Figure S1 Expression of PHLDA family in MM and lung adenocarcinoma (LUAD) tumors cores included in tissue microarray (TMA). Homogeneity observed between expression levels in different tumor cores. Original magnification 4×. PHLDA, pleckstrin homology domain family A; MM, malignant mesothelioma.

Oncomine dataset

Analysis Type by Cancer	Cancer vs. Normal		Analysis Type by Cancer	Cancer vs. Normal		Analysis Type by Cancer	Cancer vs. Normal	
Bladder Cancer	1		Bladder Cancer			Bladder Cancer		
Brain and CNS Cancer	14		Brain and CNS Cancer	3		Brain and CNS Cancer		
Breast Cancer		5	Breast Cancer	4		Breast Cancer	1	
Cervical Cancer		2	Cervical Cancer			Cervical Cancer		
Colorectal Cancer	22		Colorectal Cancer	4		Colorectal Cancer	1	
Esophageal Cancer		8	Esophageal Cancer	4		Esophageal Cancer		2
Gastric Cancer			Gastric Cancer			Gastric Cancer	1	
Head and Neck Cancer	1	1	Head and Neck Cancer	5		Head and Neck Cancer		
Kidney Cancer	4		Kidney Cancer	3		Kidney Cancer	1	
Leukemia	2	1	Leukemia		1	Leukemia	3	
Liver Cancer		2	Liver Cancer			Liver Cancer		
Lung Cancer	1		Lung Cancer	8		Lung Cancer		
Lymphoma	6	4	Lymphoma	10		Lymphoma	5	
Melanoma	5		Melanoma			Melanoma		
Myeloma	1		Myeloma			Myeloma		
Other Cancer	4		Other Cancer	4	1	Other Cancer	5	
Ovarian Cancer	1		Ovarian Cancer	3		Ovarian Cancer		
Pancreatic Cancer	5		Pancreatic Cancer	5		Pancreatic Cancer	2	
Prostate Cancer			Prostate Cancer			Prostate Cancer		
Sarcoma	1	2	Sarcoma		1	Sarcoma	1	6
Significant Unique Analyses	66	24	Significant Unique Analyses	53	3	Significant Unique Analyses	18	8
Total Unique Analyses	457		Total Unique Analyses	436		Total Unique Analyses	360	

PHLDA1	PHLDA2	PHLDA3

Figure S2 Oncomine analysis of *PHLDA1*, *PHLDA2* and *PHLDA3* mRNA expression in different types of cancer, showing the differences in expression levels between tumor and normal tissue. Red cells represent overexpression of genes in tumor tissue compared to normal, whereas blue cells indicate underexpression, satisfying the thresholds P<0.05; fold change ≥1.5; gene rank ≤10%. PHLDA, pleckstrin homology domain family A.

PHLDA1 Expression

A Hou Lung Statistics

B Selamat Lung Statistics

C Su Lung Statistics

Legend

0. Lung (n=65)
1. Large Cell Lung Carcinoma (n=19); *P*= 0.14; FC= 1.16
2. Lung Adenocarcinoma (n=45); *P*= 0.03; FC= 1.18
3. Squamous Cell Lung Carcinoma (n=27); *P*= 0.03; FC= 1.25

Legend

1. Lung (n=58)
2. Lung Adenocarcinoma (n=58); *P*= 0.61; FC= -1.030

Legend

1. Lung (n=30)
2. Lung Adenocarcinoma (n=27); *P*<0.01; FC= -1.71

PHLDA2 Expression

D Hou Lung Statistics

E Selamat Lung Statistics

F Su Lung Statistics

Legend

0. Lung (n=65)
1. Large Cell Lung Carcinoma (n=19); *P*= 0.06; FC= 1.06
2. Lung Adenocarcinoma (n=45); *P*<0.01; FC= 2.21
3. Squamous Cell Lung Carcinoma (n=27); *P*<0.01; FC= 1.173

