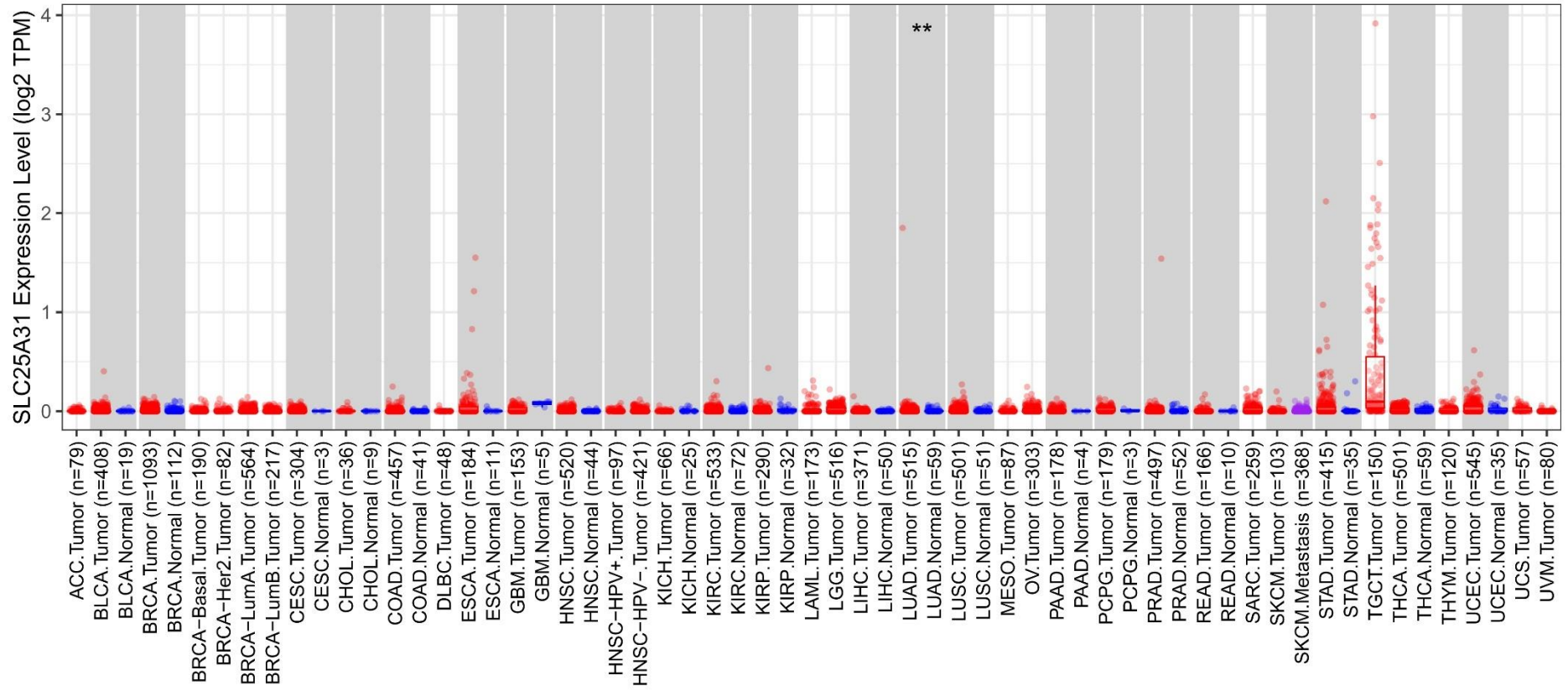


## Supplementary Materials



Supplementary Figure S1. SLC25A31\_AAC4 expression levels in 21 “cancer vs healthy” tissue pairs available on TCGA, analysed through Tumor2.

Survival difference in KIRC (n=533)

Cox Proportional Hazard Model:

```
SLC25A4 in KIRC (n=533):
Model: Surv(OS, EVENT) ~ SLC25A4
529 patients with 173 dying ( 4 missing obs. )
      coef  HR se(coef)  95%CI_L  95%CI_U    z  p signif
SLC25A4 -0.706 0.494   0.094   0.411  0.593 -7.541 0 ***
Rsquare = 0.095 (max possible = 0.75e-01)
Likelihood ratio test p = 3.8e-13
Wald test p = 4.05e-14
Score (logrank) test p = 2.24e-13
```

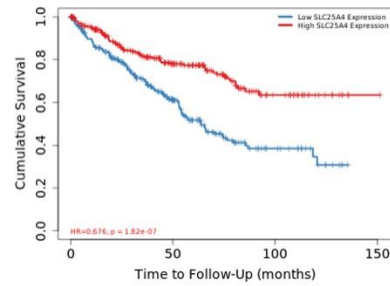
Kaplan-Meier Curve Parameters:

