

## 1    **Supplementary Information**

2    **Supplementary Table 1.** Top 50 upregulated genes in pancreatic adenocarcinoma cells exposed  
3    to pancreatic stellate cells in the microarray dataset GSE36775. The microarray dataset was  
4    downloaded from Gene Expression Omnibus (GEO) at <https://www.ncbi.nlm.nih.gov/geo/>. We  
5    analyzed the dataset with GEO2R at <https://www.ncbi.nlm.nih.gov/geo/geo2r/> to obtain  
6    log2-transformed fold change values and adjusted p-values for multiple comparisons.

| Gene symbol | Log fold change | Adjusted p-value |
|-------------|-----------------|------------------|
| SAA1        | 2.17            | 0.0018           |
| FCGBP       | 1.94            | 0.00201          |
| PIGR        | 1.91            | 0.00167          |
| SAA2        | 1.91            | 0.00167          |
| TFF3        | 1.77            | 0.0018           |
| ATP10B      | 1.75            | 0.00243          |
| HLA-DRA     | 1.69            | 0.00243          |
| RNASE1      | 1.68            | 0.00165          |
| AGR2        | 1.67            | 0.00243          |
| S100A8      | 1.67            | 0.00165          |
| RARRES1     | 1.65            | 0.0101           |
| DMBT1       | 1.63            | 0.00165          |
| CDC42EP5    | 1.57            | 0.00109          |
| ASS1        | 1.54            | 0.00964          |
| CFB         | 1.49            | 0.00667          |
| CD74        | 1.45            | 0.00435          |
| HLA-DPA1    | 1.42            | 0.00331          |
| GBP2        | 1.36            | 0.00684          |
| HSD17B2     | 1.33            | 0.00165          |
| MUC1        | 1.33            | 0.00443          |
| PSCA        | 1.33            | 0.01877          |
| RARRES3     | 1.29            | 0.02695          |

|               |             |                |
|---------------|-------------|----------------|
| CEACAM1       | 1.26        | 0.02399        |
| PDZK1IP1      | 1.23        | 0.03226        |
| PRR15L        | 1.23        | 0.00312        |
| HLA-DRB6      | 1.18        | 0.00243        |
| CAPN5         | 1.17        | 0.00697        |
| CYP3A5        | 1.17        | 0.01538        |
| LGALS4        | 1.16        | 0.00547        |
| CD24          | 1.14        | 0.00667        |
| PI3           | 1.14        | 0.04351        |
| SERPINA3      | 1.14        | 0.04645        |
| CCPG1         | 1.13        | 0.03932        |
| HLA-DMA       | 1.13        | 0.0018         |
| MB            | 1.13        | 0.0018         |
| VSIG2         | 1.11        | 0.01812        |
| WIP1          | 1.11        | 0.0083         |
| <b>S100A9</b> | <b>1.10</b> | <b>0.02042</b> |
| AZGP1         | 1.09        | 0.00167        |
| KLHL24        | 1.08        | 0.02311        |
| SAA4          | 1.08        | 0.00697        |
| TRAPPC6A      | 1.07        | 0.0018         |
| ALDH3B2       | 1.07        | 0.00264        |
| PRSS1         | 1.06        | 0.01563        |
| PLA2G10       | 1.04        | 0.00167        |
| TSPAN1        | 1.03        | 0.00243        |

8 **Supplementary Table 2.** Top 50 upregulated genes in pancreatic cancer cell lines with high  
 9 metastatic and growth potential under normoxic growth conditions in the microarray dataset  
 10 GSE9350. The microarray dataset was downloaded from Gene Expression Omnibus (GEO) at  
 11 <https://www.ncbi.nlm.nih.gov/geo/>. We analyzed the dataset with GEO2R at  
 12 <https://www.ncbi.nlm.nih.gov/geo/geo2r/> to obtain log2-transformed fold change values and  
 13 adjusted p-values for multiple comparisons.

