SUPPLEMENTARY FIGURE LEGENDS

Table. S1: List of 30 TCGA tumor types. The abbreviated TCGA tumor types are annotated.

Table. S2: List of all Immune synapse genes. The HLA, co-stimulatory and immune checkpoint genes studied.

Table. S3: List of Illumina 450 probes for immune synapse genes. The probeID, the location within the gene locus, the R correlation coefficient between probe β-value and gene expression for all probes used in the study are summarized.

Table. S4: List of 75 selected probes for PCA. The probes located within TSS1500, TSS200, 5'UTR within a gene with negative correlation to its expression are selected for PCA.

Figure S1. The methylation pattern for *HHLA2* and *CD40*. β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *HHLA2* (**A**) and *CD40* (**B**) derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color. Heatmap of the correlation coefficient between all the probes within *HHLA2* (**C**) and *CD40* (**D**) genes across all tumor types.

Figure S2. The methylation pattern for *CEACAM1*. (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *CEACAM1* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression. Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S3. The methylation pattern for *LGALS9* (Galectin9). (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *LGALS9 (Galectin9)* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression. Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S4. The methylation pattern for *CD274* (*PDL1*). (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *CD274 (PDL1)* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5’UTR are plotted against gene expression. Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S5. The methylation pattern for *PDCD1LG2* (*PDL2*). (**A**) β-values of methylation probes for TSS1500, TSS200, 5’UTR, body, and 3’UTR of *PDCD1LG2 (PDL2)* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5’UTR are plotted against gene expression. Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S6. The methylation pattern for *C10orf54* (*VISTA*). (**A**) β-values of methylation probes for TSS1500, TSS200, 5’UTR, body, and 3’UTR of *C10orf54 (VISTA)* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression. Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S7. The methylation pattern for *CD276* (*B7-H3*). (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *CD276 (B7-H3)* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression. Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S8. The methylation pattern for *VTCN1* (*B7-H4*). (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *VTCN1 (B7-H4)* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression.

Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S9. The methylation pattern for *CD86* (B7-2). (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *CD86* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression. Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S10. The methylation pattern for *CD80* (*B7-1*). (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *CD80* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression.

Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S11. The methylation pattern for *PVR (*CD155*)*. (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *PVR* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression. Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S12. The methylation pattern for *LGALS3* (Galectin3). (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *LGALS3 (Galectin3)* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression. Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S13. The methylation pattern for *TNFSF14* (*LIGHT*). (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *TNFSF14 (LIGHT)* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression. Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S14. The methylation pattern for *TNFSF4* (*OX40L*). (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *TNFSF4 (OX40L)* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression. Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S15. The methylation pattern for *TNFSF9* (*CD173L*). (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *TNFSF9 (CD173L)* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression. Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

Figure S16. The methylation pattern for *HLA-A*. (**A**) β-values of methylation probes for TSS1500, TSS200, 5'UTR, body, and 3'UTR of *HLA-A* gene derived from all tumor samples (blue) and normal adjacent tissues (red) are depicted. The methylation level for each probe is represented by a box-plots. The left most column indicates the presence of CpG-island, while the second column colors indicate where on the gene the probe is located. The genomic location is listed on the left y-axis and the probe id is shown on the right y-axis the probes selected for further analysis is marked with blue color (**B**) Heatmap of the correlation coefficient between all the probes within a gene across all tumor types. (**C**) The average β-values for selected probes within TSS1500, TSS200, and 5'UTR are plotted against gene expression.

Each circle represents an individual tissue sample. (**D**) A box plot of average β-values for selected probes from tumor (blue) and normal adjacent tissue (red) are shown.

