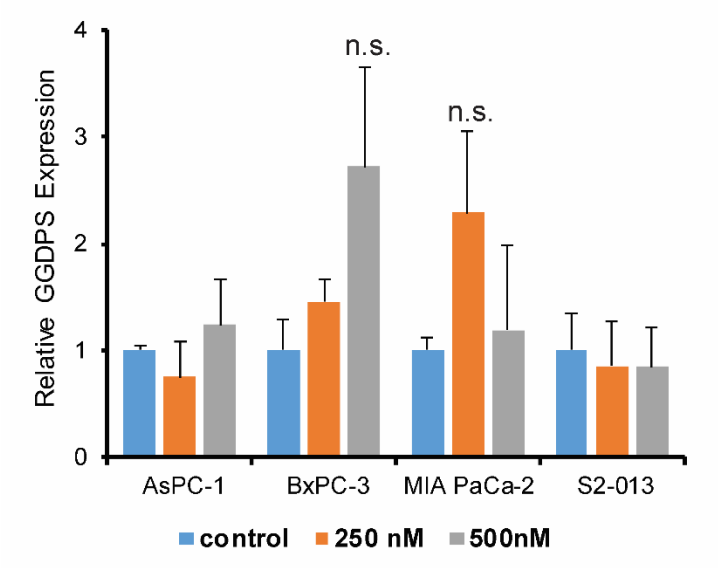
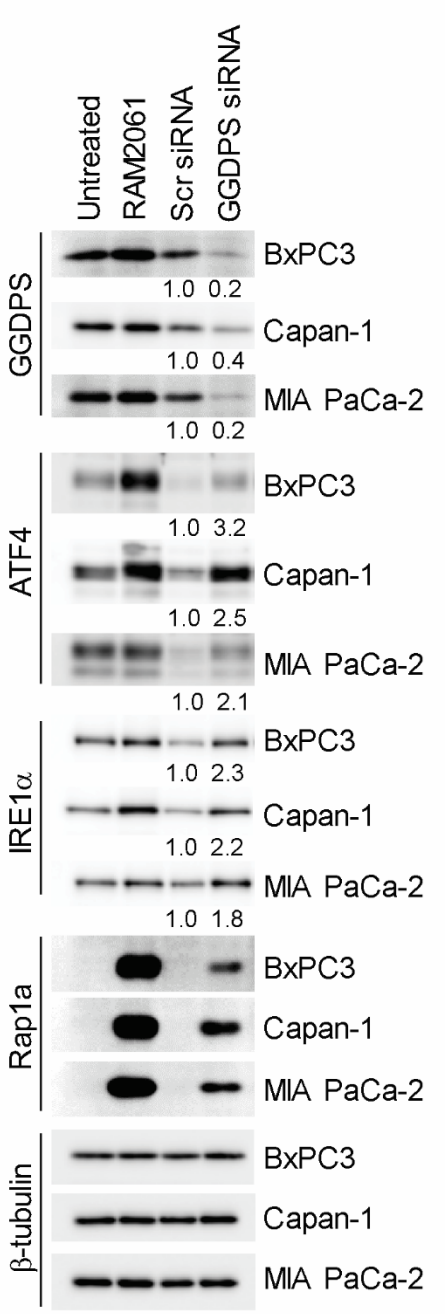
