Supplementary material.

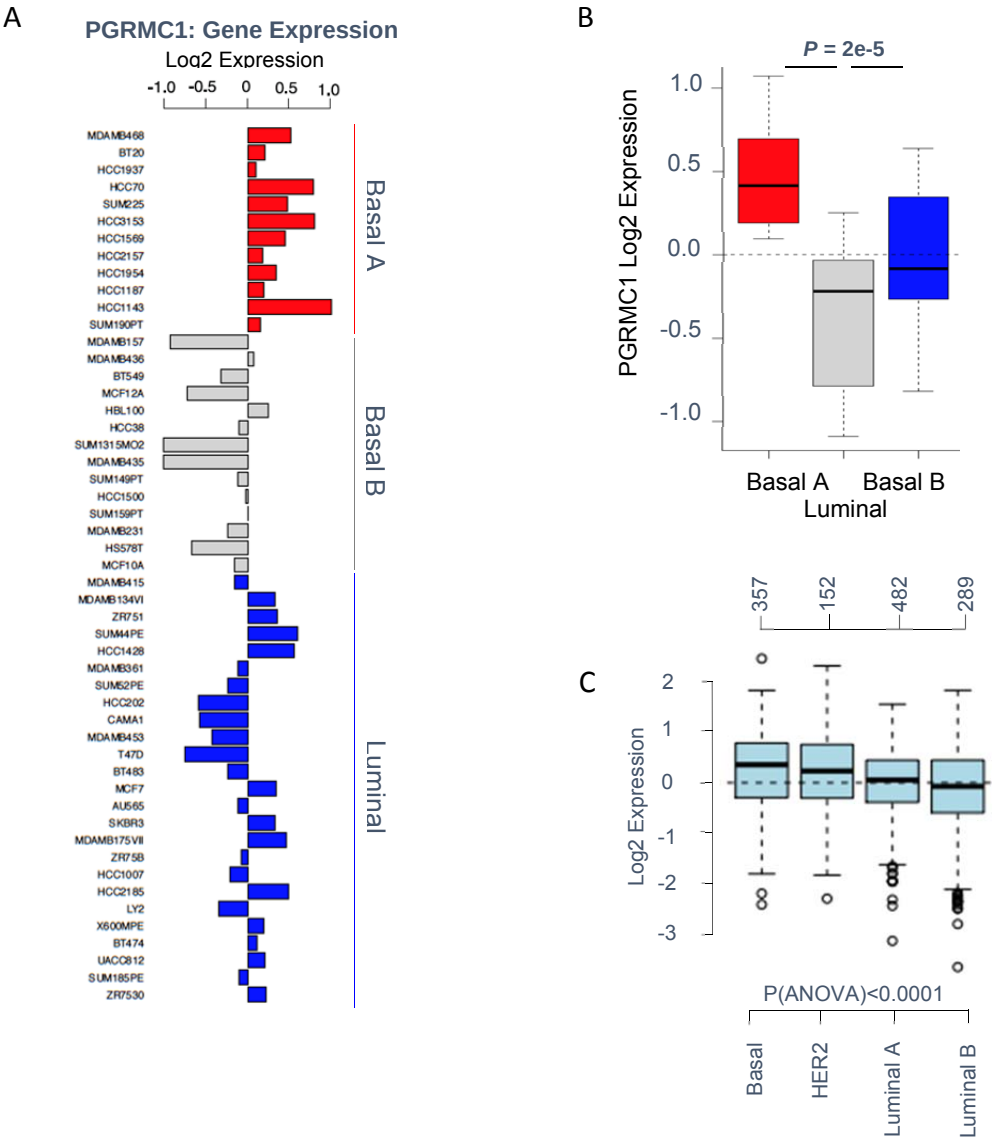



Fig. S1. **PGRMC1 is highly expressed in ER-positive and TNBCs.**

A. available gene expression repository, Gene expression-based Outcome for Breast Cancer (GOBO) was analyzed to observe PGRMC1 relative mRNA expression from a panel of 51 malignant and non-malignant breast cells, Basal A, B and Luminal epithelial cells. B. Box-plots displaying distribution of data the 51 breast cells. C. Box-plots displaying PGRMC1 expression in Basal (n=357), HER2 (n=152), Luminal A (n=482) and B (n=289) malignant breast tissue (n=number of tissue samples).