Legend

0. Lung (n=58)
1. Lung Adenocarcinoma (n=58); *P*<0.01; FC= 2.39

Legend

1. Lung (n=30)
2. Lung Adenocarcinoma (n=27); *P*<0.01; FC= 3.63

PHLDA3 Expression

G Hou Lung Statistics

H Selamat Lung Statistics

I Su Lung Statistics

Legend

0. Lung (n=65)
1. Large Cell Lung Carcinoma (n=19); *P*= 1.00; FC= -1.81
2. Lung Adenocarcinoma (n=45); *P*=0.98; FC= -1.14
3. Squamous Cell Lung Carcinoma (n=27); *P*=0.28; FC= 1.05

Legend

0. Lung (n=58)
1. Lung Adenocarcinoma (n=58); *P*<0.01; FC= 1.29

Legend

1. Lung (n=30)
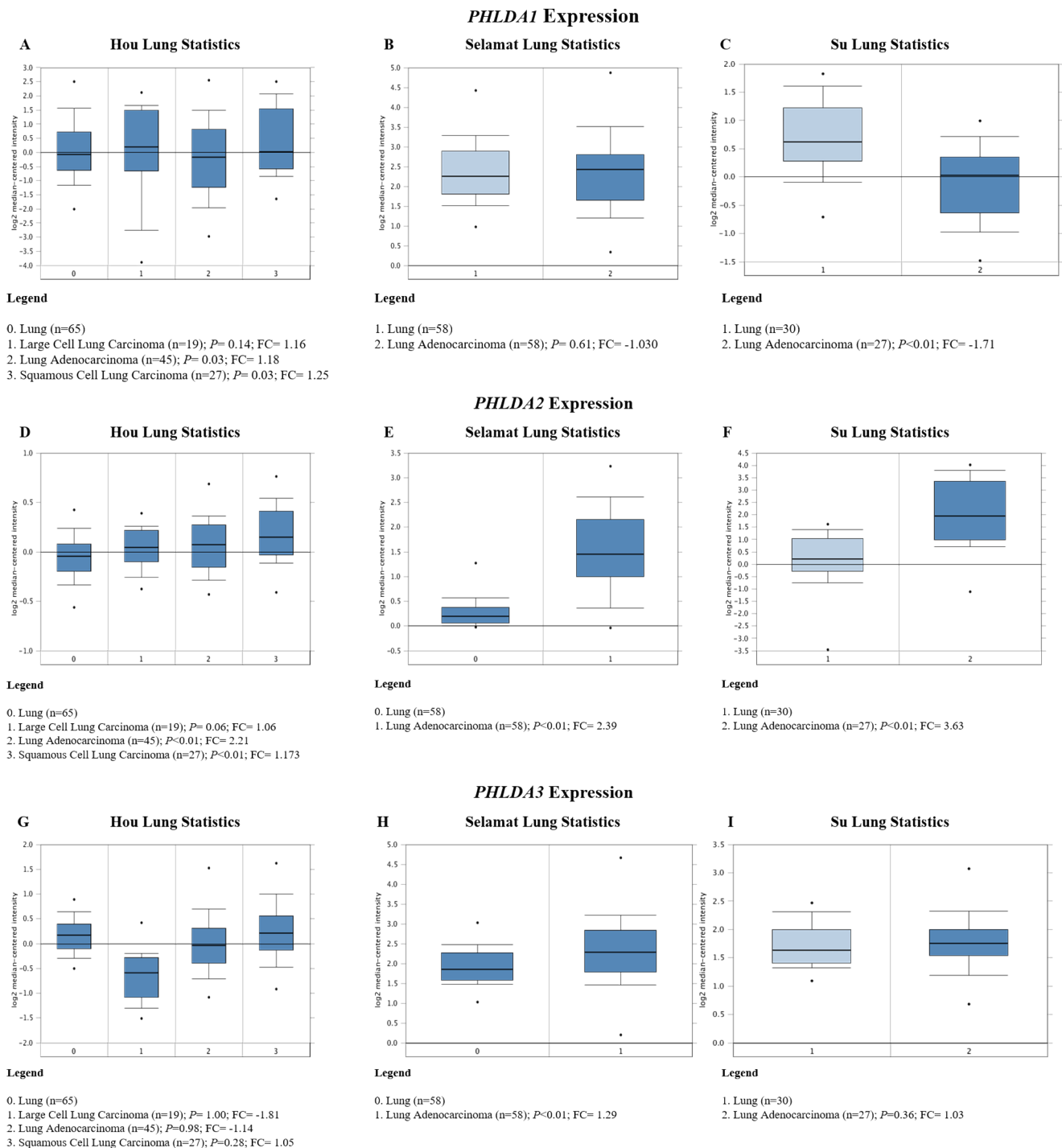2. Lung Adenocarcinoma (n=27); *P*=0.36; FC= 1.03

Figure S3 Oncomine analysis of *PHLDA1*, *PHLDA2* and *PHLDA3* expression in NSCLC and their corresponding normal tissues. (A) In the Hou Lung