| Gene symbol | Log fold change | Adjusted p-value |
|-------------|-----------------|------------------|
| SOSTDC1     | 6.657           | 0.0000911        |
| NTRK2       | 6.496           | 0.0001743        |
| IL1R1       | 5.191           | 0.0012128        |
| BCHE        | 4.9             | 0.0002484        |
| PLAT        | 4.524           | 0.0002185        |
| PTPRZ1      | 4.441           | 0.0005813        |
| HLA-DRA     | 4.384           | 0.0000806        |
| PHLDA1      | 4.241           | 0.0002185        |
| MUC2        | 4.131           | 0.0015504        |
| PTHLH       | 3.949           | 0.00111          |
| MPPED2      | 3.946           | 0.0006904        |
| SAGE1       | 3.933           | 0.0002284        |
| PHLDA1      | 3.875           | 0.0013092        |
| DUSP6       | 3.851           | 0.0012311        |
| ALDH1A3     | 3.838           | 0.0006904        |
| HS3ST1      | 3.675           | 0.0005678        |
| NTRK2       | 3.603           | 0.0002302        |
| DKK3        | 3.327           | 0.0007911        |
| SLC6A15     | 3.284           | 0.0004901        |
| PAK3        | 3.249           | 0.000486         |
| GLUL        | 3.22            | 0.0000806        |

|               |              |                  |
|---------------|--------------|------------------|
| MME           | 3.173        | 0.0014382        |
| PIK3AP1       | 3.172        | 0.0004212        |
| PADI3         | 3.07         | 0.0002484        |
| PAK3          | 3.065        | 0.0005813        |
| DUSP6         | 3.048        | 0.001214         |
| GLUL          | 3.017        | 0.0001232        |
| GCNT3         | 3.013        | 0.0002187        |
| ABCA1         | 2.973        | 0.0003563        |
| VEGFC         | 2.934        | 0.00111          |
| <b>S100A9</b> | <b>2.933</b> | <b>0.0003563</b> |
| PHLDA1        | 2.813        | 0.0007405        |
| STC1          | 2.801        | 0.0015455        |
| GLUL          | 2.79         | 0.0001284        |
| TNFSF10       | 2.763        | 0.0012251        |
| MPPED2        | 2.723        | 0.000737         |
| ABCA1         | 2.627        | 0.0003407        |
| GBP6          | 2.603        | 0.0006904        |
| TNFSF10       | 2.403        | 0.0014056        |
| LINC00673     | 2.275        | 0.000822         |
| SLC6A15       | 2.259        | 0.0016643        |
| CEP19         | 2.245        | 0.000822         |
| CEP19         | 2.24         | 0.0011113        |
| TIPARP        | 2.238        | 0.0002915        |
| B4GALT6       | 2.218        | 0.0003563        |
| NFKBIZ        | 2.198        | 0.0004531        |
| IL18R1        | 2.192        | 0.0006686        |
| IKZF2         | 2.178        | 0.0002187        |
| EDNRA         | 2.115        | 0.001755         |
| NRP2          | 2.049        | 0.00111          |

15 **Supplementary Table 3.** Primer pairs for real-time PCR

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|                |    |                         |    |
|----------------|----|-------------------------|----|
| S100A8 F:      | 5' | GGGGAATTTCCATGCCGTCTAC  | 3' |
| S100A8 R:      | 5' | CTGCCACGCCCATCTTTATCAC  | 3' |
| S100A9 F:      | 5' | TCAAAGAGCTGGTGCGAAAAGAT | 3' |
| S100A9 R:      | 5' | CCTCGCCATCAGCATGATGAACT | 3' |
| Cyclophilin F: | 5' | ATACGGGTCCTGGCATCTTGTC  | 3' |
| Cyclophilin R: | 5' | GGTGATCTTCTTGCTGGTCTTG  | 3' |

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**Supplementary Table 4.** Clinical and pathological characteristics of the study cohort from The

Human Protein Atlas website.

We obtained data from 176 patients with pancreatic ductal carcinoma via The Human Protein

Atlas website (<https://www.proteinatlas.org/>). The patients were divided into high and low

expression groups based on the default setting on the website. *p* values were calculated via \*

t-test, \*\* chi-square test, or \*\*\* Fisher's exact test.  $\alpha$ -SMA:  $\alpha$ -smooth muscle actin.