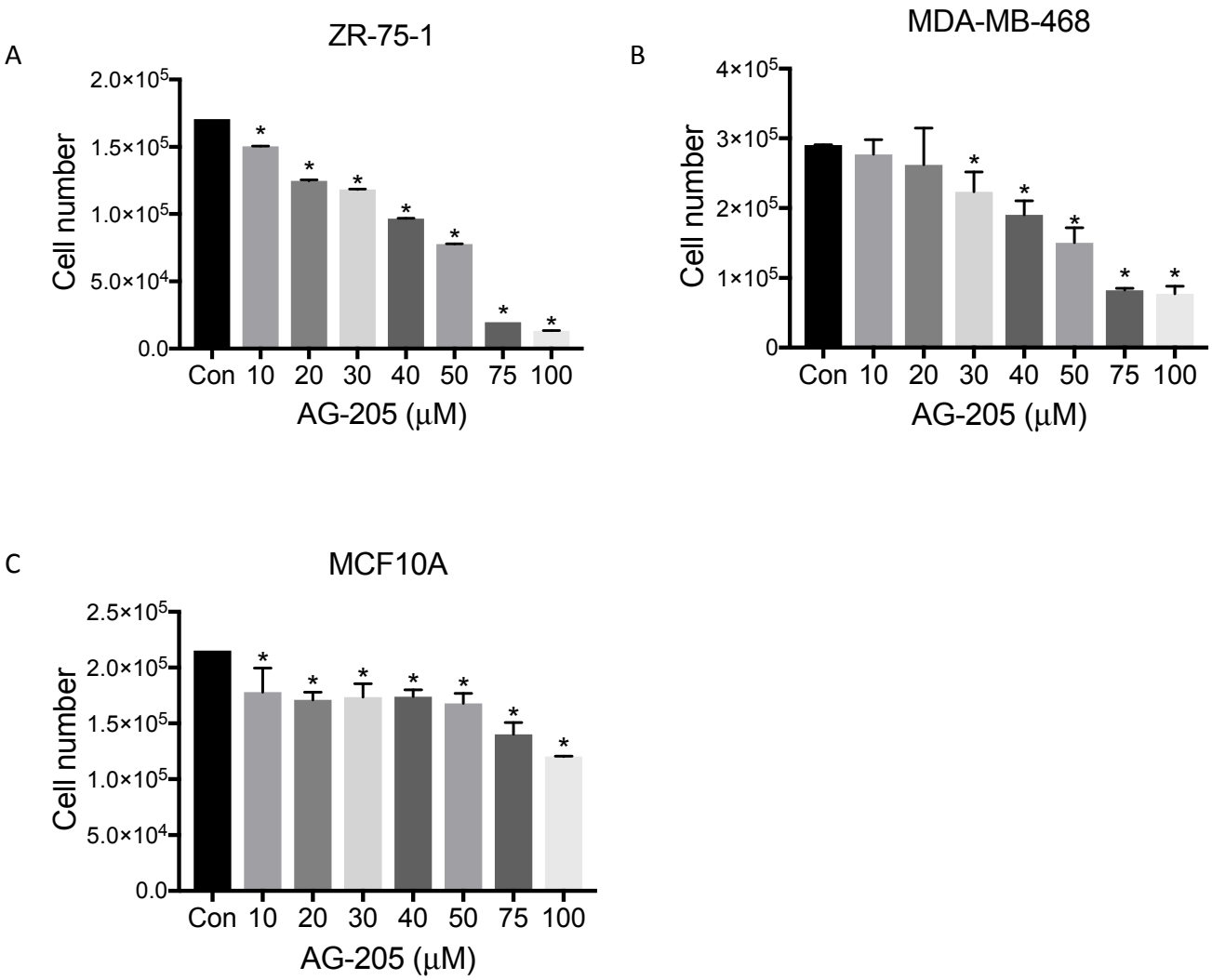
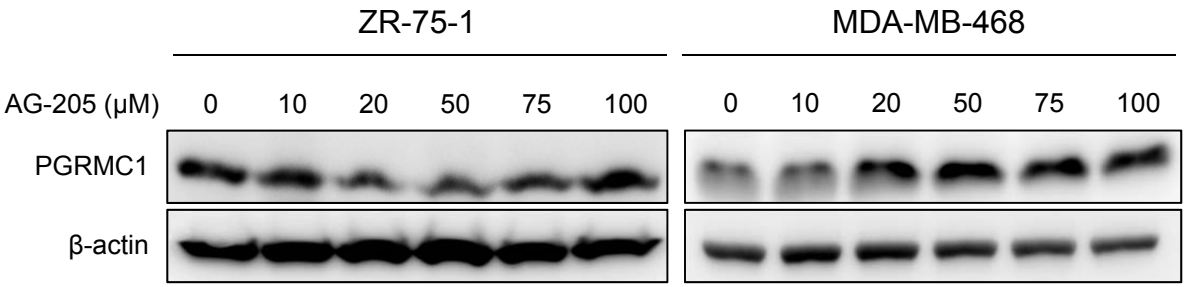



Fig. S2. **AG-205 selectively inhibits ER-positive and TNBC cell growth and survival.**

A. Dose dependent cell proliferation by hemocytometer following trypan blue staining of ZR-75-1, MDA-MB-468 breast cancer cells and normal breast MCF10A cells following 10, 20, 30, 40, 50, 75 and 100μM AG-205 treatment for 24 hours.

