

Table S1 Immune cell types between non-solid and solid adenocarcinoma in TCGA cohort

Characteristic	Non-solid (n=112)	Solid (n=74)	P value
B-cells (median, IQR)	0.03 (0.00, 0.09)	0.05 (0.01, 0.11)	0.081
CD4+ T-cells (median, IQR)	0.000 (0.000, 0.000)	0.000 (0.000, 0.002)	0.069
CD4+ Tcm (median, IQR)	0.000 (0.000, 0.012)	0.000 (0.000, 0.000)	0.001
CD4+ Tem (median, IQR)	0.007 (0.000, 0.028)	0.002 (0.000, 0.025)	0.3
CD4+ memory T-cells (median, IQR)	0.000 (0.000, 0.004)	0.004 (0.000, 0.012)	0.001
CD4+ naive T-cells (median, IQR)	0.000 (0.000, 0.001)	0.000 (0.000, 0.000)	0.7
CD8+ T-cells (median, IQR)	0.01 (0.00, 0.04)	0.02 (0.00, 0.06)	0.3
CD8+ Tcm (median, IQR)	0.01 (0.00, 0.05)	0.03 (0.00, 0.08)	0.054
CD8+ Tem (median, IQR)	0.000 (0.000, 0.000)	0.000 (0.000, 0.014)	0.01
CD8+ naive T-cells (median, IQR)	0.001 (0.000, 0.006)	0.003 (0.000, 0.009)	0.023
DC (median, IQR)	0.05 (0.02, 0.10)	0.04 (0.02, 0.10)	0.8
Macrophages (median, IQR)	0.10 (0.05, 0.13)	0.13 (0.09, 0.16)	0.002
Macrophages M1 (median, IQR)	0.06 (0.04, 0.09)	0.09 (0.07, 0.12)	<0.001
Macrophages M2 (median, IQR)	0.04 (0.03, 0.08)	0.05 (0.03, 0.07)	>0.9
Th1 cells (median, IQR)	0.11 (0.08, 0.15)	0.14 (0.11, 0.18)	<0.001
Th2 cells (median, IQR)	0.03 (0.00, 0.08)	0.10 (0.02, 0.21)	<0.001
Tregs (median, IQR)	0.000 (0.000, 0.017)	0.009 (0.000, 0.035)	0.008
aDC (median, IQR)	0.06 (0.00, 0.13)	0.08 (0.01, 0.16)	0.2
cDC (median, IQR)	0.14 (0.06, 0.38)	0.14 (0.05, 0.34)	0.6
iDC (median, IQR)	0.44 (0.25, 0.69)	0.48 (0.24, 0.74)	0.7
pDC (median, IQR)	0.000 (0.000, 0.007)	0.011 (0.000, 0.038)	<0.001
Immune score (median, IQR)	0.19 (0.09, 0.26)	0.25 (0.16, 0.35)	0.014
Stroma score (median, IQR)	0.02 (0.01, 0.06)	0.02 (0.00, 0.05)	0.2
Microenvironment score (median, IQR)	0.24 (0.12, 0.33)	0.28 (0.17, 0.36)	0.077

Table S2 Immune cell types between non-solid and solid adenocarcinoma in ACC cohort

