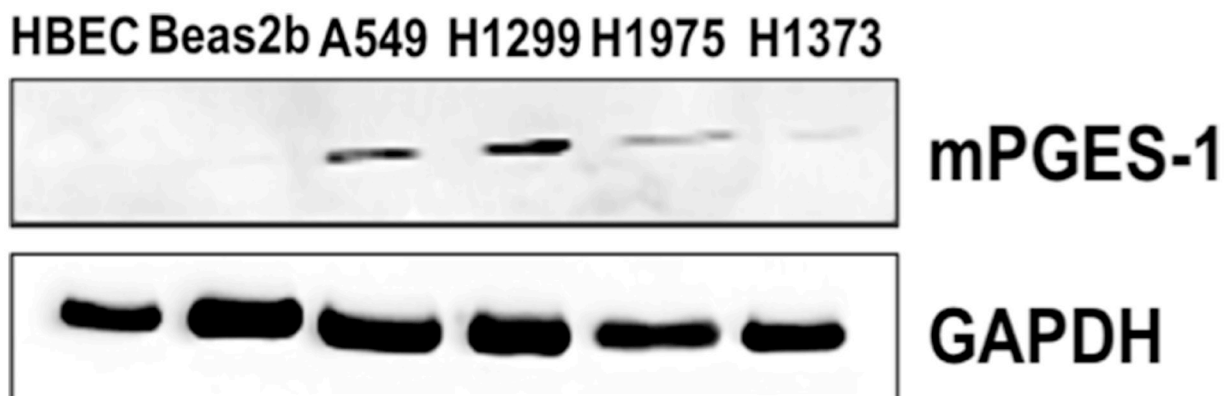
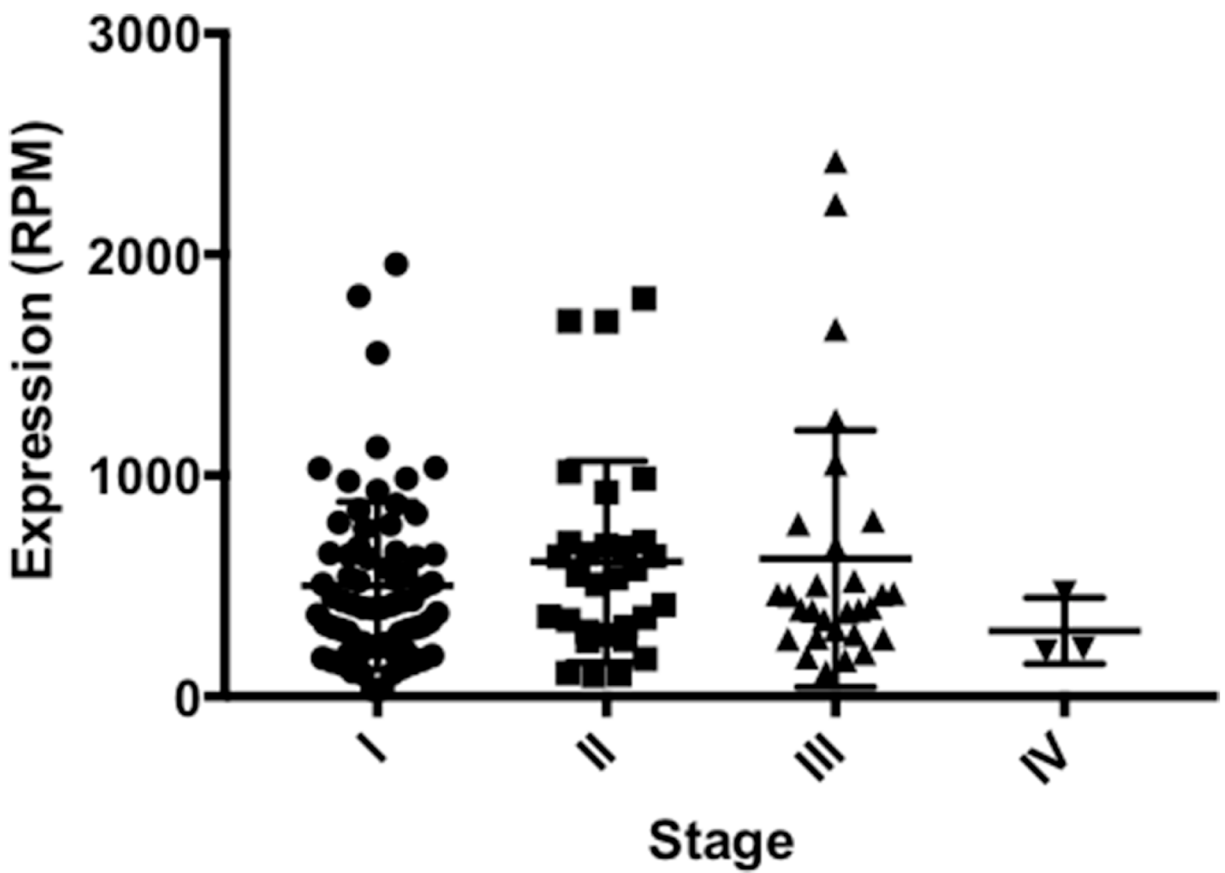