A




B

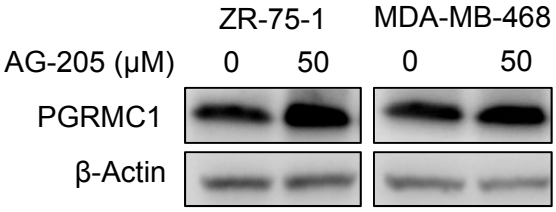



Fig. S3. **AG-205 has minimal effects on PGRMC1 expression.**

A. PGRMC1 expression by western blot following 10, 20, 50, 75 and 100 μM AG-205 treatment for 24 hours in ZR-75-1 and MDA-MB-468 breast cancer cells. B. Expression of PGRMC1 following 50 μM AG-205 treatment in ZR-75-1 and MDA-MB-468 breast cancer cells.

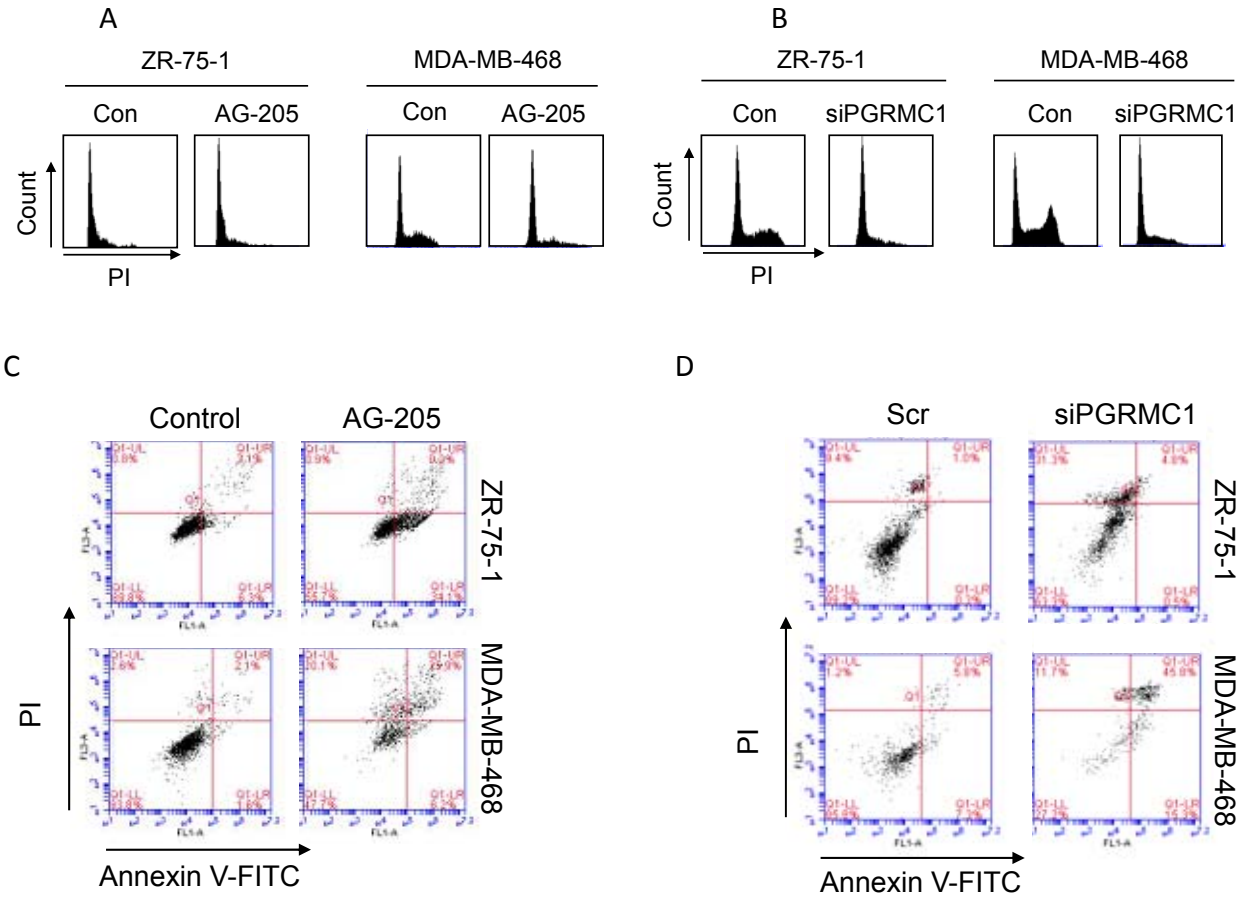
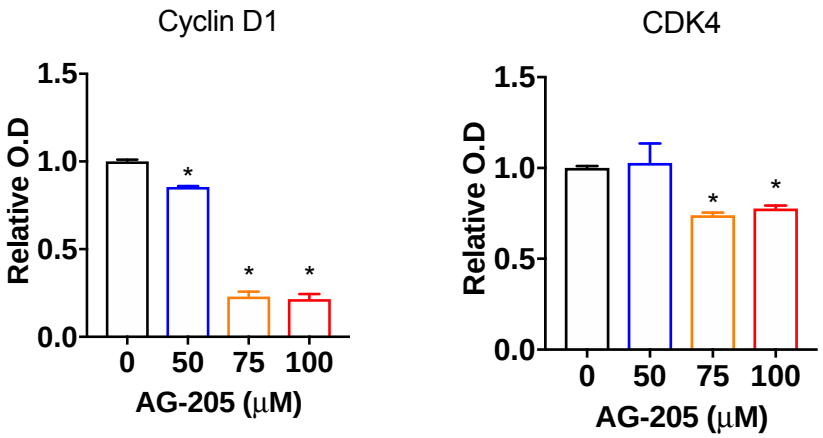