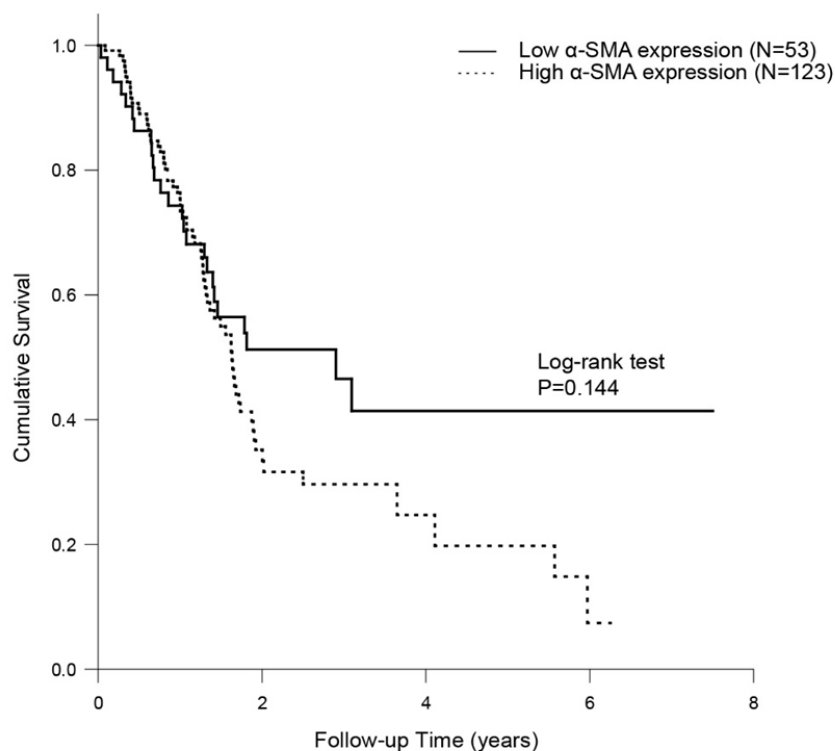
| Characteristics     | S100A9 level    |               | <i>p</i> value |
|---------------------|-----------------|---------------|----------------|
|                     | Low             | High          |                |
|                     | N=37            | N=139         |                |
| Age (Years)         | 63.1 $\pm$ 10.5 | 65.1 $\pm$ 11 | 0.303*         |
| Sex                 |                 |               |                |
| Male                | 24              | 72            | 0.156**        |
| Female              | 12              | 67            |                |
| Stage               |                 |               |                |
| I-II                | 32<br>(18.2%)   | 134 (76.1%)   | 0.036***       |
| III-IV              | 4 (2.3%)        | 3 (1.7%)      |                |
| Not available       | 1 (0.6%)        | 2 (1.1%)      |                |
| $\alpha$ -SMA level |                 |               |                |
| Low                 | 24              | 29            | <0.001**       |
| High                | 13              | 110           |                |

24 **Supplementary Table 5.** Univariate and multivariate Cox regression analyses of potential  
 25 factors affecting patient survival in 176 patients with pancreatic ductal carcinoma from the  
 26 Human Protein Atlas database (<https://www.proteinatlas.org/>).  $\alpha$ -SMA:  $\alpha$ -smooth muscle actin.

| Factor        | Univariate model |                | Multivariate model |                |
|---------------|------------------|----------------|--------------------|----------------|
|               | HR (95%CI)       | <i>p</i> value | HR (95%CI)         | <i>p</i> value |
| Age           | 1.03 (1.01-1.05) | 0.006          | 1.03 (1-1.05)      | 0.019          |
| Male          | 0.82 (0.54-1.24) | 0.344          |                    |                |
| Stage         |                  |                |                    |                |
| I             | 0.46 (0.21-0.99) | 0.028          |                    |                |
| II            | 2.37 (1.22-4.59) | 0.005          |                    |                |
| III           | 0.6 (0.08-4.32)  | 0.581          |                    |                |
| IV            | 1 (0.25-4.12)    | 0.99           |                    |                |
| S100A9        | 2 (1.14-3.49)    | 0.009          | 1.82(1.04-3.21)    | 0.037          |
| expression    |                  |                |                    |                |
| $\alpha$ -SMA | 1.41 (0.89-2.24) | 0.136          |                    |                |
| expression    |                  |                |                    |                |