## miR-708-5p targets oncogenic prostaglandin E2 production to suppress a pro-tumorigenic phenotype in lung cancer cells

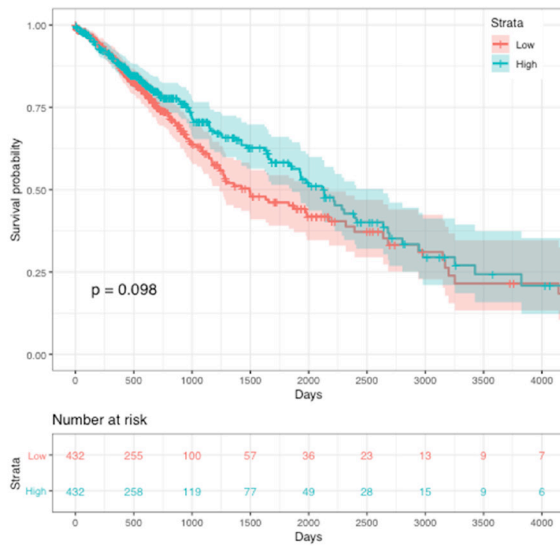
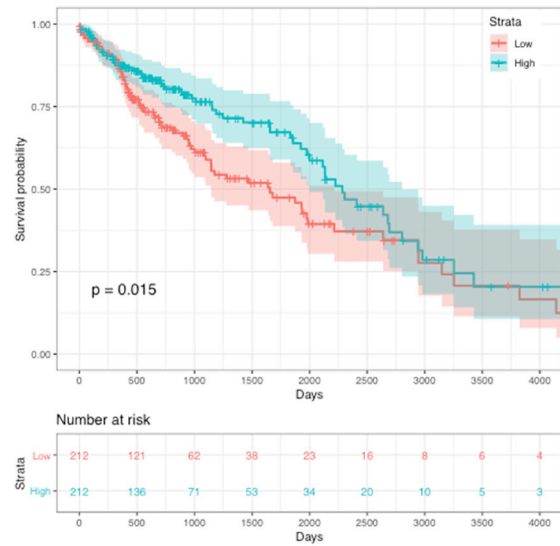
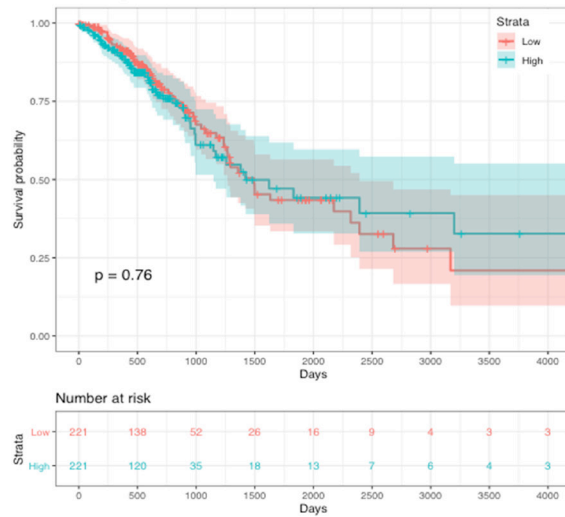
### SUPPLEMENTARY MATERIALS