Fig. S4. **PGRMC1 signal inhibition and silencing promote cell cycle arrest and apoptosis.** A. Cell cycle analysis by flow cytometry following 50μM AG-205 treatment or B. silencing PGRMC1 in ZR-75-1 and MDA-MB-468 cells. C. Apoptosis analysis by flow cytometry following 50μM AG-205 treatment or C. silencing PGRMC1 in ZR-75-1 and MDA-MB-468 cells.

**ZR-75-1**

A




**MDA-MB-468**

B

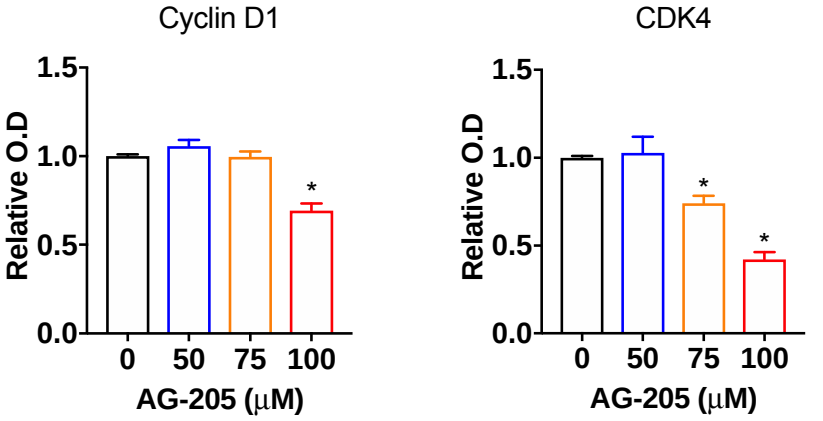
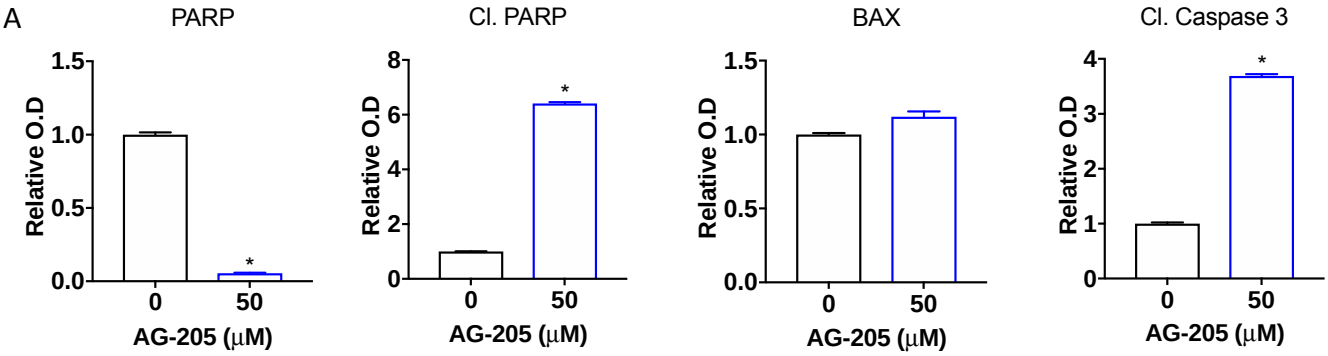



Fig. S5. **Densitometric analysis of cell cycle proteins following AG-205 treatment.**

A-B. Densitometric analysis of cell cycle proteins, Cyclin D1 and CDK4 following 50, 75 and 100μM of AG-205 treatment in ZR-75-1 and MDA-MB-468 cells.