Split Percentage of Patients: (%)

5%  50%

Survival Time Between: (Month)

0  2000



Survival difference in KIRC (n=533)

Cox Proportional Hazard Model:

```
SLC25A5 in KIRC (n=533):
Model: Surv(OS, EVENT) ~ SLC25A5
529 patients with 173 dying ( 4 missing obs. )
      coef  HR se(coef)  95%CI_L  95%CI_U    z  p signif
SLC25A5 -0.340 0.709   0.103   0.570  0.866 -3.359 0.001 **
Rsquare = 0.022 (max possible = 0.75e-01)
Likelihood ratio test p = 6.43e-04
Wald test p = 7.82e-04
Score (logrank) test p = 1.07e-03
```

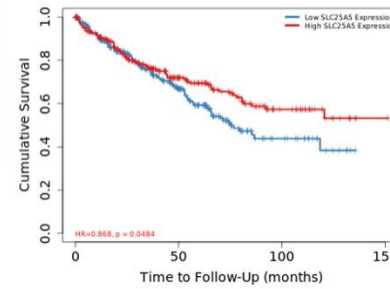
Kaplan-Meier Curve Parameters:

Split Percentage of Patients: (%)

5%  50%

Survival Time Between: (Month)

0  2000



Survival difference in KIRC (n=533)

Cox Proportional Hazard Model:

```
SLC25A6 in KIRC (n=533):
Model: Surv(OS, EVENT) ~ SLC25A6
529 patients with 173 dying ( 4 missing obs. )
      coef  HR se(coef)  95%CI_L  95%CI_U    z  p signif
SLC25A6 -0.205 0.815   0.121   0.643  1.033 -1.691 0.091
Rsquare = 0.005 (max possible = 0.75e-01)
Likelihood ratio test p = 1.02e-01
Wald test p = 9.08e-02
Score (logrank) test p = 0.35e-02
```

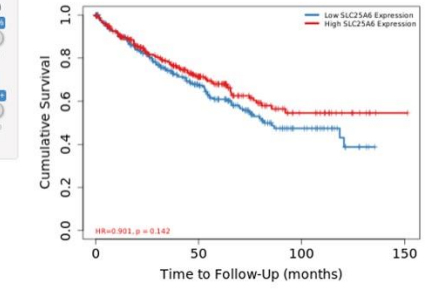
Kaplan-Meier Curve Parameters:

Split Percentage of Patients: (%)

5%  50%

Survival Time Between: (Month)

0  2000



Survival difference in KIRP (n=290)

Cox Proportional Hazard Model:

```
SLC25A4 in KIRP (n=290):
Model: Surv(OS, EVENT) ~ SLC25A4 + Age + Gender + Stage
255 patients with 39 dying ( 35 missing obs. )
      coef  HR se(coef)  95%CI_L  95%CI_U    z  p signif
SLC25A4 -0.541 0.552   0.186   0.465  0.637 -2.916 0.004 **
Age      0.088 1.008   0.014  0.980  1.036  0.553 0.580
Gendermale -0.369 0.691   0.361  0.341  1.403 -1.023 0.306
Stage2   0.065 1.007   0.770  0.236  4.823  0.084 0.033
Stage3  -1.536 4.644   0.384  2.188  9.057  3.999 0.000 ***
Stage4  -2.388 10.892  0.463  4.396 26.987  5.158 0.000 ***
Rsquare = 0.171 (max possible = 7.61e-01)
Likelihood ratio test p = 1.24e-08
Wald test p = 9.23e-10
Score (logrank) test p = 8.35e-15
```

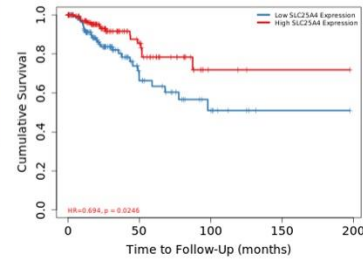
Kaplan-Meier Curve Parameters:

Split Percentage of Patients: (%)

5%  50%

Survival Time Between: (Month)

0  2000



Survival difference in KIRP (n=290)

Cox Proportional Hazard Model:

```
SLC25A5 in KIRP (n=290):
Model: Surv(OS, EVENT) ~ SLC25A5 + Age + Gender + Stage
255 patients with 39 dying ( 35 missing obs. )
      coef  HR se(coef)  95%CI_L  95%CI_U    z  p signif
SLC25A5 -0.069 0.933   0.172  0.667  1.307 -0.401 0.689
Age      0.064 1.004   0.014  0.976  1.032  0.250 0.803
Gendermale -0.353 0.702   0.359  0.347  1.420 -0.984 0.325
Stage2   0.046 1.048   0.768  0.232  4.723  0.060 0.952
Stage3  -1.564 4.779   0.390  2.226 10.259  4.013 0.000 ***
Stage4  -2.672 14.473  0.471  5.750 36.426  5.074 0.000 ***
Rsquare = 0.144 (max possible = 7.61e-01)
Likelihood ratio test p = 5.24e-07
Wald test p = 4.93e-08
Score (logrank) test p = 1.25e-12
```