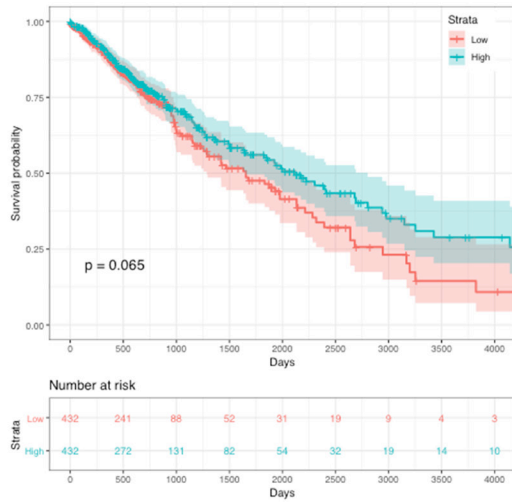
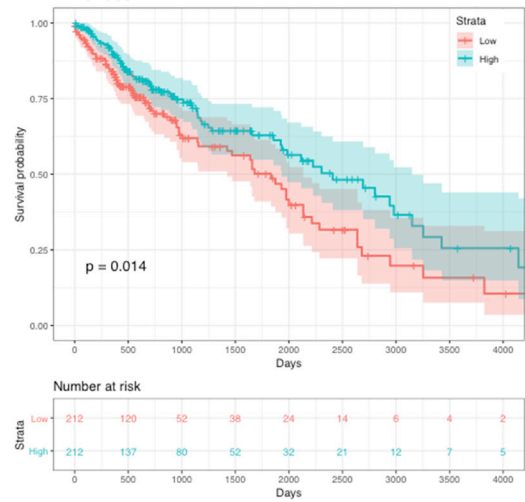
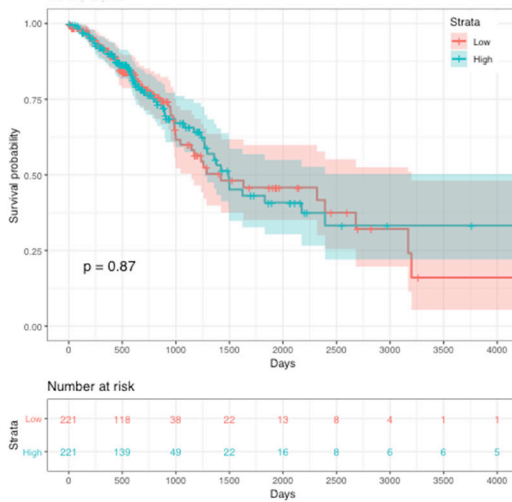
**Supplementary Figure 1: mPGES-1 is overexpressed in lung cancer cell lines.** Western blot analysis of baseline mPGES-1 protein levels in non-cancerous (HBEC, Beas2b) and cancerous (A549, H1299, H1975, H1373) lung cell lines. GAPDH served as a loading control. All western blots are representative of 3 independent experiments.



**Supplementary Figure 2: miR-708 expression is not associated with lung TNM stage.** Box plot from TCGA data measuring the mean expression of miR-708 by tumor-node metastasis (TNM) stage in LUSC patients. Stage I:  $n = 72$ , Stage II:  $n = 30$ , Stage III:  $n = 29$ , Stage IV:  $n = 3$ .

**A****B****C**

**Supplementary Figure 3: ODZ4 mRNA expression is associated with increased survival rates in LUSC patients and phenocopies miR-708.** Kaplan–Meier plots from TCGA data measuring the effects of high (blue) or low (red) *ODZ4* mRNA expression in (A) NSCLC ( $p = .0905$ ,  $n = 864$ ), (B) LUSC ( $p = .015$ ,  $n = 424$ ), and (C) LUAD ( $p = .76$ ,  $n = 442$ ) on patient survival rates. The bottom of each graph indicates the number of patients at risk for each time point.

**A****B****C**

**Supplementary Figure 4: CHOP mRNA expression is associated with increased survival rates in LUSC patients.** Kaplan–Meier plots from TCGA data measuring the effects of high (blue) or low (red) CHOP mRNA expression in (A) NSCLC ( $p = .065$ ,  $n = 864$ ), (B) LUSC ( $p = .014$ ,  $n = 424$ ), and (C) LUAD ( $p = .87$ ,  $n = 442$ ) on patient survival rates. The bottom of each graph indicates the number of patients at risk for each time point.