Characteristic	Non-solid (n=86)	Solid (n=26)	P value
B cells (median, IQR)	0.01 (0.00, 0.07)	0.07 (0.03, 0.10)	0.001
CD4+ Tcells (median, IQR)	0.000 (0.000, 0.001)	0.000 (0.000, 0.002)	0.20
CD4+ Tcm (median, IQR)	0.000 (0.000, 0.008)	0.000 (0.000, 0.000)	0.094
CD4+ Tem (median, IQR)	0.02 (0.00, 0.06)	0.03 (0.00, 0.05)	0.90
CD4+ memory Tcells (median, IQR)	0.000 (0.000, 0.000)	0.000 (0.000, 0.000)	0.09
CD4+ naive Tcells (median, IQR)	0.002 (0.000, 0.016)	0.024 (0.000, 0.039)	0.009
CD8+ Tcells (median, IQR)	0.03 (0.00, 0.06)	0.07 (0.03, 0.12)	0.007
CD8+ Tcm (median, IQR)	0.03 (0.01, 0.07)	0.10 (0.02, 0.14)	0.005
CD8+ Tem (median, IQR)	0.006 (0.000, 0.028)	0.032 (0.007, 0.061)	0.003
CD8+ naive T-cells (median, IQR)	0.005 (0.001, 0.008)	0.005 (0.002, 0.012)	0.20
DC (median, IQR)	0.04 (0.02, 0.07)	0.04 (0.01, 0.05)	0.40
Macrophages (median, IQR)	0.05 (0.03, 0.08)	0.08 (0.02, 0.11)	0.30
Macrophages M1 (median, IQR)	0.03 (0.02, 0.05)	0.06 (0.02, 0.09)	0.016
Macrophages M2 (median, IQR)	0.021 (0.008, 0.038)	0.011 (0.004, 0.030)	0.12
Th1 cells (median, IQR)	0.000 (0.000, 0.005)	0.009 (0.000, 0.042)	0.009
Th2 cells (median, IQR)	0.03 (0.00, 0.06)	0.10 (0.07, 0.14)	<0.001
Tregs (median, IQR)	0.000 (0.000, 0.000)	0.000 (0.000, 0.010)	0.063
aDC (median, IQR)	0.12 (0.08, 0.18)	0.12 (0.09, 0.18)	>0.9
cDC (median, IQR)	0.24 (0.11, 0.40)	0.20 (0.07, 0.28)	0.21
iDC (median, IQR)	0.33 (0.09, 0.57)	0.32 (0.10, 0.51)	>0.9
pDC (median, IQR)	0.000 (0.000, 0.002)	0.030 (0.008, 0.044)	<0.001
Immune score (median, IQR)	0.15 (0.07, 0.24)	0.25 (0.09, 0.32)	0.052
Stroma score (median, IQR)	0.07 (0.03, 0.15)	0.05 (0.03, 0.10)	0.33
Microenvironment score (median, IQR)	0.24 (0.15, 0.38)	0.32 (0.15, 0.44)	0.31

Table S3 RNA expression of immune checkpoint molecule between non-solid and solid adenocarcinoma in TCGA cohort

Characteristic	Non-solid (n=112)	Solid (n=74)	P value
FOXP3 (median, IQR)	1.39 (0.89, 2.78)	2.28 (1.04, 3.41)	0.017
ICOS (median, IQR)	0.63 (0.31, 1.17)	0.93 (0.48, 1.77)	0.014
LAG3 (median, IQR)	1.01 (0.65, 1.95)	2.28 (0.75, 3.23)	0.003
TIGIT (median, IQR)	0.88 (0.39, 1.71)	1.31 (0.61, 2.37)	0.017
PDCD1 (PD-1) (median, IQR)	0.87 (0.46, 1.53)	1.42 (0.64, 2.45)	0.012
HAVCR2 (Tim-3) (median, IQR)	5.7 (2.6, 8.6)	7.3 (4.8, 10.8)	<0.001
CTLA4 (median, IQR)	1.02 (0.49, 1.87)	1.62 (0.87, 2.88)	0.007
CD274 (PD-L1) (median, IQR)	1.46 (0.92, 2.38)	3.08 (1.62, 5.48)	<0.001
Cytolytic activity score (median, IQR)	5 (3, 9)	6 (4, 13)	0.043

Table S4 RNA expression of immune checkpoint molecule between non-solid and solid adenocarcinoma in ACC cohort

Characteristic	Non-solid (n=86)	Solid (n=26)	P value
FOXP3 (median, IQR)	2.56 (1.53, 3.99)	3.18 (2.27, 4.91)	0.11
ICOS (median, IQR)	1.65 (1.02, 2.53)	3.09 (1.77, 5.73)	0.003
LAG3 (median, IQR)	2.2 (1.2, 3.6)	4.1 (2.5, 10.2)	<0.001
TIGIT (median, IQR)	3.8 (2.4, 5.8)	5.7 (4.4, 8.4)	0.003
PDCD1 (PD1) (median, IQR)	1.50 (0.93, 2.78)	3.16 (1.70, 5.81)	<0.001
HAVCR2 (Tim3) (median, IQR)	18 (11, 26)	24 (14, 36)	0.11
CTLA4 (median, IQR)	2.09 (1.14, 3.47)	3.36 (1.74, 6.36)	0.008
CD274 (PDL1) (median, IQR)	3.5 (1.8, 5.4)	5.7 (3.6, 8.8)	0.005
Cytolytic activity score (median, IQR)	12 (8, 18)	18 (10, 31)	0.009