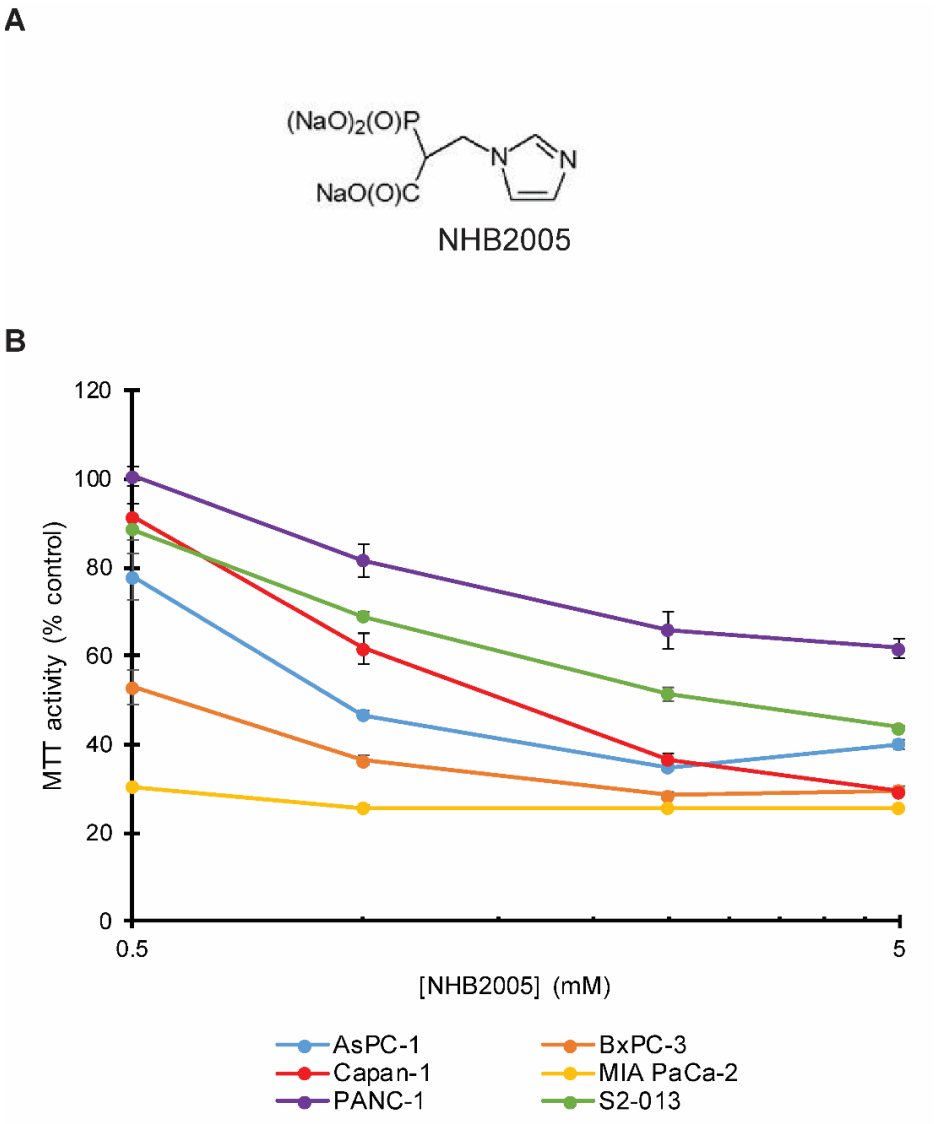


