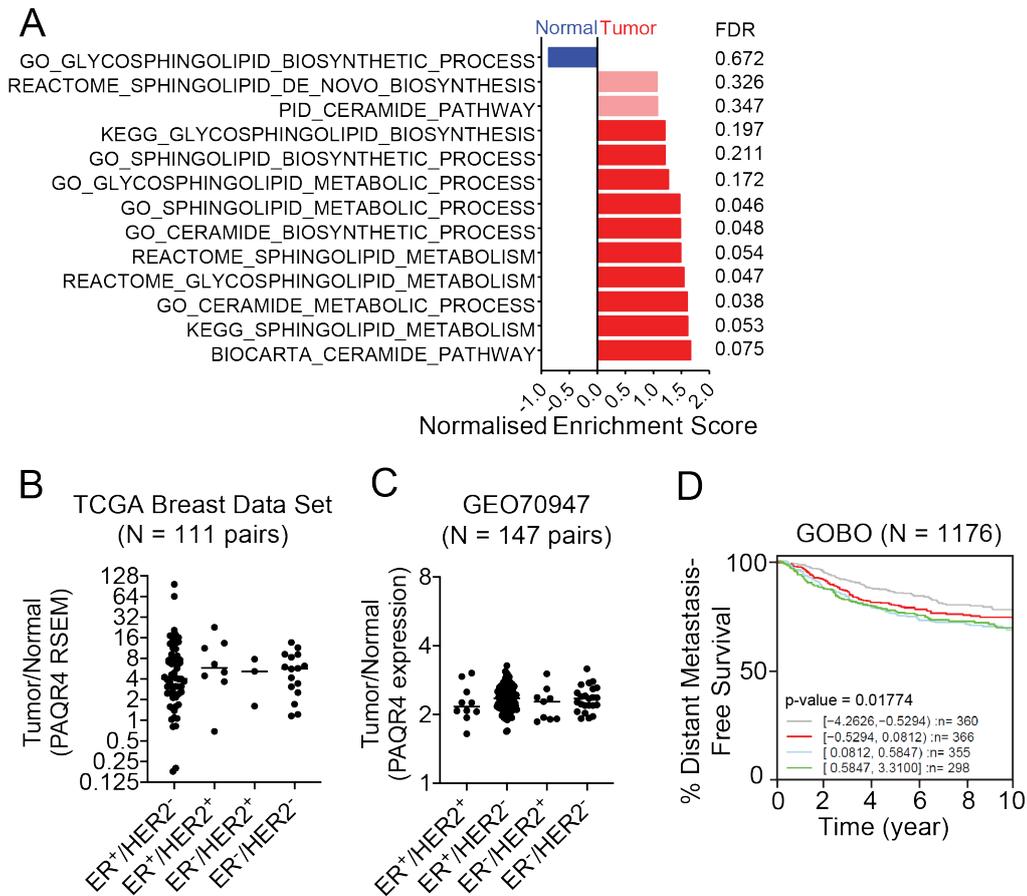


Supplementary Figure 1:



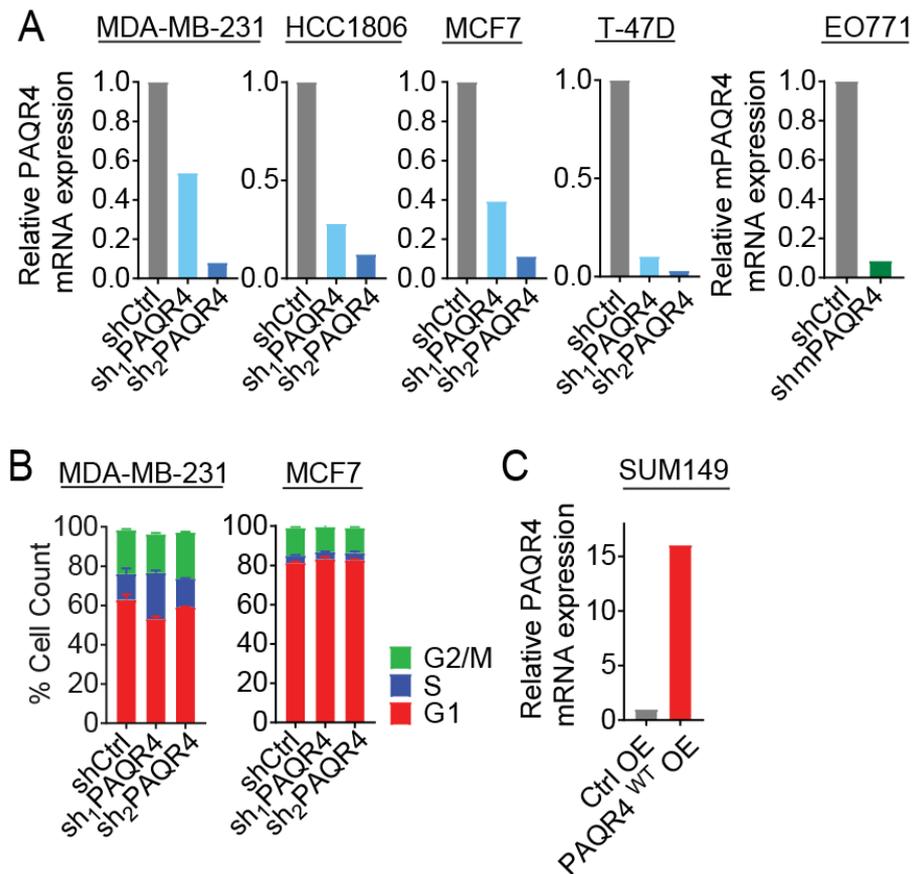
A) Gene Set Enrichment Analysis (GSEA) of sphingolipid related pathways comparing the transcriptomics of paired normal and tumor tissues from breast cancer patients (N=111) obtained from The Cancer Genome Atlas (TCGA). NES = Normalized Enrichment Score. FDR = False Discovery Rate.