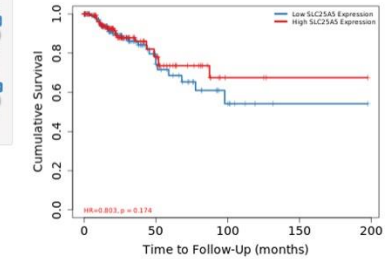
Kaplan-Meier Curve Parameters:

Split Percentage of Patients: (%)

5%  50%

Survival Time Between: (Month)

0  2000



Survival difference in KIRP (n=290)

Cox Proportional Hazard Model:

```
SLC25A6 in KIRP (n=290):
Model: Surv(OS, EVENT) ~ SLC25A6 + Age + Gender + Stage
255 patients with 39 dying ( 35 missing obs. )
      coef  HR se(coef)  95%CI_L  95%CI_U    z  p signif
SLC25A6 -0.220 0.803   0.253  0.489  1.317 -0.870 0.384
Age      0.080 1.000   0.015  0.971  1.029 -0.012 0.991
Gendermale -0.500 0.601   0.494  0.272  1.328 -1.258 0.208
Stage2   0.067 1.069   0.768  0.237  4.820  0.067 0.931
Stage3  -1.608 4.994   0.390  2.324 10.734  4.120 0.000 ***
Stage4  -2.656 14.242  0.459  5.798 34.983  5.793 0.000 ***
Rsquare = 0.146 (max possible = 7.61e-01)
Likelihood ratio test p = 4e-07
Wald test p = 4.53e-08
Score (logrank) test p = 1.09e-12
```

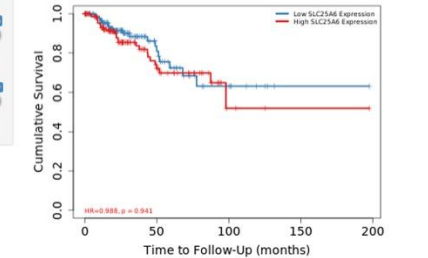
Kaplan-Meier Curve Parameters:

Split Percentage of Patients: (%)