**ZR-75-1**




**MDA-MB-468**

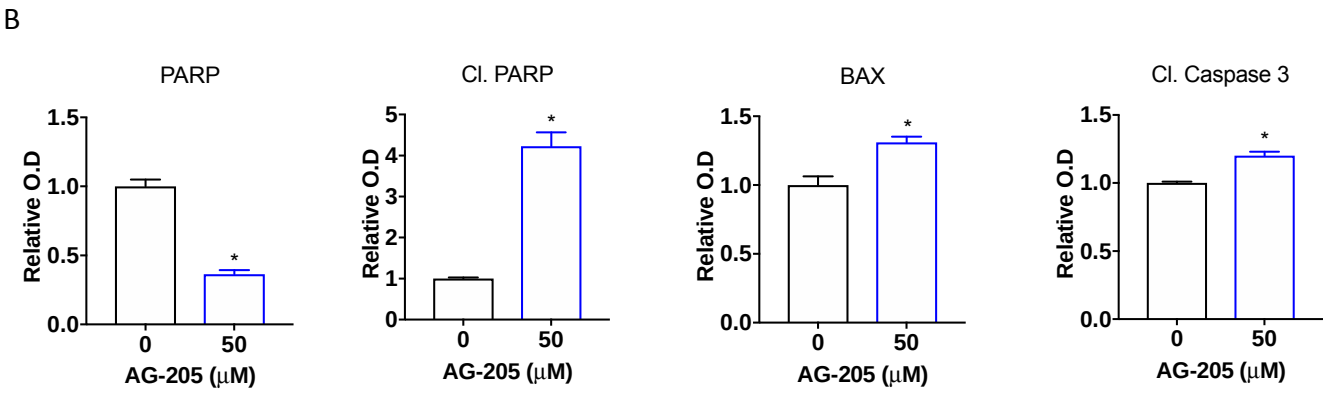
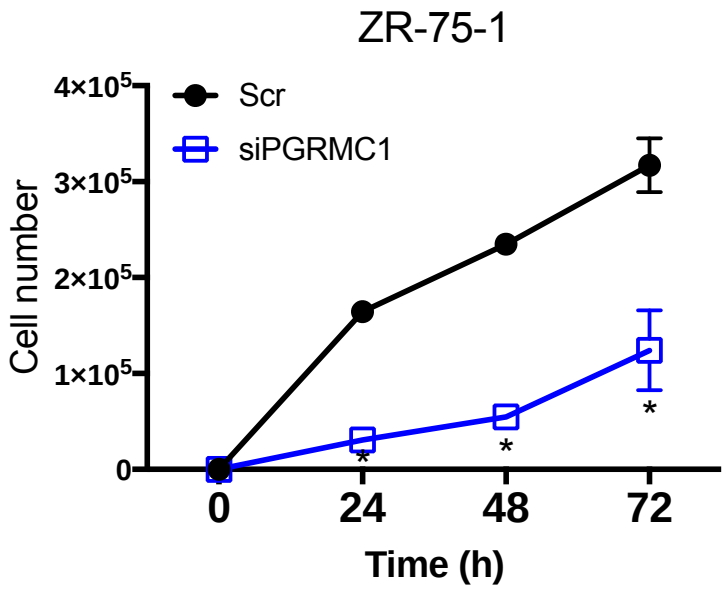



Fig. S6. **Densitometric analysis of apoptotic proteins following AG-205 treatment.**

A-B. Densitometric analysis of apoptotic proteins, PARP, Cl. PARP, BAX and Cl. Caspase 3 following 50µM treatment of AG-205 in ZR-75-1 and MDA-MB-468 cells.