B, C) Relative *PAQR4* expression in tumor compared to normal tissue samples with different estrogen, progesterone and HER2 receptor status subtypes in the TCGA and GEO70947 datasets. *PAQR4* RSEM represents the normalized number of reads mapped to *PAQR4* gene.

D) *PAQR4* expression negatively correlates with patient survival as determined by Kaplan-Meier curves of distant metastasis-free survival based on *PAQR4* expression

stratified into four quantiles using Gene expression-based Outcome for Breast cancer Online (GOBO) (n = 1176 breast cancer patients) (Ringner et al., 2011).

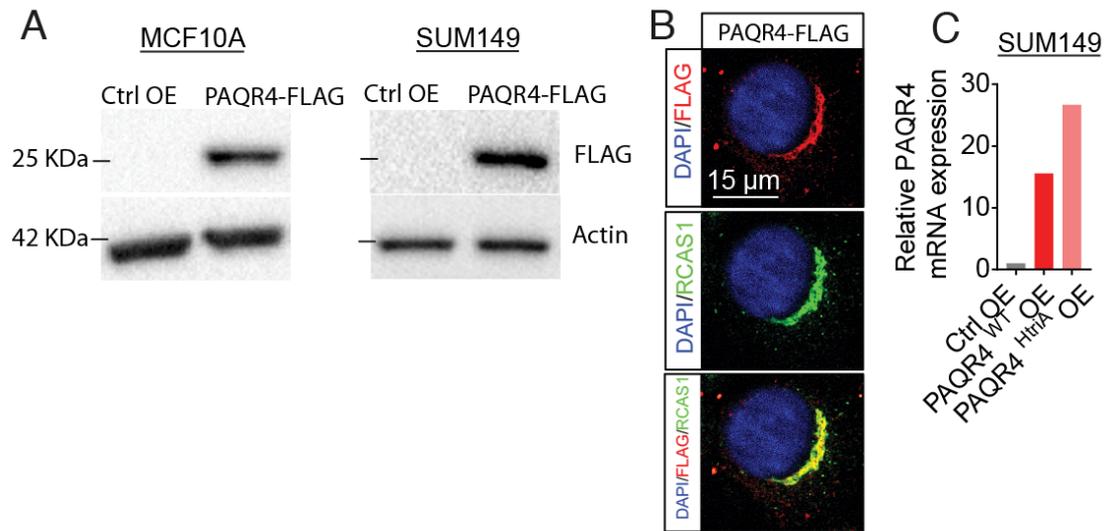
Supplementary Figure 2:



A) Expression level of *PAQR4* determined by qPCR in cell lines stably transfected with shRNAs targeting *PAQR4*. *PAQR4* expression is calculated relative to control cells. The data shown is one representative of three or more experiments.

B) Cell cycle distribution analysis of MDA-MB-231 and MCF7 cells depleted for *PAQR4* as determined by PI staining and flow cytometry of fixed cells. Data are presented as mean \pm SEM from one of three independent experiments.

Supplementary Figure 4:

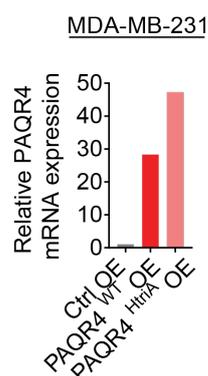


A) Western blot analysis of lysates from MCF10A and SUM149 cells engineered to express PAQR4 containing a N-terminal flag tag. anti-Flag were used to detect PAQR4-flag and anti-actin antibody for assessing equal loading.

B) Confocal immunofluorescent images of breast cancer cell line SUM149 expressing Flag-tagged PAQR4. The tagged protein co-localizes with the Golgi marker RCAS1.

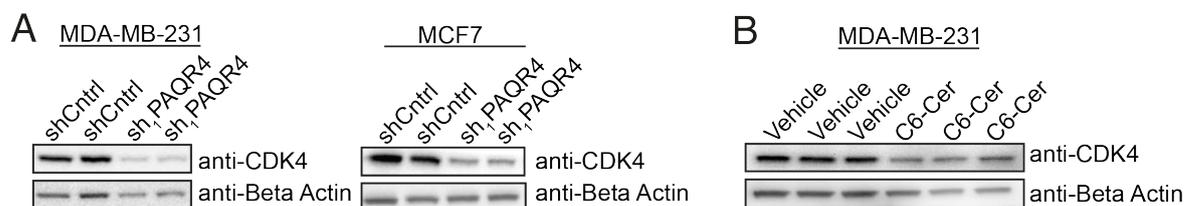
C) Expression level of wild type and mutated (HtriA) *PAQR4* in SUM149 cells with retroviral-mediated overexpression as determined by RT-qPCR. PAQR4 expression is calculated relative to the control cells. The presented figure is one representative of more than three experiments.

Supplementary Figure 5:



Expression level of wild type and mutated (HtriA) *PAQR4* in MDA-MB-231 cells with retroviral mediated overexpression as determined by RT-qPCR. *PAQR4* expression is calculated relative to the control cells. The presented figure is one representative of more than three experiments.

Supplementary Figure 6:



A) Western blot analysis of CDK4 expression in lysates from MDA-MB-231 and MCF7 control and knockdown cells using anti-CDK4 and anti-actin antibody as a loading control. **B)** Western blot analysis of CDK4 expression in lysates from MDA-MB-231 following exposure to exogenous C6-Ceramides.

Movie S1: Molecular Dynamics Simulation of the PAQR4 Model Containing Docked a C18-Ceramide Molecule Embedded in the Phospholipid Bilayer.