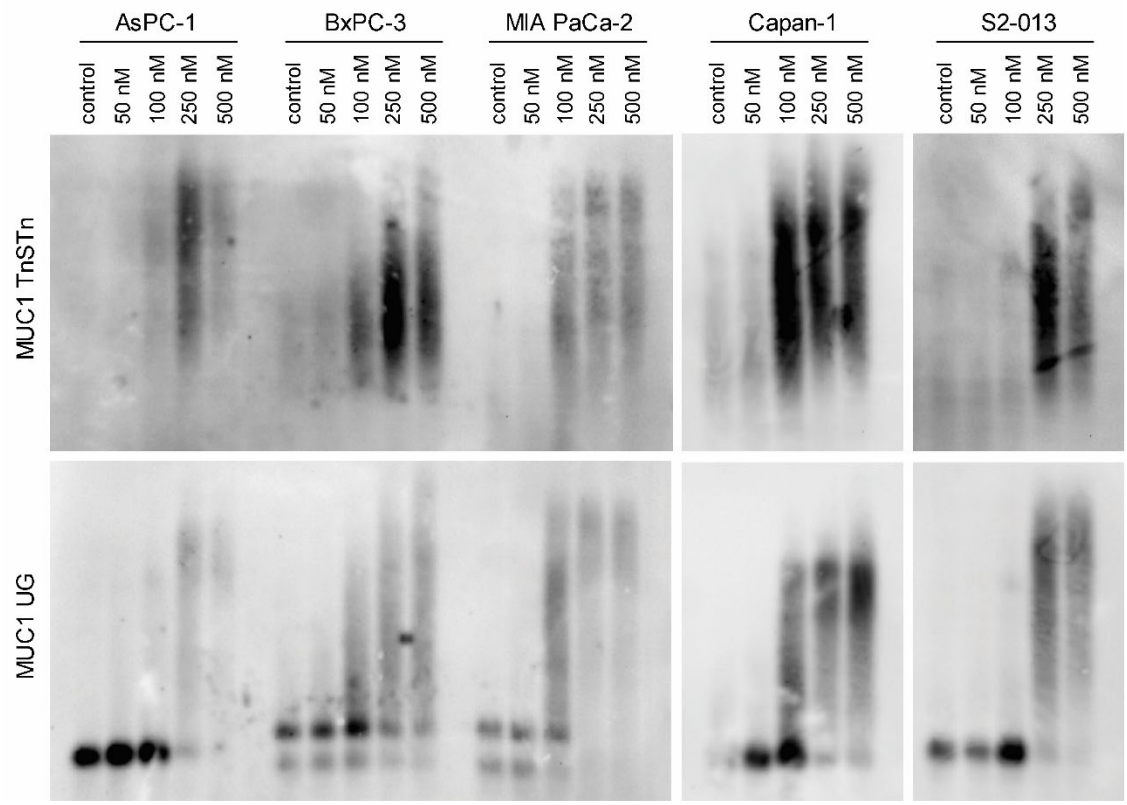

**Supplemental Figure 1. RAM2061 does not alter GGDPS expression.** qRT-PCR analysis of GGDPS expression in human PDAC cell lines. Cells were treated with or without RAM2061 for 48 hours. Data are normalized to control. Data are shown a mean ± standard deviation (n=3).



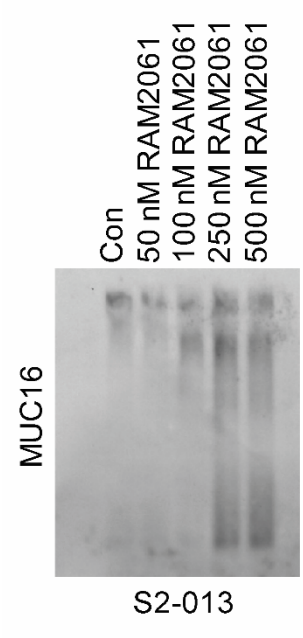

**Supplemental Figure 2. siRNA mediated knockdown of GGDPS induces the UPR.** Immunoblot analysis showing protein levels of GGDPS, ATF4, IRE1α, Rap1a, and β-tubulin (loading control) in human PDAC cell lines. Cells were treated with either scrambled siRNA or GGDPS siRNA and protein was isolated after 96 hours. Untreated and RAM2061 (100 nM) cells are shown as negative and positive controls, respectively. Densitometry measurement for GGDPS knockdown relative to the scrambled control are shown.



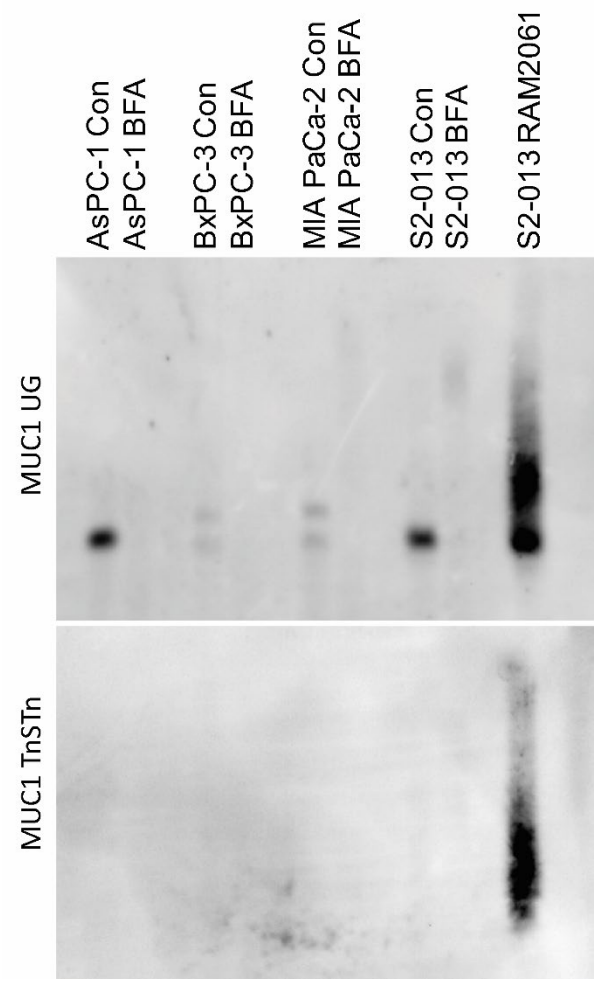

**Supplemental Figure 3. GGTase II inhibition induces cytotoxic effects in human PDAC cells.** (A) Structure of the GGTase II inhibitor (NHB2005) used in these studies. (B) MTT assays were performed following a 72-hour incubation period with NHB2005 in six human PDAC cell lines. Data are shown a mean ± standard deviation (n=4).