A




B

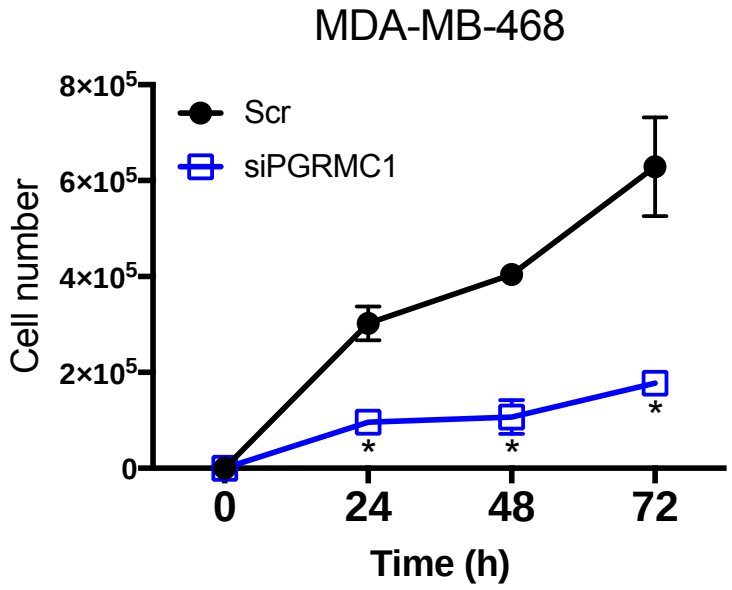
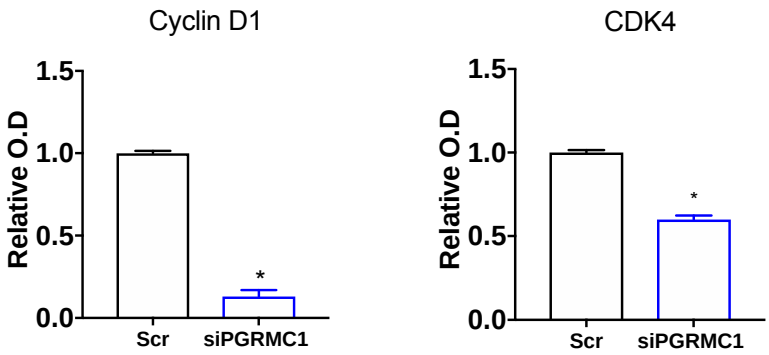



Fig S7**. Silencing PGRMC1 inhibits growth and survival of breast cancer cells**

A – B. Time dependent cell proliferation by hemocytometer following trypan blue staining following PGRMC1 silencing by siRNA in ZR-75-1 and MDA-MB-468 cells.

**ZR-75-1**

A




**MDA-MB-468**

B

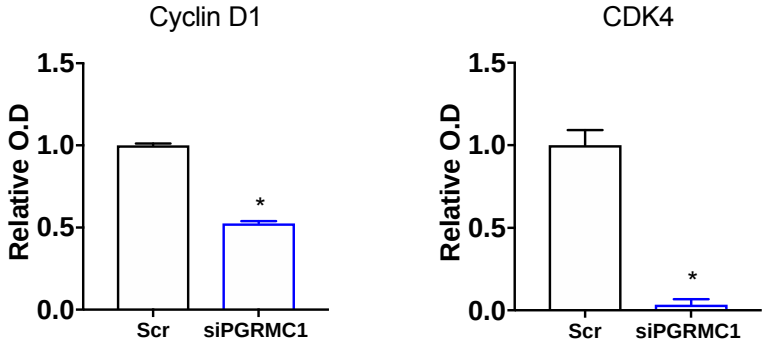
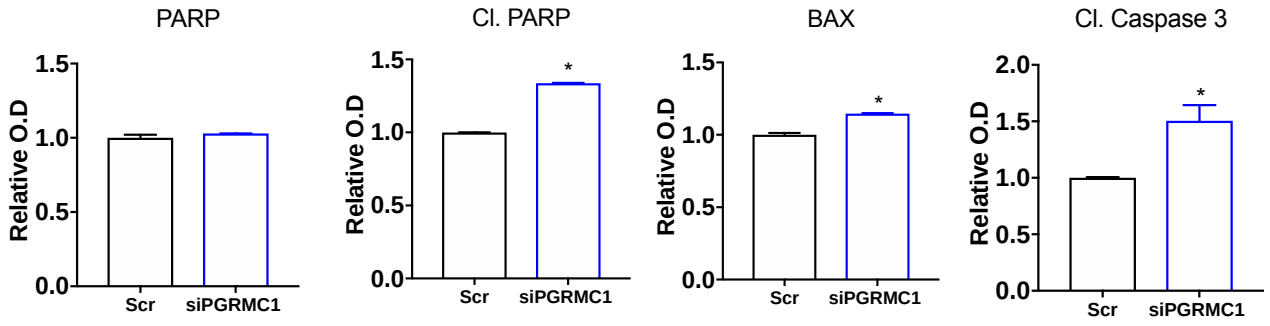



Fig. S8. **Densitometric analysis of cell cycle proteins following PGRMC1 silencing.**

A-B. Densitometric analysis of cell cycle proteins, Cyclin D1 and CDK4 following PGRMC1 silencing in ZR-75-1 and MDA-MB-468 cells.