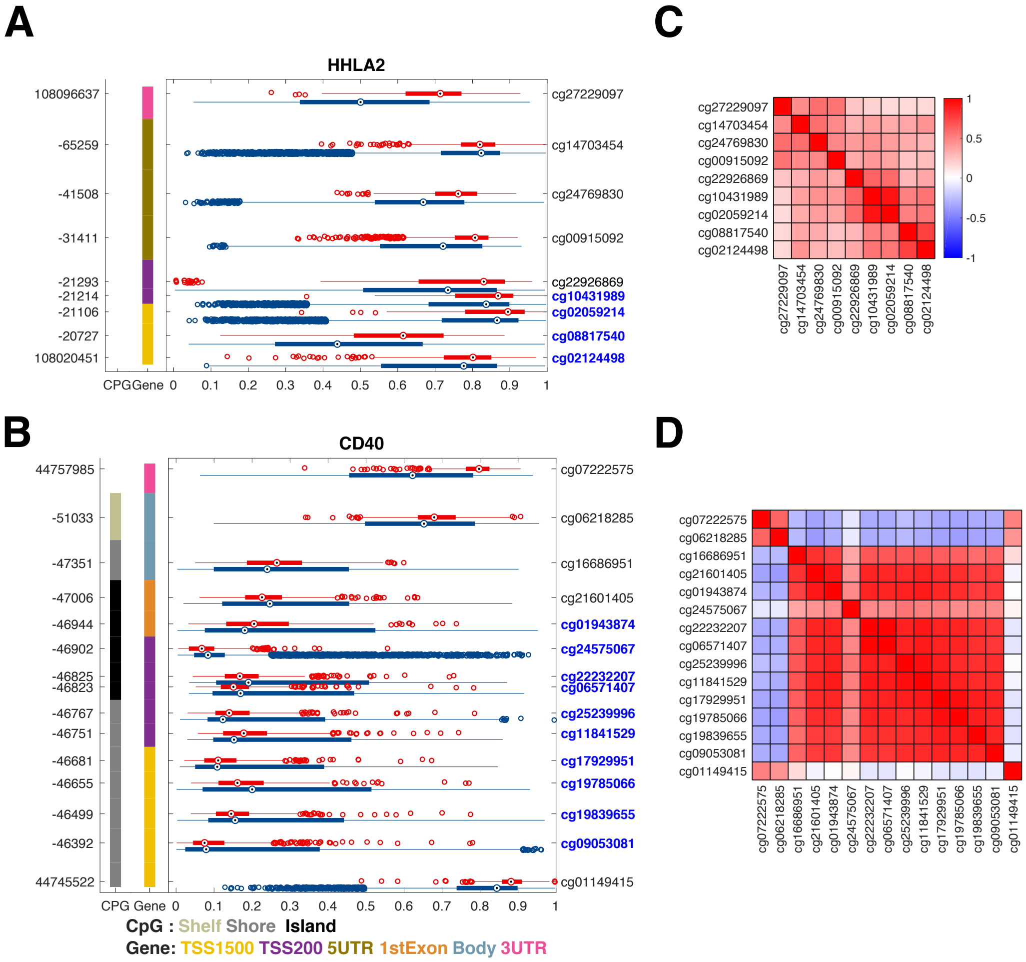
Figure S17. Correlation of PC1 and PC2 with CSG and ICG. (A) A scatter plot of PC1 score vs. average β-values of CSG probes is shown. (B) A scatter plot of PC2 score vs. average β-values of ICG probes is shown. (C) The PCA loadings of each variable, CpG-probes, for CSG probes (Blue circles) and ICG probes (Red squares) are depicted. A box plot of average β-values of CSG probes (C) and average β-values of ICG probes (D) for tumor (blue) and normal adjacent tissue (red) are compared across histologic types. * $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$ by t-test.

Figure S18. PLS regression model in melanoma. The PLS model was developed by analysis of patients with longer DSS vs. shorter DSS in the training set in melanoma. Kaplan-Meier curves for DSS of the validation melanoma cohort is depicted based on the high vs. low predicted response by median.

Figure S19. PC1 predicts OS and DSS in immunogenic cancers. (A) Kaplan-Meier curves for OS of melanoma patients with high, intermediate, and low tertile of PC1 score are shown. (B, C) Kaplan-Meier curves for OS (B) and DSS (C) of lung squamous cell carcinoma with high, intermediate and low tertile of PC1 score are shown. (D, E) Kaplan-Meier curves for OS (D) and DSS (E) of lung adenocarcinoma patients with high, intermediate, and low tertile of PC1 score are shown. (F, G) Kaplan-Meier curves for OS of uterine cancer patients with MSI (F) or without MSI (G) with high, intermediate, and low tertials of PC1 score are shown.