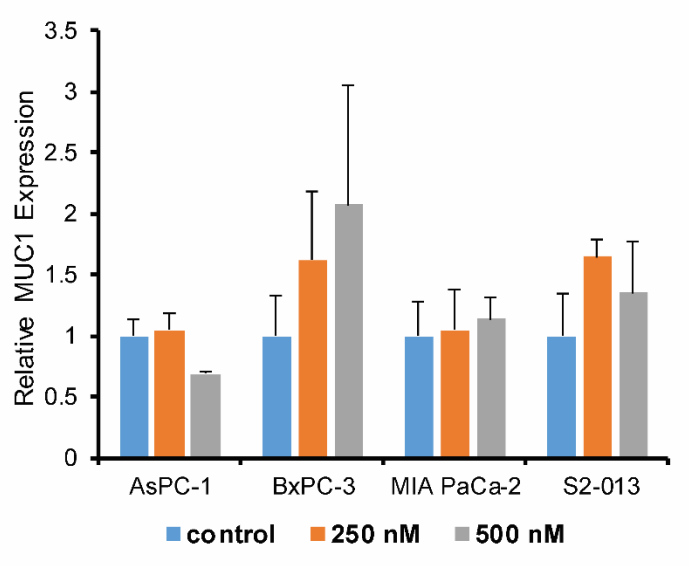

**Supplemental Figure 4. Inhibition of GGDPS results in accumulation of MUC1.** Immunoblot analysis showing protein levels of MUC1 in human PDAC cell lines incubated in the presence or absence of varying concentrations of RAM2061 for 72 hours. Antibodies specific to the TnSTn and under glycosylated (UG) MUC1 glycoprotein were used.



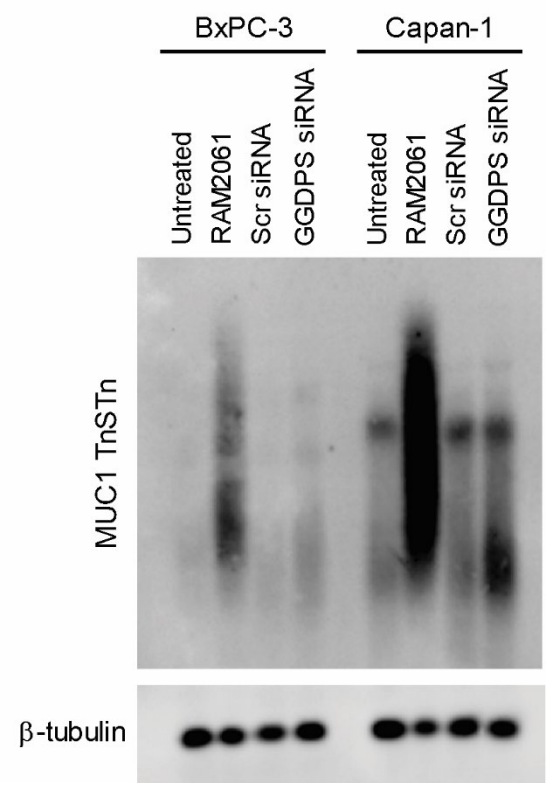

**Supplemental Figure 5. GGDPS inhibition disrupts MUC16 trafficking.** Immunoblot analysis showing protein levels of MUC16 in S2-013 cells incubated in the presence or absence of varying concentrations of RAM2061 for 48 hours.




**Supplemental Figure 6. Treatment with brefeldin A (BFA) does not induce an accumulation of MUC1.** Immunoblot analysis of MUC1 in human PDAC cells incubated in the presence or absence of BFA (0.2 μM) for 24 hours. Antibodies specific to the TnSTn and under glycosylated (UG) MUC1 glycoprotein were used. As a comparator, lysate from S2-013 cells incubated with 250 nM RAM2061 for 48 hours is shown.