**ZR-75-1**

A




**MDA-MB-468**

B

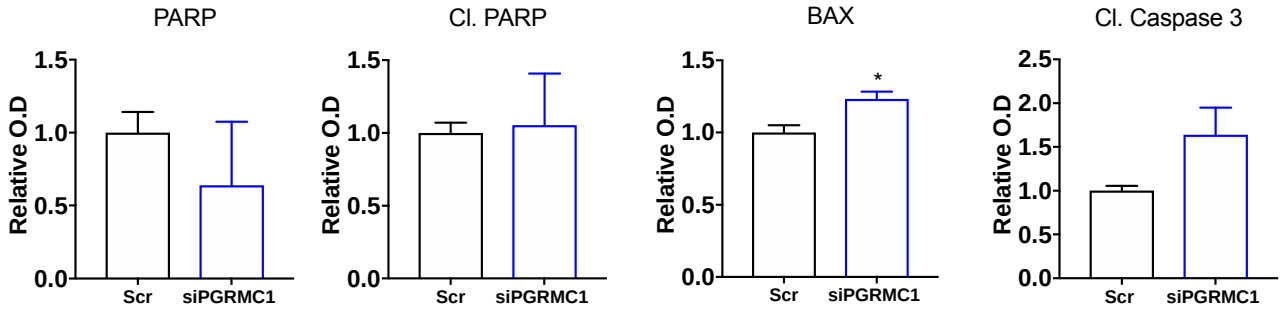



Fig. S9. **Densitometric analysis of apoptotic proteins following PGRMC1 silencing.**

A-B. Densitometric analysis of apoptotic proteins, PARP, Cl. PARP, BAX and Cl. Caspase 3 following PGRMC1 silencing in ZR-75-1 and MDA-MB-468 cells.

A **ZR-75-1**
AG-205/siPGRMC1

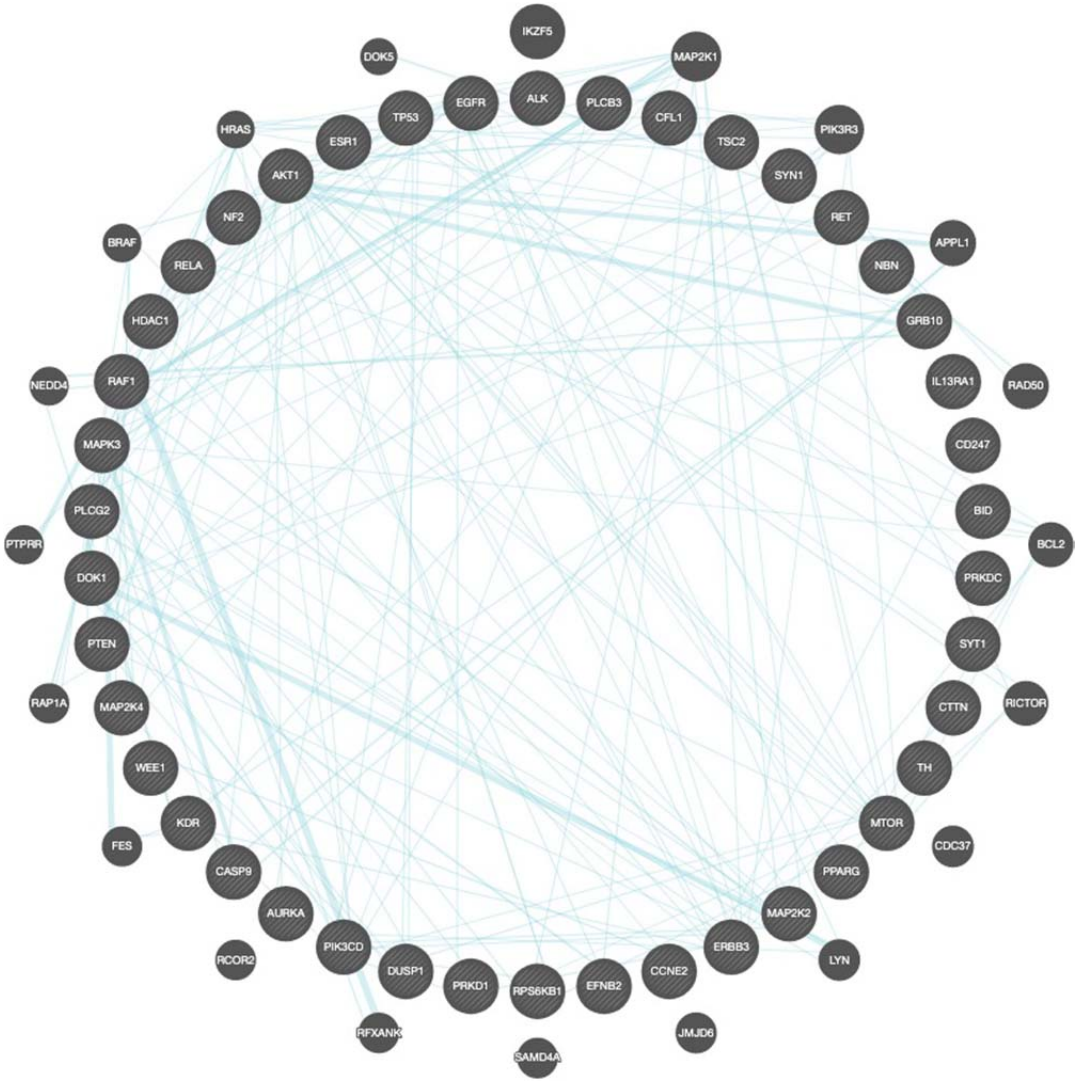



Fig. S10. **Phospho-proteome analysis connects PGRMC1 signaling to breast cancer proliferation.**