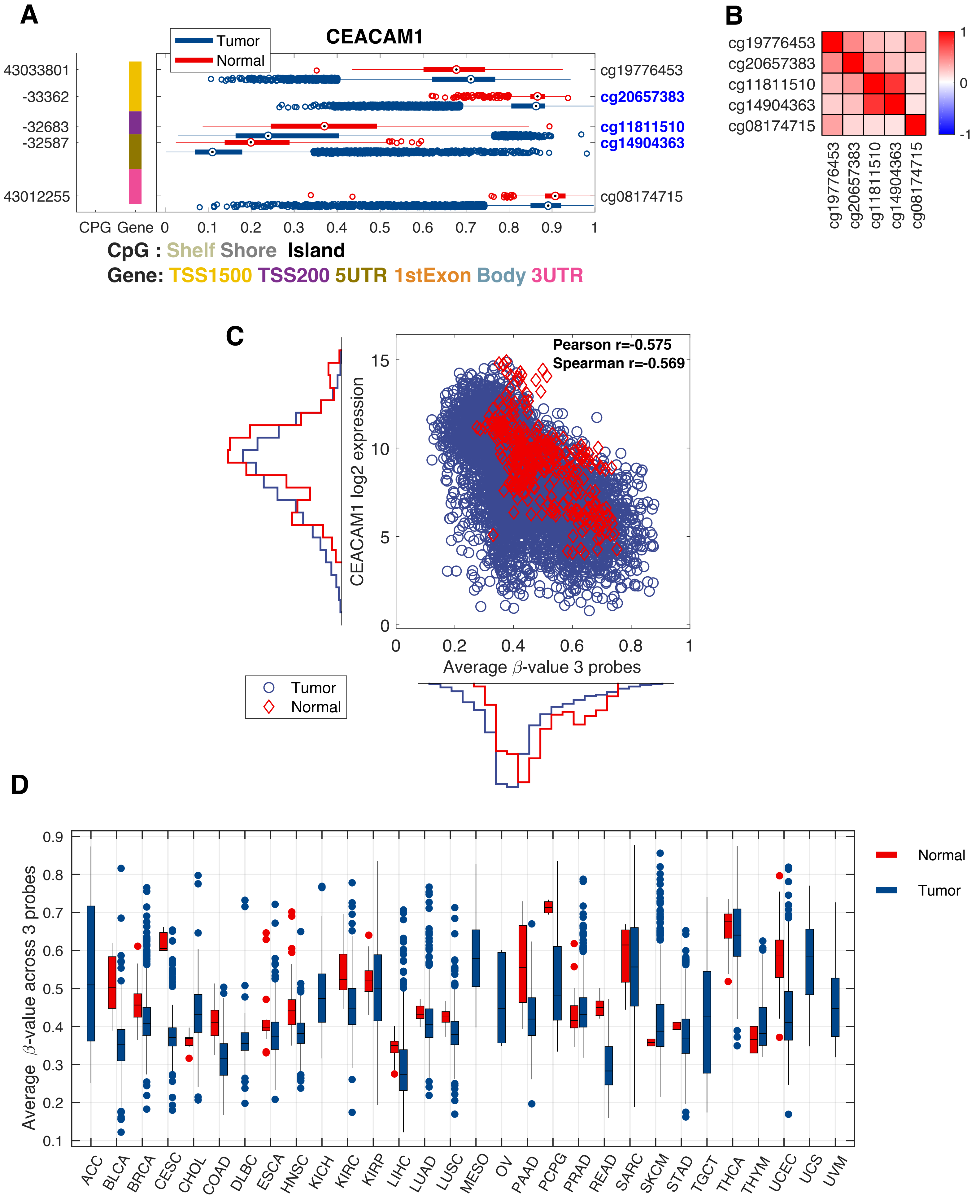
Figure S20. PC2 predicts OS and DSS in immunogenic cancers. (A, B) Kaplan-Meier curves for OS (B) and DSS (C) of head and neck squamous cell carcinoma with high, intermediate and low tertile of PC2 score are shown. (C, D) Kaplan-Meier curves for OS (C) and DSS (D) of renal clear cell carcinoma patients with high, intermediate, and low tertile of PC1 score are shown. (E, F) Kaplan-Meier curves for OS (E) and DSS (F) of renal papillary carcinoma patients with high, intermediate, and low tertile of PC1 score are shown.