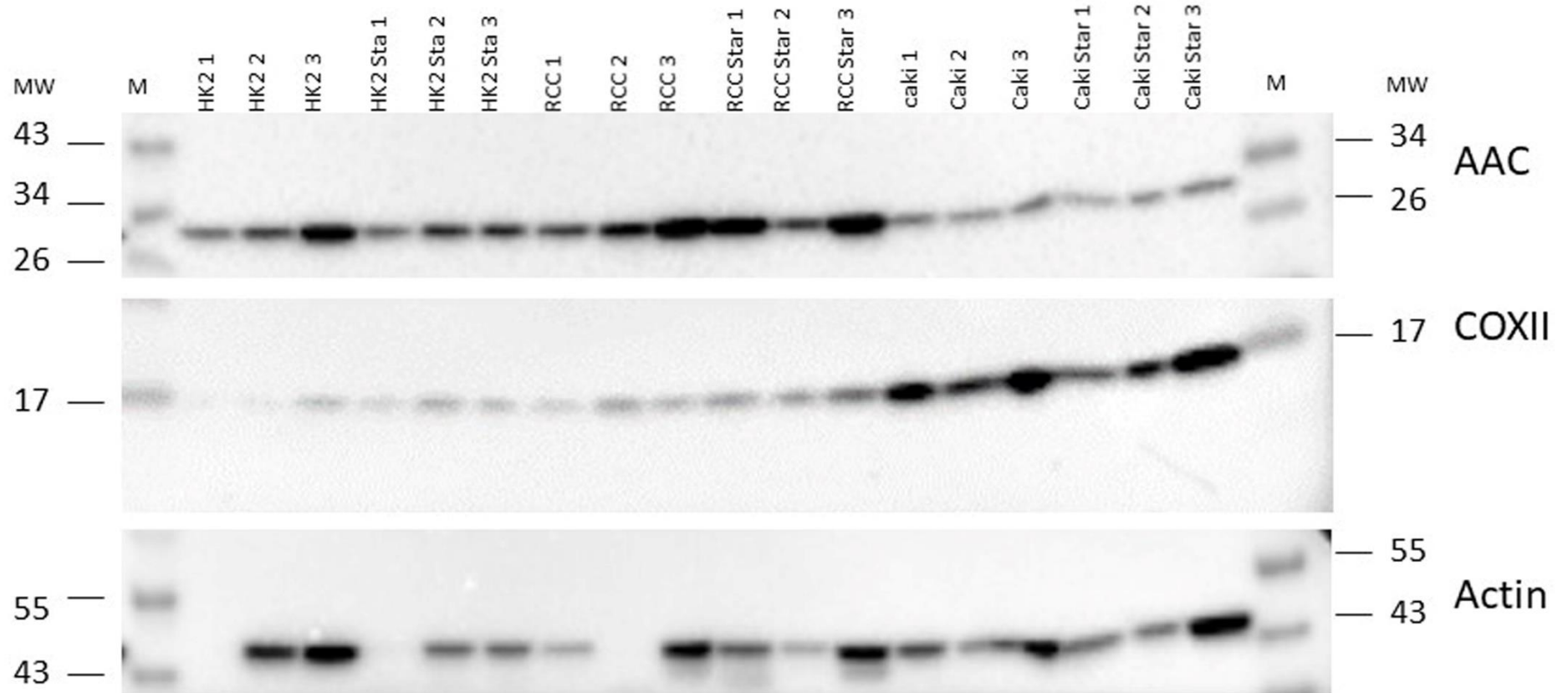
5%  50%

Survival Time Between: (Month)

0  2000



Supplementary Figure S2. Survival difference related to AACs expression in the investigated cancer tissues



**Supplementary Figure S3.** AACs protein content estimated through WB in HK2, RCC shaw and CaKi-1 cells grown in complete medium or starvation (serum-free medium, starved cell-lines are those indicated with "star" in the label) with respect to actin or COXII content. M = marker; MW Molecular Weight marker; PageRuler™ Prestained Protein Ladder; Thermo Fisher Scientific).

**Supplementary Table S1.** Pairs of primers used for qRT-PCR

<b>Name</b>	<b>Sequence</b>	<b>Length</b>
ACT-FOR	5'- GAAGATCAAGATCATTGCTCCT -3'	111
ACT-REV	5'- TACTCCTGCTTGCTGATCCA -3'	
AAC1-FOR	5'- CTGGTGCCTACCCCTTTGA-3'	129
AAC1-REV	5'- CTTGGCTCCTTCGTCTTTTG -3'	
AAC2-FOR	5'- ATCTACCGAGCCGCCTACTT -3'	105
AAC2-REV	5'- GACAGTCTGTGCGATCATCC-3'	
AAC3-FOR	5'- TGCAGGGCATCATCATCTAC-3'	106
AAC3-REV	5'- ATCATCCAGCTCACCACGAT -3'	
AAC4-FOR	5'- AAACCTGGCTTCTGGTGGAG -3'	118
AAC4-REV	5'- GAATTGTCGCTCCTCAGGAC-3'	

**Supplementary Table S2.** Table showing RNA and proteins extracted from the investigated cell-lines (from a representative replicate) for qRT-PCR and WB analyses.

Cell-line >>>>>>>>>>	HK2 complete medium	HK2 serum-free medium	RCC-shaw complete medium	RCC-shaw serum-free medium	CaKi-1 complete medium	CaKi-1 serum-free medium
Number of cells for each T75	3,8 x 10 <sup>6</sup>	4,8 x 10 <sup>6</sup>	11,8 x 10 <sup>6</sup>	12 x 10 <sup>6</sup>	12 x 10 <sup>6</sup>	12 x 10 <sup>6</sup>
Number of cells for RNA extraction	1 x 10 <sup>6</sup>	2 x 10 <sup>6</sup>	2 x 10 <sup>6</sup>	2 x 10 <sup>6</sup>	2 x 10 <sup>6</sup>	1 x 10 <sup>6</sup>
Eluted volume (uL)	40	80	80	80	80	80
Abs (260 nm)	2,03	0,952	0,314	0,667	0,453	0,341
260/280	2,09	1,94	1,72	1,96	1,92	1,97
Conc NanoDrop (ng/uL)	81,1	38,1	23,3	1,03	43	31
Dilution sample	10	10	10	10	10	10
Conc RNA (ng/uL)	811	381	233	275	430	316
Number of cells for WB	2,8 x 10 <sup>6</sup>	2,8 x 10 <sup>6</sup>	9,8 x 10 <sup>6</sup>	10 x 10 <sup>6</sup>	10 x 10 <sup>6</sup>	10 x 10 <sup>6</sup>
Volume Ripa Buffer (uL)	150	100	300	300	400	400
Sonication time (sec)	3	6	3	6	5	5
Abs (595 nm)	0,72	0,36	0,502	0,179	0,651	0,393
cuvette concentration (mg/mL)	0,716	0,678	0,985	0,237	0,65	0,415
Dilution sample	10	10	10	10	10	10
Protein concentration (mg/mL)	7,16	6,78	9,85	2,73	6,5	4,2