A. Network analysis of commonly enriched genes following both 50μM AG-205 and PGRMC1 silencing in ZR-75-1 cells. The genes observed exhibited interactions with cell proliferative and cell survival genes.

A **MDA-MB-468**
AG-205/siPGRMC1

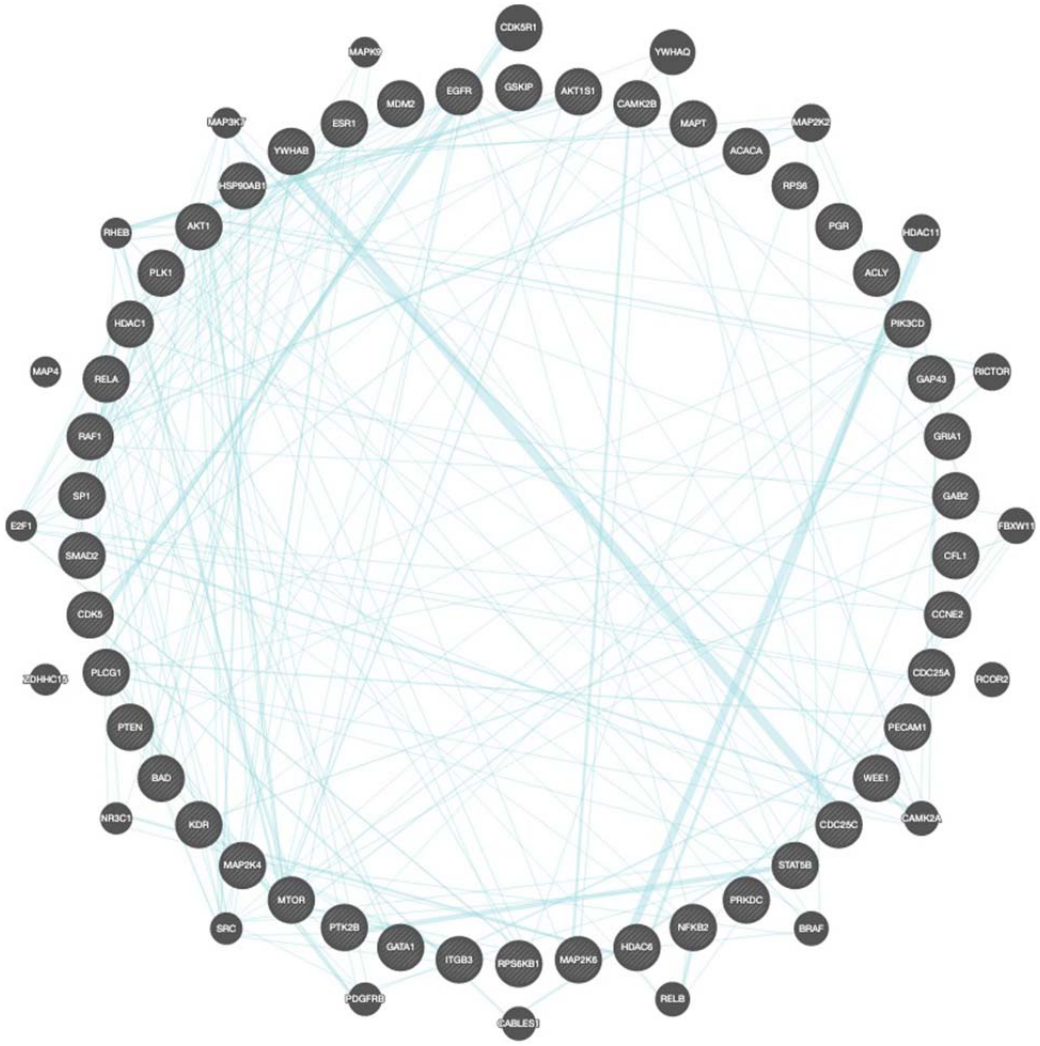



Fig. S11. **Phospho-proteome analysis connects PGRMC1 signaling to breast cancer proliferation.**

B. Network analysis of commonly enriched genes following both 50μM AG-205 and PGRMC1 silencing in MDA-MB-468 cells. The genes observed exhibited interactions with cell proliferative and cell survival genes.