Supplementary Figure 1



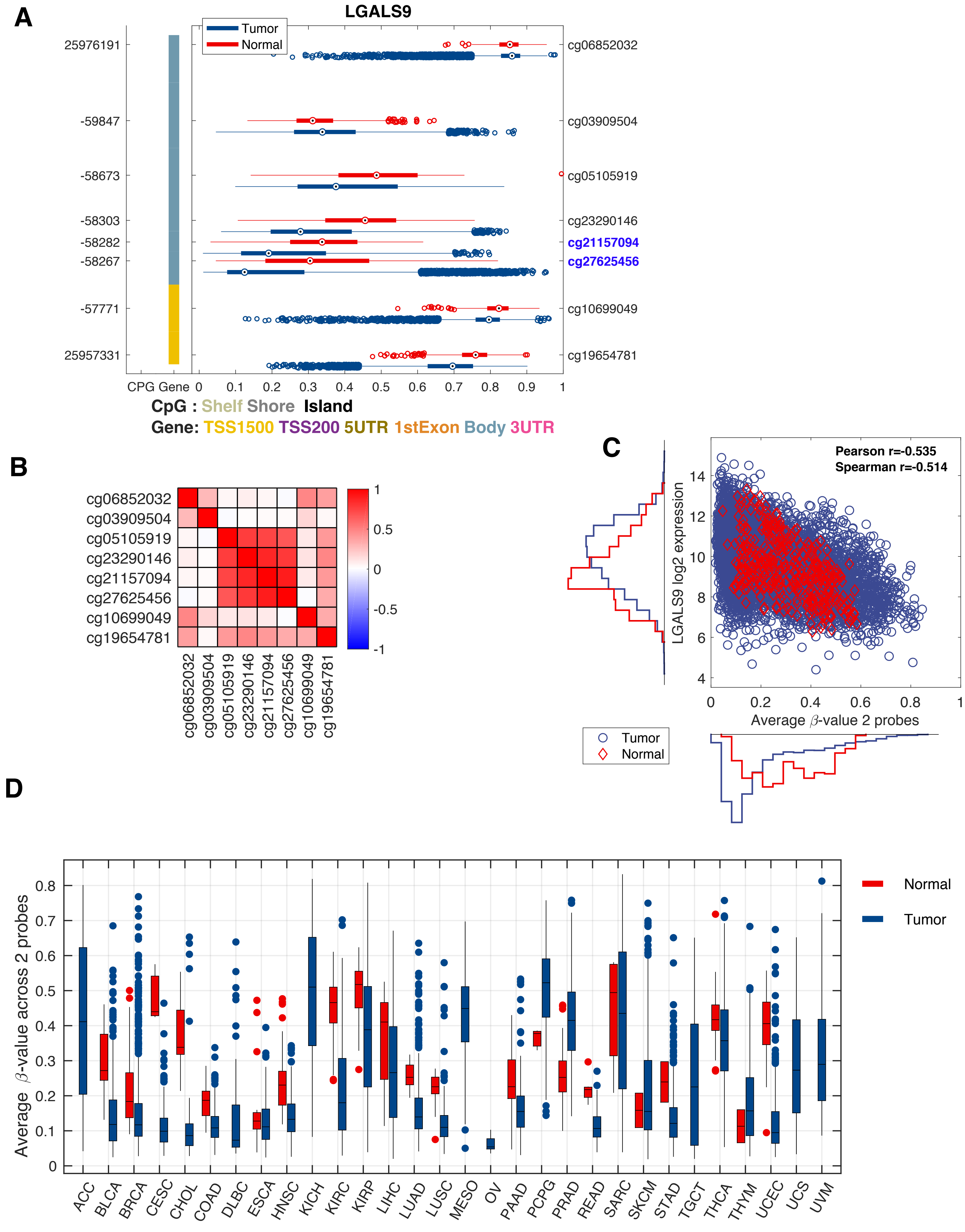
Supplementary Figure 2

CEACAM1



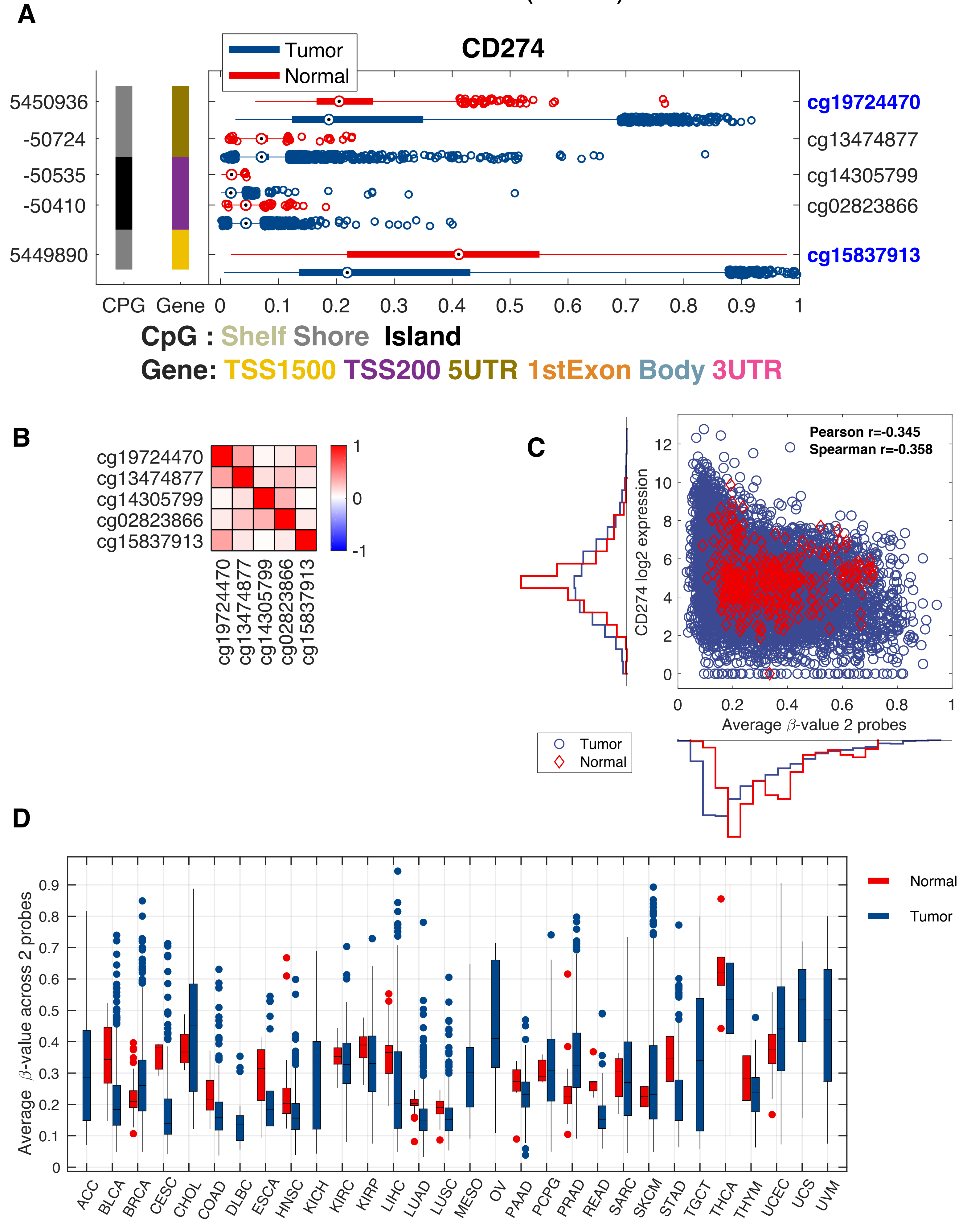
Supplementary Figure 3

LGALS9 (Galectin 9)