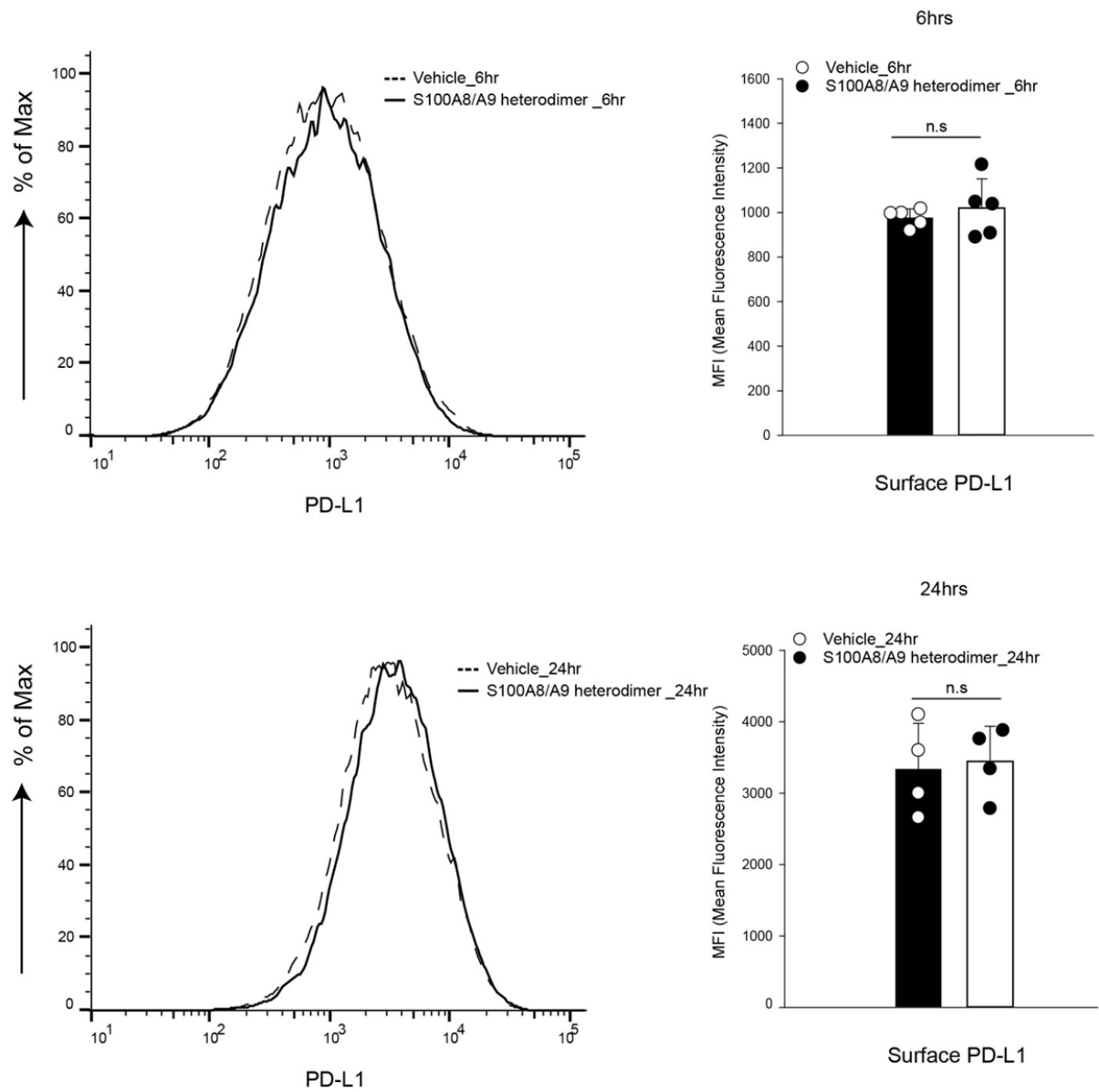
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## 28    **Supplementary Figure 1.**



29  
 30    Kaplan-Meier survival curves according to  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA) expression. We  
 31    obtained survival and immunohistochemistry staining data from 176 patients with pancreatic  
 32    ductal carcinoma from The Human Protein Atlas (<https://www.proteinatlas.org/>). Patients were  
 33    divided into high and low expression groups based on the default setting on the website. The  
 34    survival of each group was examined by Kaplan-Meier survival estimators, and the survival  
 35    outcomes of the two groups were compared by log-rank tests. The expression of  $\alpha$ -SMA did not  
 36    have a significant effect on the survival of the patients with PDAC (p=0.144, log-rank test).

Supplementary Figure 2.



Supplementary Figure 2. Stimulation with S100A8/S100A9 heterodimers in monocyte-derived IFN- $\gamma$ -primed U937 cells did not induce significant changes in the surface expression of PD-L1 in comparison with vehicle control.

42 We treated IFN- $\gamma$ -primed U937 cells with recombinant S100A8/S100A9 heterodimers, and  
43 detected the surface expression of PD-L1 with flow cytometry. We found that treatment of  
44 IFN- $\gamma$ -primed U937 cells with S100A8/S100A9 heterodimers for 6 and 24 hours did not induce  
45 significant changes in the surface expression of PD-L1 in comparison with vehicle control.