**Supplementary Table 1: miR-708 expression correlates with known miR-708 regulators in lung cancer tumors**

Gene	miRNA	NSCLC		LUAD		LUSC	
		Correlation	<i>p</i> value	Correlation	<i>p</i> value	Correlation	<i>p</i> value
<i>CHOP</i> <sup>^</sup>	miR-708	0.207	2.181E-11	<b>0.0445</b>	<b>0.3085</b>	0.188	0.00002323
<i>GRα</i> <sup>^</sup>	miR-708	<b>-0.236</b>	<b>1.825E-14</b>	<b>-0.0579</b>	<b>0.1851</b>	<b>-0.203</b>	<b>0.000004526</b>
<i>MYC</i> <sup>^</sup>	miR-708	0.333	4.618E-28	<b>-0.000522</b>	<b>0.9905</b>	0.167	0.0001741
<i>E2F1</i> <sup>^</sup>	miR-708	0.119	0.000132	0.13	0.002744	0.106	0.01712
<i>CTBP2</i> <sup>*</sup>	miR-708	<b>-0.19</b>	<b>8.999E-10</b>	<b>0.0799</b>	<b>0.06715</b>	<b>-0.0134</b>	<b>0.7638</b>
<i>RAD21</i> <sup>^</sup>	miR-708	0.206	2.502E-11	0.15	0.0005638	0.154	0.0005529
<i>C/EBP-β</i> <sup>^</sup>	miR-708	<b>-0.271</b>	<b>8.746E-19</b>	<b>0.0728</b>	<b>0.09539</b>	<b>-0.382</b>	<b>6.762E-19</b>
<i>CTCF</i> <sup>*</sup>	miR-708	0.16	2.434E-07	<b>-0.0445</b>	<b>0.3086</b>	0.0894	0.04538

TCGA mRNA/miRNA data showing correlation, and significance (*p* value) of miR-708 and various validated regulators of miR-708 expression in NSCLC (*n* = 864), LUAD (*n* = 442), and LUSC (*n* = 424) tumors. ***Bold italic*** font indicates a significant negative correlation; *italic* font represents a significant positive correlation; **bold** font indicates no significant correlation. (ˆ) represents a positive regulator of miR-708 expression, while (\*) represents a repressor of miR-708 expression.

**Supplementary Table 2: Significant correlations between miR-708 and AA pathway mRNA gene expression in LUSC tumors**

**A**

<b>Significant Negative Correlation</b>				
<b>Gene</b>	<b>miRNA</b>	<b>Correlation</b>	<b>Adj. R<sup>2</sup></b>	<b><i>p</i> value</b>
15-LOX	miR-708	-0.195	0.0361	1.10E-05
5-LO	miR-708	-0.347	0.118	1.27E-15
COX-1	miR-708	-0.279	0.0758	2.13E-10
COX-2	miR-708	-0.0916	0.00641	0.04018
CYSLTR	miR-708	-0.208	0.0412	2.69E-06
FLAP	miR-708	-0.337	0.111	9.34E-15
LTA4H	miR-708	-0.299	0.0874	8.37E-12
LTC4S	miR-708	-0.328	0.106	4.28E-14
mPGES-1	miR-708	-0.126	0.0139	0.004761
PTGDR	miR-708	-0.242	0.0565	4.23E-08
PTGDS	miR-708	-0.257	0.064	5.44E-09
PTGER1	miR-708	-0.164	0.025	0.0002207
PTGER2	miR-708	-0.301	0.0887	5.88E-12
PTGER4	miR-708	-0.111	0.0104	0.01261
PTGIR	miR-708	-0.274	0.073	4.49E-10
PTGIS	miR-708	-0.279	0.0758	2.13E-10
TBXAS1	miR-708	-0.357	0.126	1.45E-16

**B**

<b>Significant Positive Correlation</b>				
<b>Gene</b>	<b>miRNA</b>	<b>Correlation</b>	<b>Adj. R<sup>2</sup></b>	<b><i>p</i> value</b>
mPGES-2	miR-708	0.155	0.0221	0.0004902
LTB4R2	miR-708	0.0974	0.0075	0.02918
cPGES	miR-708	0.199	0.0377	7.09E-06
12-LOX	miR-708	0.142	0.0182	0.001421

TCGA mRNA/miRNA data displaying correlation, adjusted R<sub>2</sub>, and significance for miR-708 vs AA pathway genes in LUSC tumor ( $n = 424$ ). Supplementary Table 1 (A) indicates genes significantly negatively correlated with miR-708 expression, while (B) shows genes significantly positively correlated with miR-708 expression.