and (B) Selamat datasets, there was no apparent change in *PHLDA1* gene expression in lung adenocarcinoma (LUAD) (fold change =1.18 and –1.03, respectively), whereas in the (C) Su dataset, there was a trend for underexpression of *PHLDA1* in LUAD tissue (fold change =–1.71). *PHLDA2* was overexpressed according to (D) Hou Lung (fold change = 2.21), (E) Selamat (fold change =2.39), and (F) Su (fold change =3.63) datasets. No changes were found in the expression levels of *PHLDA3* in LUAD according to (A) Hou Lung (fold change =–1.14), (B) Selamat (fold change =1.29) and (C) Su (fold change =1.03) datasets. PHLDA, pleckstrin homology domain family A.

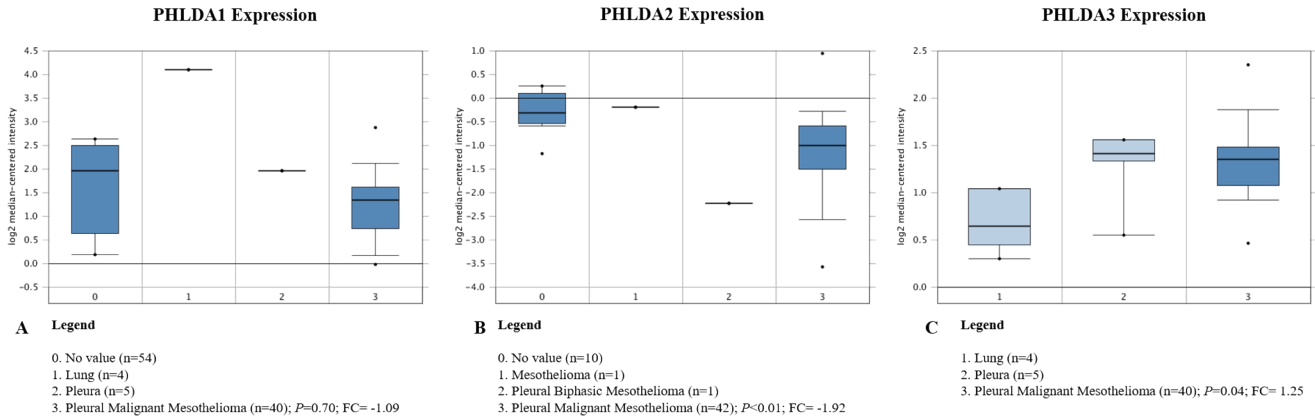**PHLDA Expression in Gordon Mesothelioma**
Grouped by Cancer Type