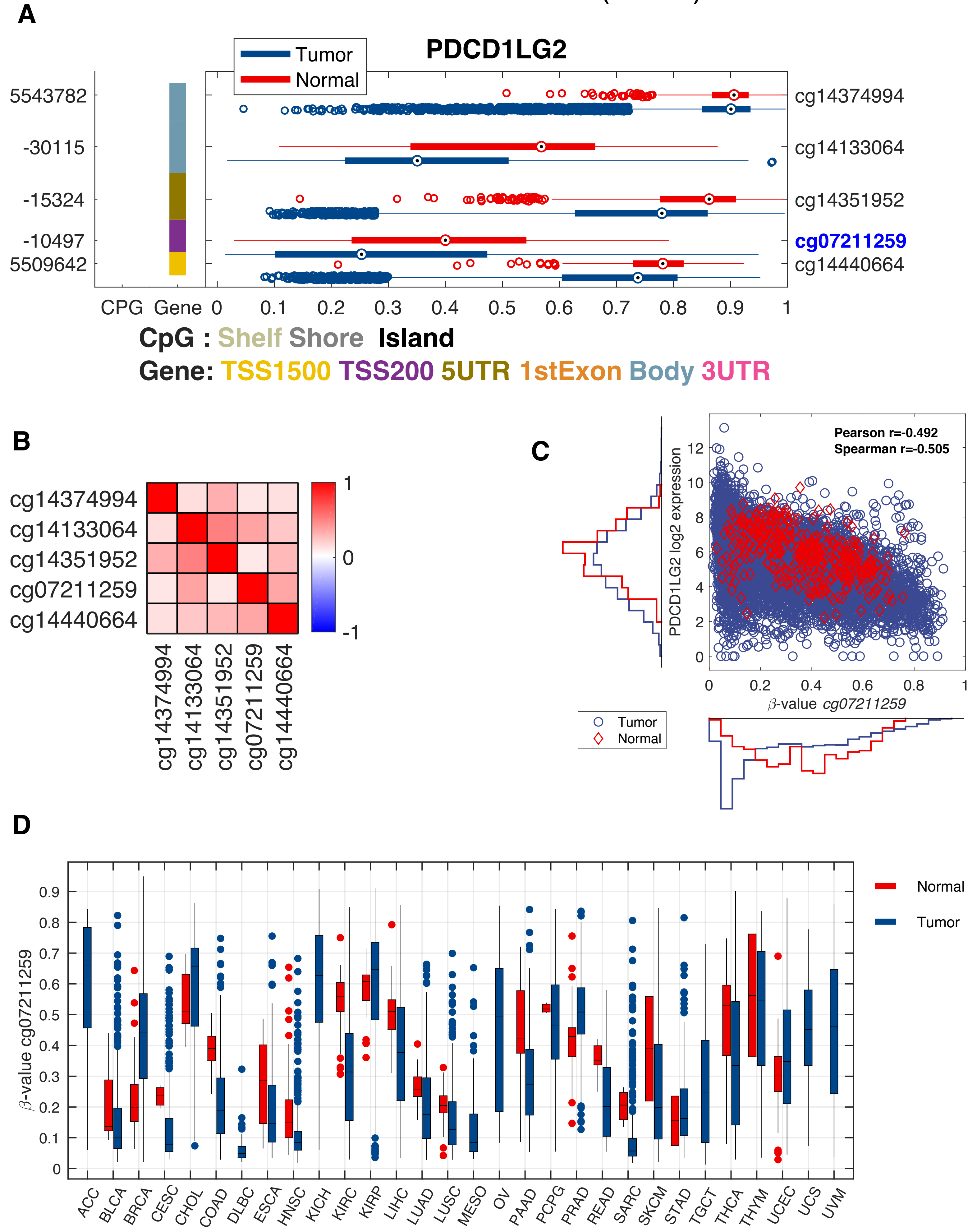
Supplementary Figure 4

CD274 (PDL1)