Table S5 Flow cytometry using fresh tumor digests among patients in ACC cohort

Characteristic	Non-solid (n=25)	Solid (n=11)	P value
CD4+ (median, IQR)	0.66 (0.56, 0.75)	0.54 (0.47, 0.68)	0.047
CD8+ (median, IQR)	0.24 (0.19, 0.35)	0.41 (0.26, 0.46)	0.021
CD4+/CD39+,CD103+ (median, IQR)	0.06 (0.02, 0.11)	0.02 (0.01, 0.08)	0.20
CD8+/CD39+,CD103+ (median, IQR)	0.16 (0.10, 0.26)	0.38 (0.25, 0.49)	0.007
CD4+PD-1 (median, IQR)	4,077 (2,848, 5,083)	5,202 (4,928, 6,170)	0.008
CD8+PD-1 (median, IQR)	4,003 (2,734, 5,402)	4,038 (3,094, 4,706)	0.80

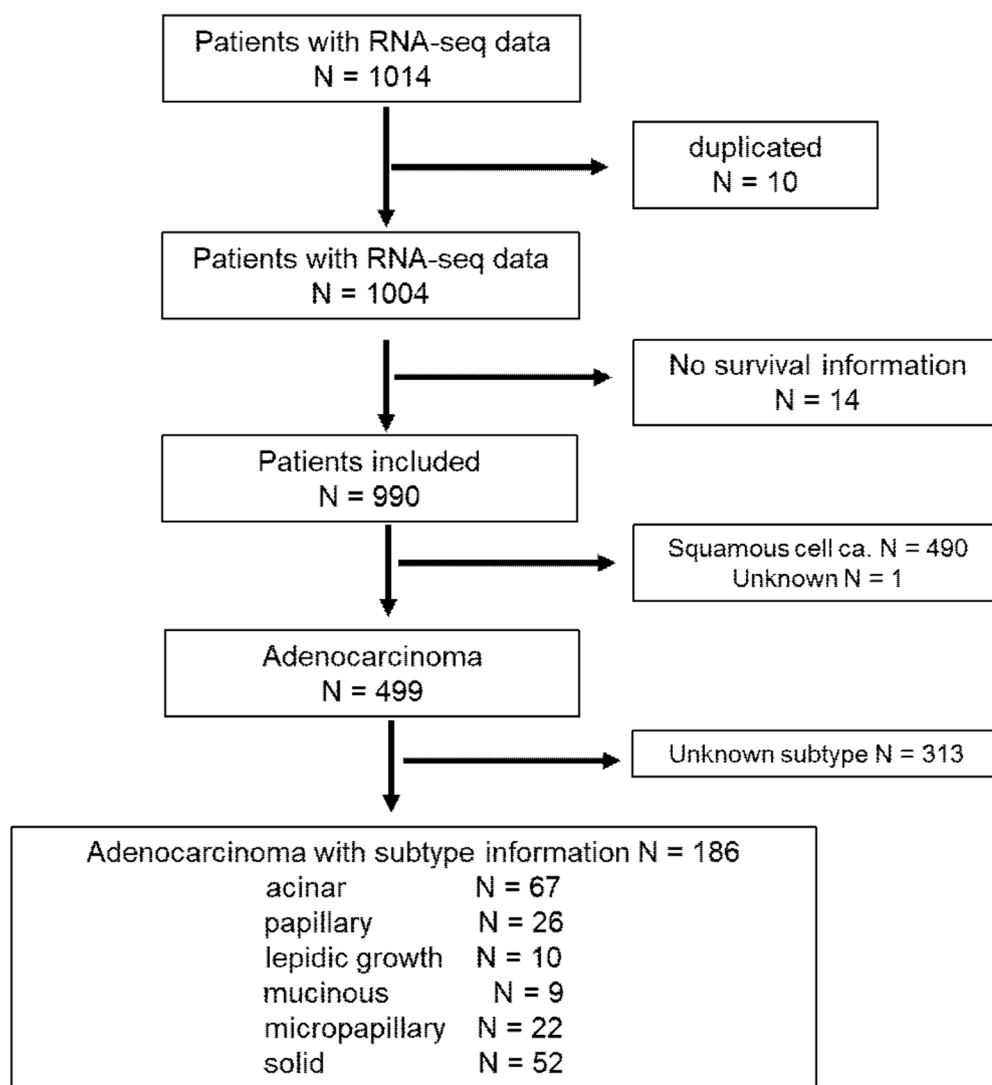


Figure S1 The flow diagram of patients' selection in TCGA data.

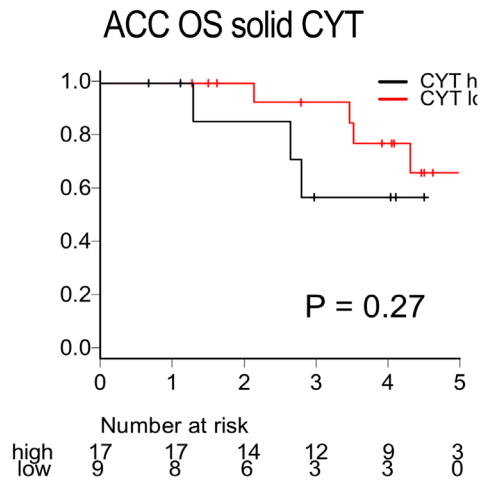
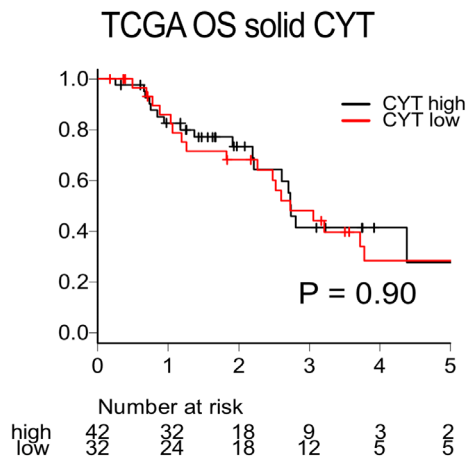
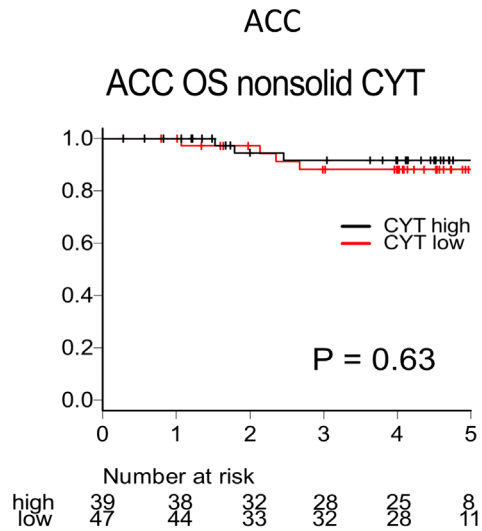
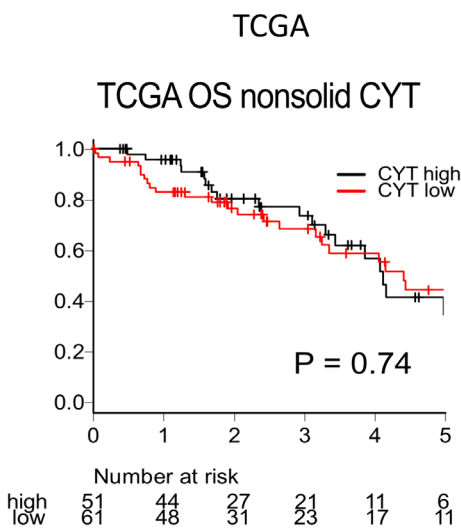


Figure S2 The survival analysis between the cytolytic activity (CYT) score high and low group in each subtype (upper; solid, lower; non-solid) in TCGA (left) and ACC (right).