PHLDA1 Expression

A Legend
0. No value (n=54)
1. Lung (n=4)
2. Pleura (n=5)
3. Pleural Malignant Mesothelioma (n=40); *P*=0.70; FC= -1.09

PHLDA2 Expression

B Legend
0. No value (n=10)
1. Mesothelioma (n=1)
2. Pleural Biphasic Mesothelioma (n=1)
3. Pleural Malignant Mesothelioma (n=42); *P*<0.01; FC= -1.92

PHLDA3 Expression

C Legend
1. Lung (n=4)
2. Pleura (n=5)
3. Pleural Malignant Mesothelioma (n=40); *P*=0.04; FC= 1.25

Figure S4 *PHLDA* gene expression in malignant mesothelioma (MM) according to the Gordon Mesothelioma dataset. *PHLDA1* (A) and *PHLDA3* (C) were not significantly expressed in tumors compared to normal tissue (fold change =−1.09 and 1.25, respectively), (B) *PHLDA2* was underexpressed in MM (fold change=−1.92). The X-axis of the plot represents normal vs. pleural malignant mesothelioma, the Y-axis represents mRNA expression in log2 median-centered intensity; the line in the middle represents the median value. P<0.05 was considered significant. PHLDA, pleckstrin homology domain family A.
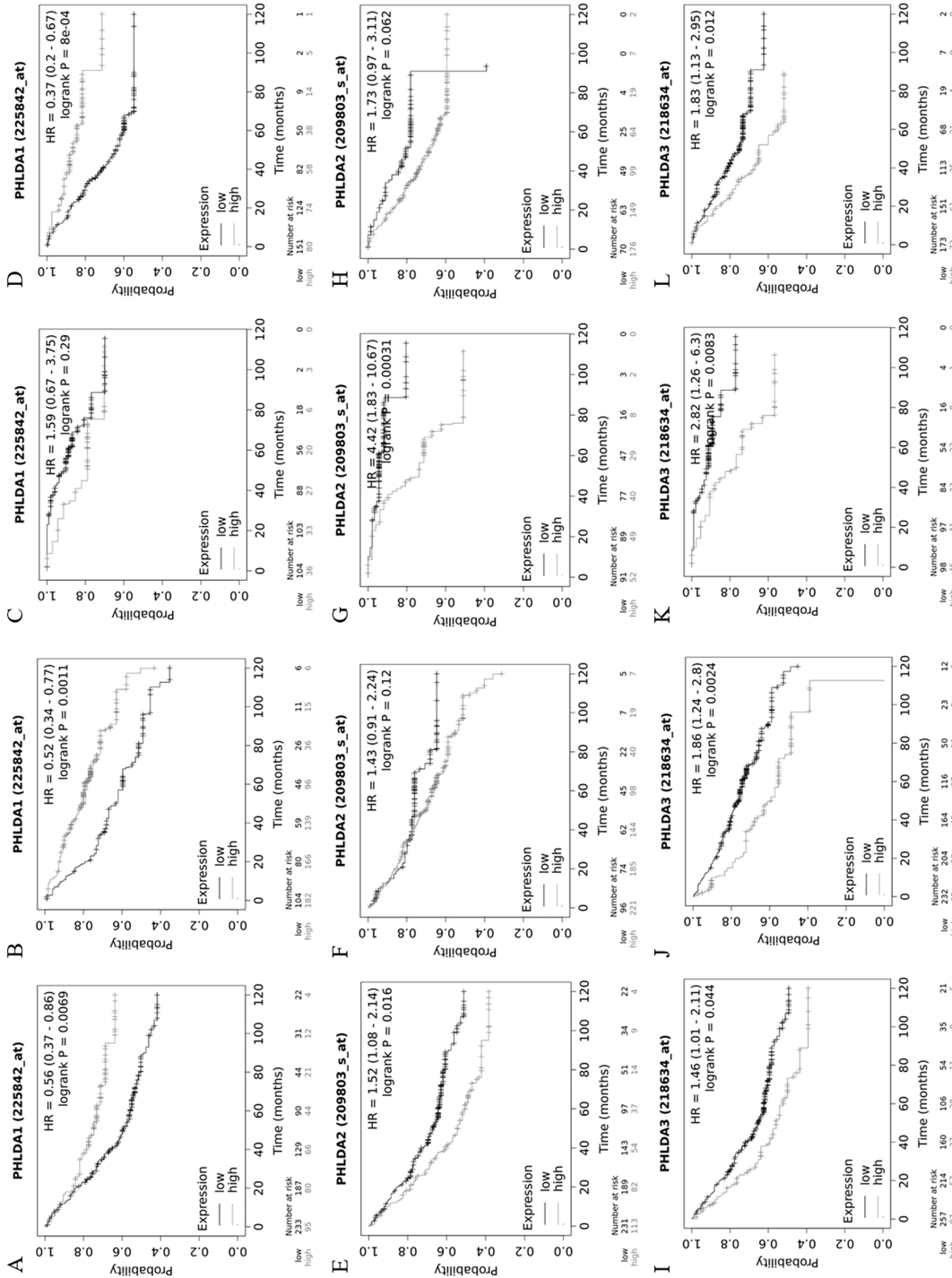
Figure S5 This Kaplan Meier survival curve shows the correlation between pleckstrin homology domain family A (PHLDA) gene expression and overall survival (OS) in lung adenocarcinoma (LUAD) patients, according to the Kaplan–Meier plotter database. Low PHLDA1 expression was significantly related to worse survival in male patients (HR =0.56; 95% CI: 0.37–0.86, P<0.01) (A), female patients (HR =0.52; 95% CI: 0.34–0.77, P<0.01) (B), and smokers (HR =0.37; 95% CI: 0.2–0.67, P<0.01) (D). (C) PHLDA1 expression was not statistically significant in never smokers. High PHLDA2 expression was significantly related to worse survival in male patients (HR =1.52; 95% CI: 1.08–2.14, P=0.02) (E), and non-smokers (HR =4.42; 95% CI: 1.83-10.67, P<0.01) (G). PHLDA2 gene expression was not statistically significant in female patients (F), and smokers (H). High PHLDA3 expression correlated with worse survival in male patients (HR =1.46; 95% CI: 1.01–2.11, P=0.04) (I), female patients (HR =1.86; 95% CI: 1.24–2.8, P<0.01) (J), non-smokers (HR =2.82; 95% CI: 1.26–6.3, P<0.01) (K), and smokers (HR =1.83; 95% CI: 1.13–2.95, P=0.01) (L).