**Supplemental Figure 7. RAM2061 treatment does not alter MUC1 mRNA expression.** qRT-PCR analysis of MUC1 expression in human PDAC cell lines. Cells were treated with or without varying concentrations of RAM2061 for 48 hours. Data are normalized to control. Data are shown a mean ± standard deviation (n=3).




**Supplementary Figure 8. siRNA mediated knockdown of GGDPS causes accumulation of MUC1.** Immunoblot analysis showing protein levels of MUC1 in human PDAC cell lines. Cells were treated with either scrambled siRNA or GGDPS siRNA and protein was isolated after 96 hours. Lysates from untreated and RAM2061 (100 nM)-treated cells are shown as negative and positive controls, respectively.

| Antibody | Company | Cat. # | Dilution |
|---|---|---|---|
| ATF-4 | Cell Signaling | 11815 | 1:1000 |
| Cleaved Caspase 3 | Cell Signaling | 9664 | 1:500 |
| Cleaved Caspase 8 | Cell Signaling | 9496 | 1:500 |
| Cleaved Caspase 9 | Cell Signaling | 9501 | 1:500 |
| eIF2α | Cell Signaling | 9722 | 1:1000 |
| GGDPS | Santa Cruz | sc-271680 | 1:250 |
| p-eIF2α | Cell Signaling | 3597 | 1:1000 |
| IRE1α | Cell Signaling | 3294 | 1:2000 |
| PARP | Santa Cruz | sc-7150 | 1:10,000 |
| PERK | Santa Cruz | sc-13073 | 1:500 |
| β-Tubulin | Sigma | T5201 | 1:25,000 |
| Rap1a | Santa Cruz | sc-373968 | 1:500 |
| MUC1 underglycosylated | Millipore | mabc1613 | 1:1000 |
| MUC1 TnSTn | Clone 5E5 | Citation 1 | 1:2500 |
| MUC1 tandem repeat | Clone AR20.5 | Citation 2 | 1:2500 |
| MUC16 | Clone AR9.6 | Citation 3 | 1:2500 |
| MUC5ac | Millipore | mab2011 | 1:2500 |

**Supplemental Table 1. Antibodies used for western blotting.**

| | |
|---|---|
| **ATF4** | |
| **F** | AAGCCTAGGTCTCTTAGATG |
| **R** | TTCCAGGTCATCTATACCCA |
| **β-ACTIN** | |
| **F** | ACGTTGCTATCCAGGCTGTGCTAT |
| **R** | TTAATGTCACGCACGATTTCCCGC |
| **CHOP** | |
| **F** | TCTTCACCACTCTTGACCCTGCTT |
| **R** | GTTCTTTCTCCTTCATGCGCTGCT |
| **IRE1** | |
| **F** | AGACTTTGTCATCGGCCTTTGCAG |
| **R** | ATTCACTGTCCACAGTCACCACCA |
| **GGDPS** | |
| **F** | GGCTGAAAGTTCCAGAGGACAAGCTA |
| **R** | ACTGCATCTGGGTGATCAAGGGTT |
| **MUC1** | |
| **F** | GGTTTTCTGGGCCTCTCCA |
| **R** | ACGTCGTGGACATTGATGGT |
| **PERK** | |
| **F** | GCAACAACGTTTATTGTGCGCAGG |
| **R** | AAACAACTCCAAAGCCACCACGTC |
| **XBP-1** | |
| **F** | GTTGAGAACCAGGAGTTAAGACAG |
| **R** | CAGAGGGTATCTCAAGACTAGG |

**Supplemental Table 2. Primer sequences.**

**Supplemental References**


1. Sorensen AL, Reis CA, Tarp MA, Mandel U, Ramachandran K, Sankaranarayanan V, et al. Chemoenzymatically synthesized multimeric Tn/STn MUC1 glycopeptides elicit cancer-specific anti-MUC1 antibody responses and override tolerance. *Glycobiology* 2006; 16: 96-107.
2. Qi W, Schultes BC, Liu D, Kuzma M, Decker W, Madiyalakan R. Characterization of an anti-MUC1 monoclonal antibody with potential as a cancer vaccine. *Hybrid Hybridomics* 2001; 20: 313-24.
3. Radhakrishnan P, Mohr AM, Grandgenett PM, Steele MM, Batra SK, Hollingsworth MA. MicroRNA-200c modulates the expression of MUC4 and MUC16 by directly targeting their coding sequences in human pancreatic cancer. *PLoS One* 2013;8(10):e73356.