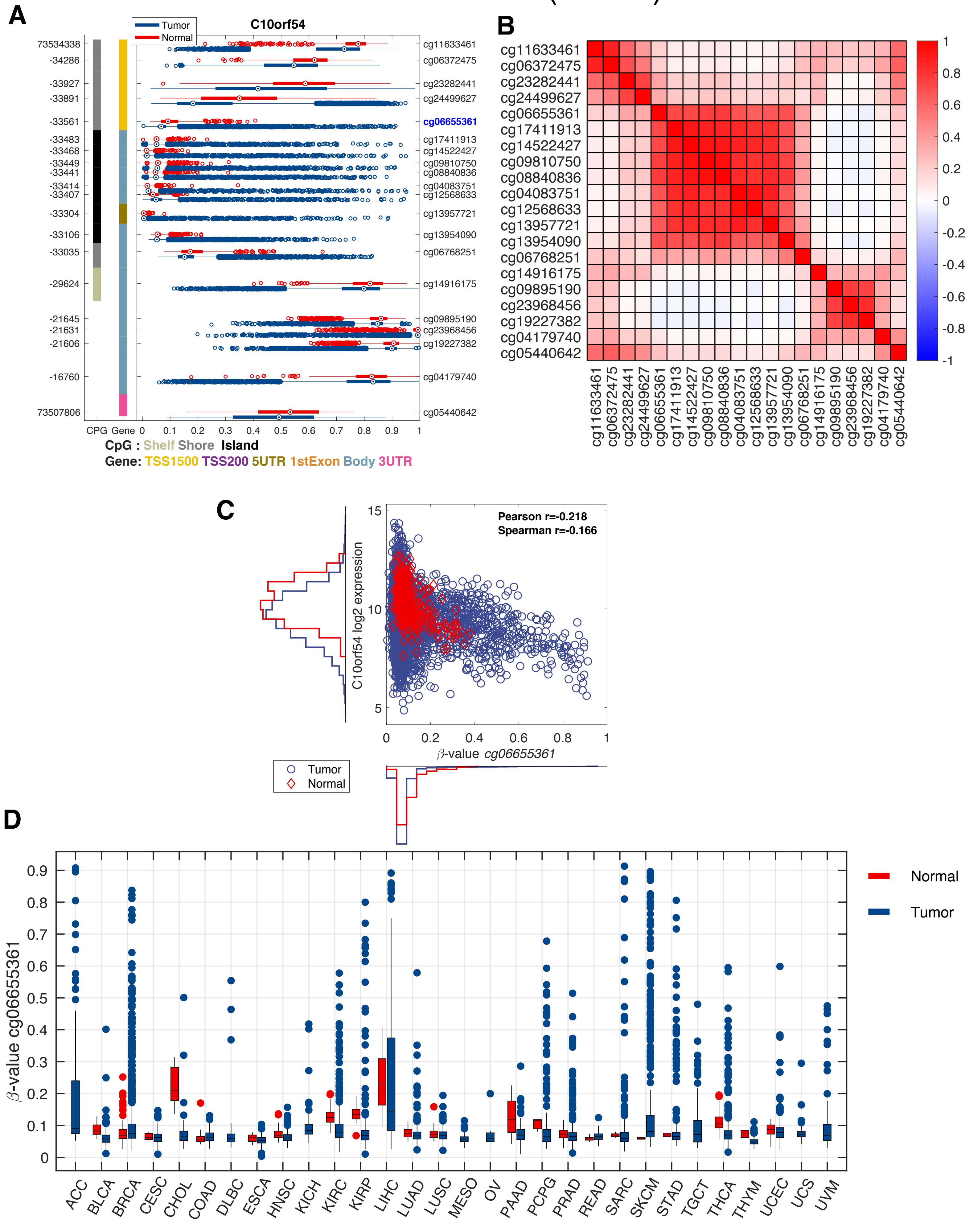
Supplementary Figure 5

PDCD1LG2 (PDL2)