Table S1 Variables associated with overall survival (OS) of 87 patients diagnosed with Malignant mesothelioma. Univariate and multivariate analysis employed a Cox proportional hazards model using the Mesothelioma TCGA Firehose Legacy database by UCSC Xena tool

Variables	Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age	0.76 (0.3-1.8)	0.53		
Sex (Male *vs.* Female)	0.90 (0.5-1.6)	0.73		
TP53 (Mutated *vs.* Wild type)	1.04 (0.5-2.0)	0.92		
Lymph node (Positive *vs.* Negative)	0.91 (0.6-1.5)	0.71		
Stage		0.77		
Stage (II *vs.* I)	0.64 (0.3-1.5)	0.31		
Stage (III *vs.* I)	0.78 (0.4-1.6)	0.51		
Stage (IV *vs.* I)	0.71 (0.3-1.7)	0.44		
PHLDA3 (High *vs.* Low)	1.29 (0.8-2.0)	0.27		
PHLDA1 (High *vs.* Low)	1.80 (1.1-2.9)	0.01	1.64 (1.0-2.6)	0.04
PHLDA2 (High *vs.* Low)	1.87 (1.2-3.0)	<0.01	1.71 (1.1-2.7)	0.03

HR: Hazard ratio; 95% CI: 95% confidence intervals.