclear fractions were extracted from MCF7 whole cell lysate using high-speed centrifugation. Fractionated cell lysates were subjected to SDS-PAGE and analyzed via immunoblot for indicated proteins. **C)** MCF7 cells cultured in full serum media were fixed and stained for DAPI and endogenous GREB1. Immunofluorescence microscopy was used to visualize GREB1 localization under normal growth conditions.

Supplemental Figure S5- Endogenous GREB1 regulates Akt activation MCF7 cells transduced with lentivirus expressing non-specific shRNA (shNS) or one of two shRNAs targeted to GREB1 (shGREB1 #1 or shGREB1 #2) were placed in serum/phenol red free media for 16 hours followed by 1 hour of activation with 1ng/ml EGF. Cells were harvested and lysates analyzed via immunoblot for Akt activation pathway.

A

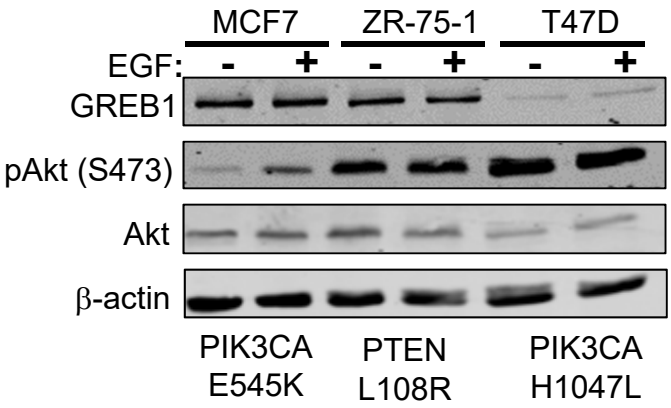


B

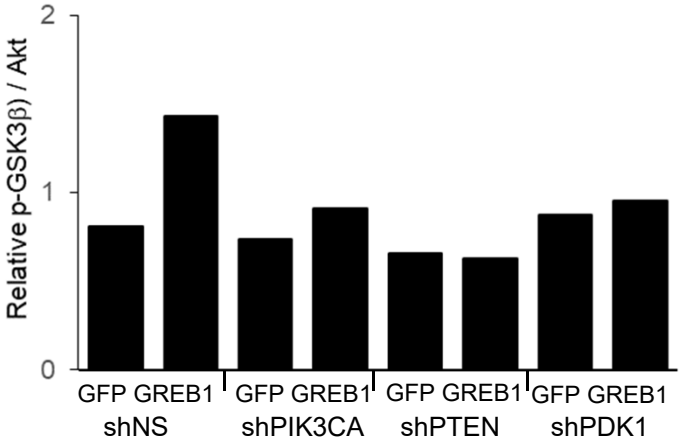


Supplemental Figure 1

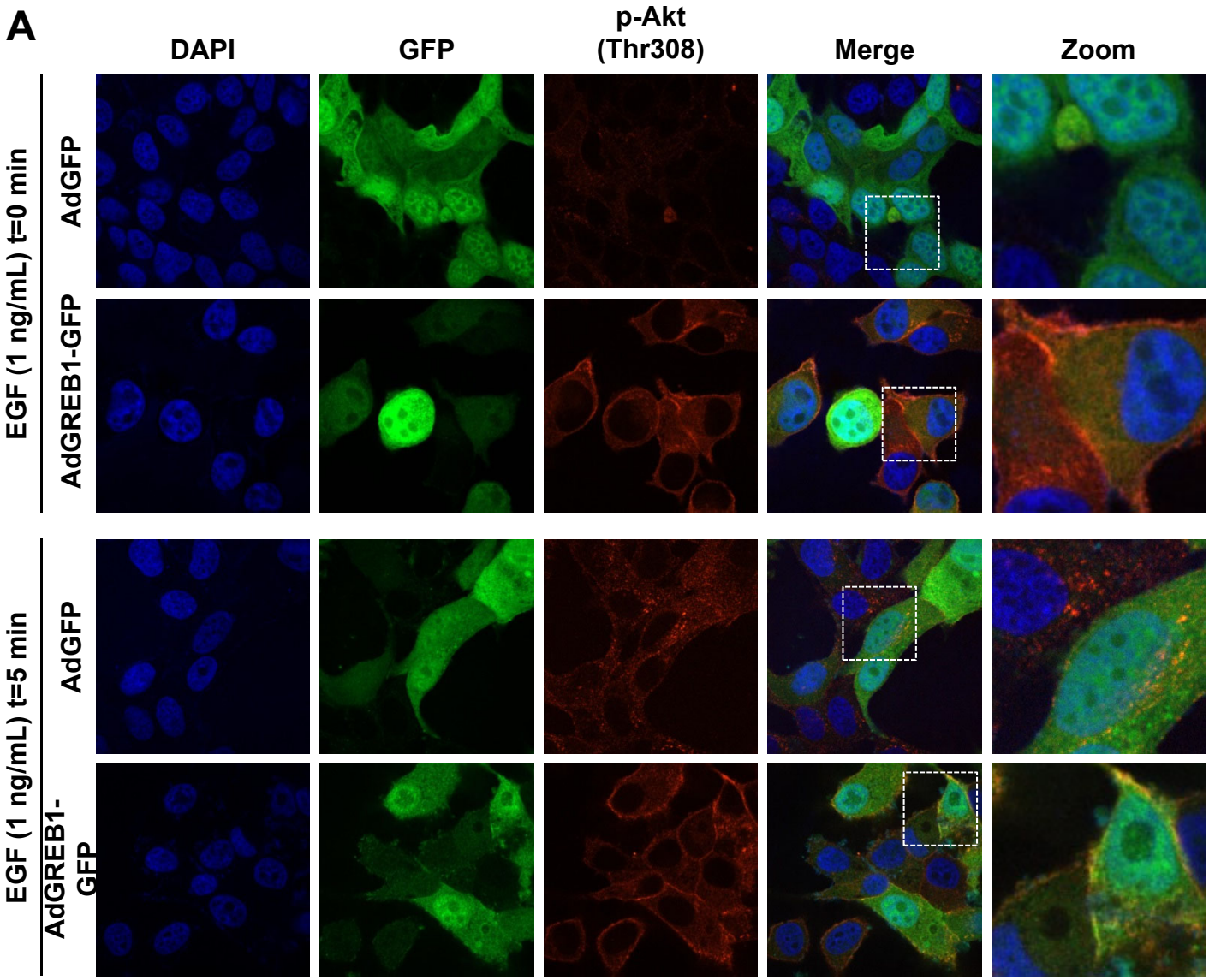
A



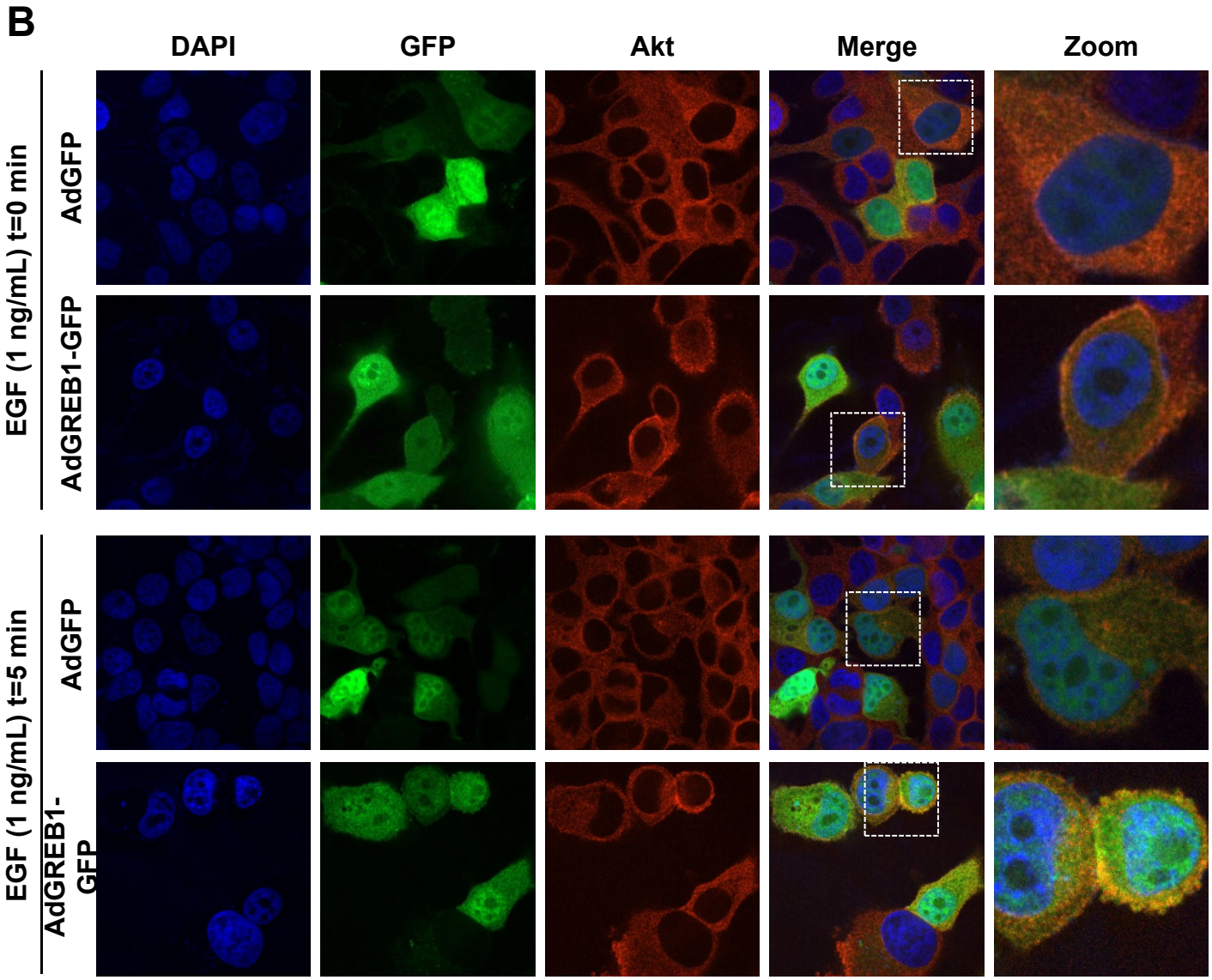
B



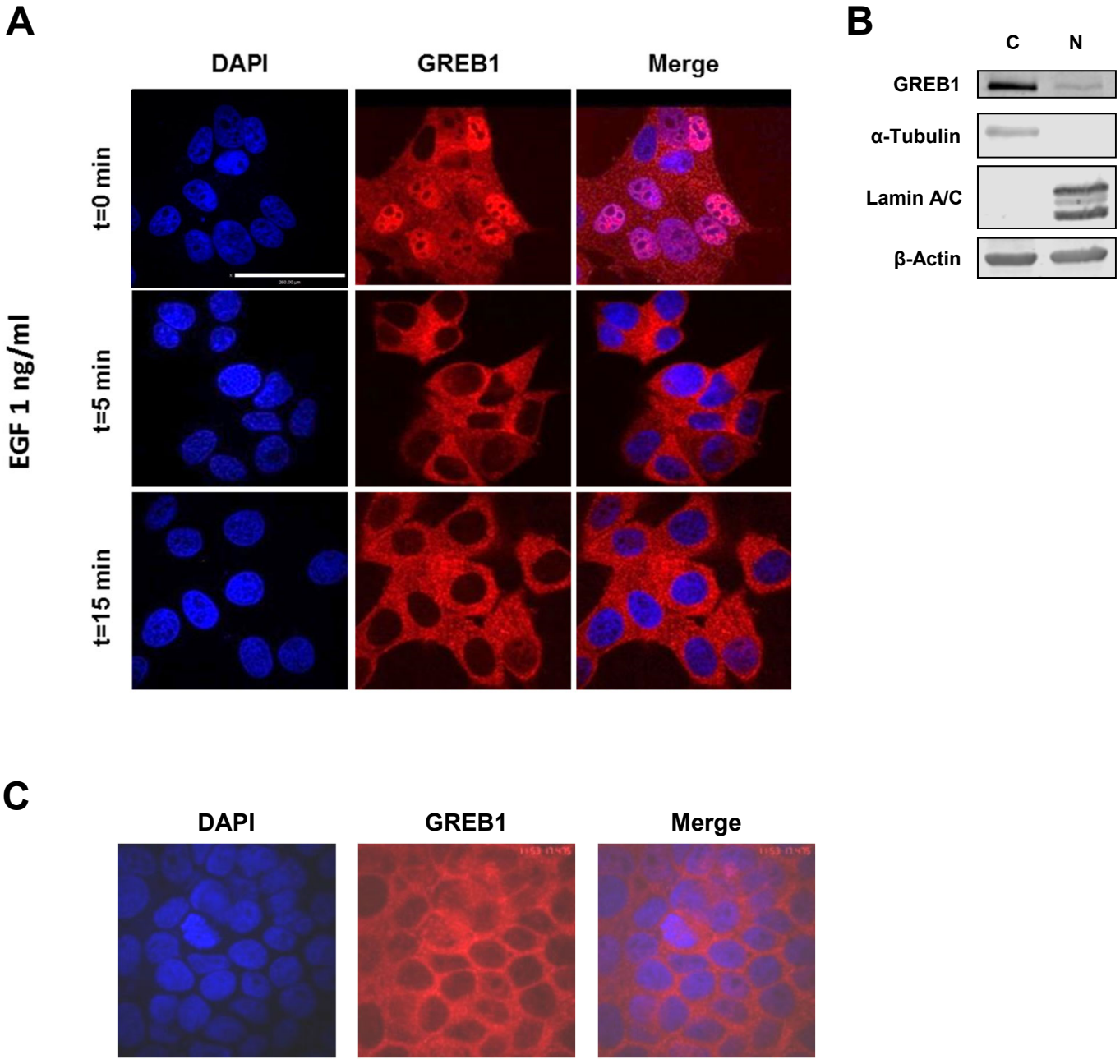
Supplemental Figure 2



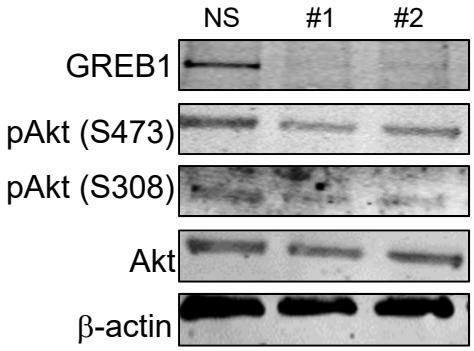
Supplemental Figure 3



Supplemental Figure 3 (continued)



Supplemental Figure 4



Supplemental Figure 5