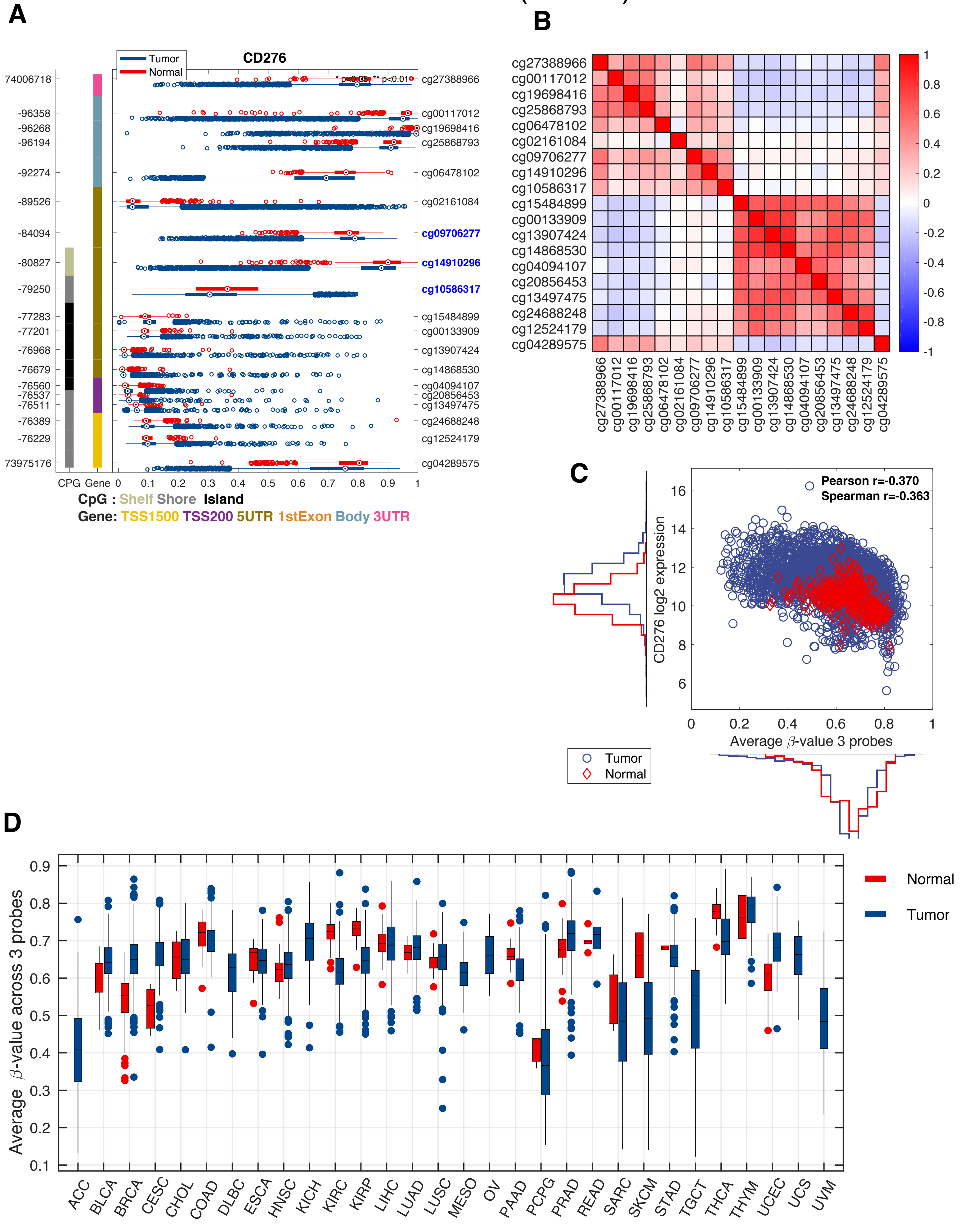
Supplementary Figure 6

C10orf54 (VISTA)



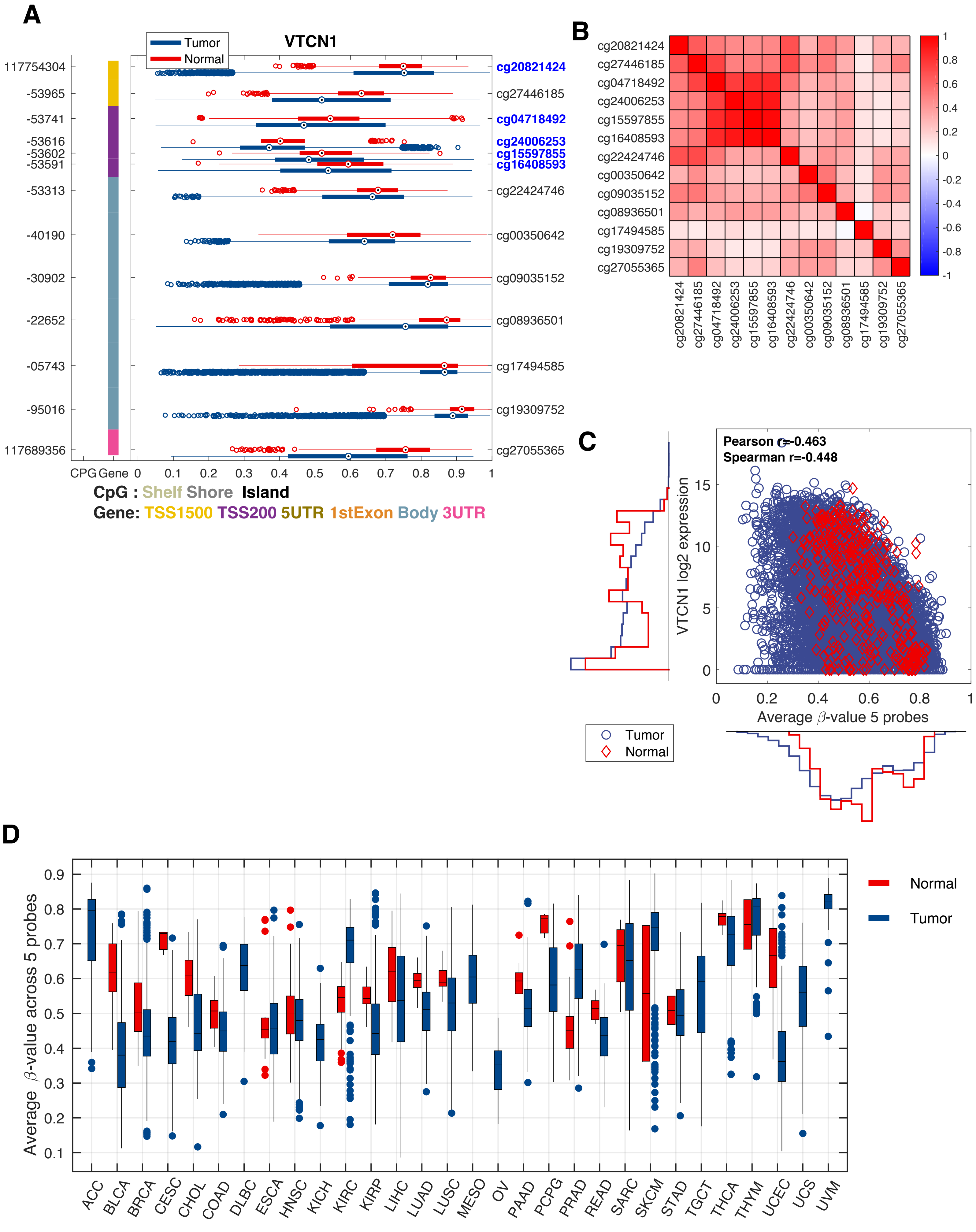
Supplementary Figure 7

CD276 (B7-H3)



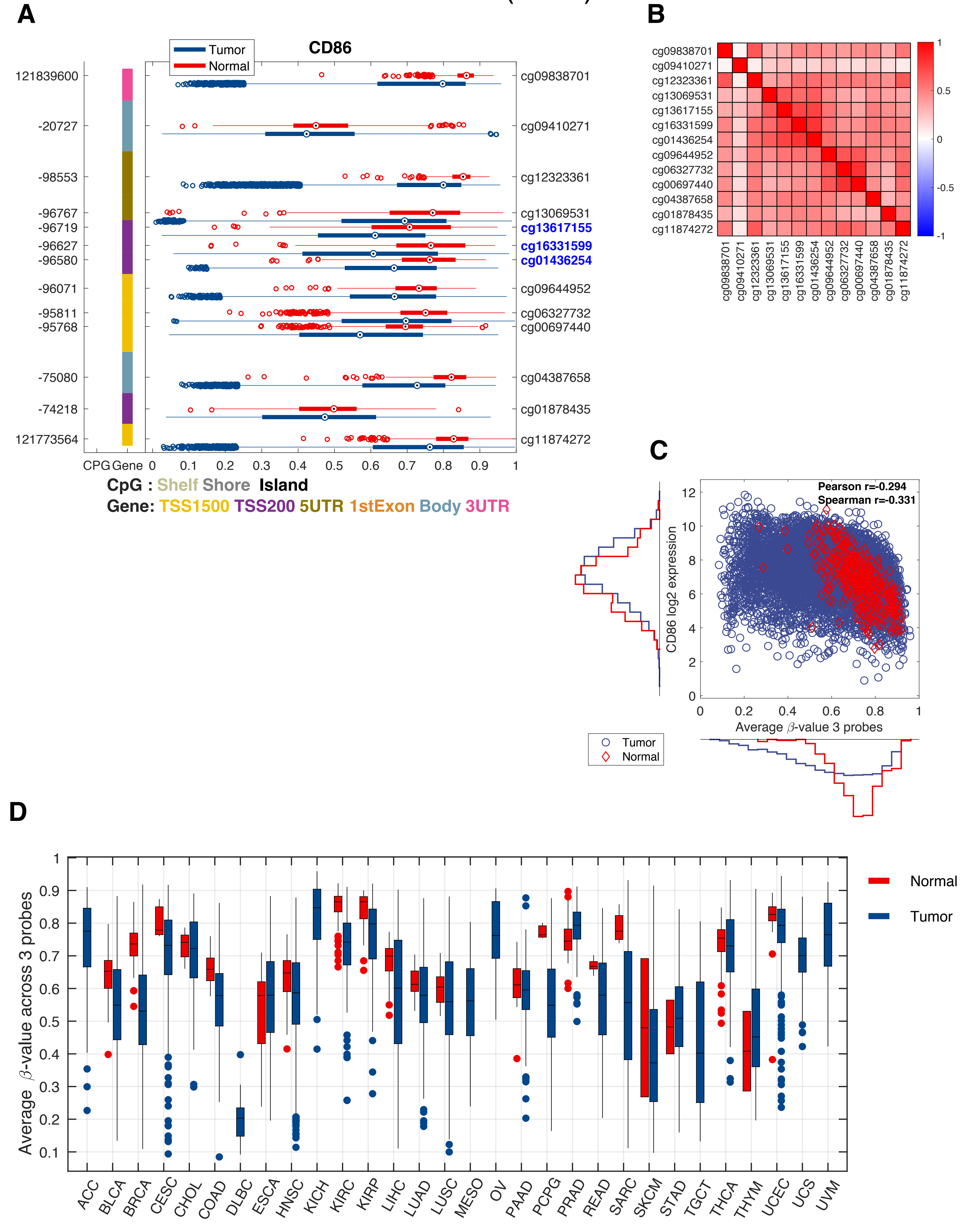
Supplementary Figure 8

VTCN1 (B7-H4)



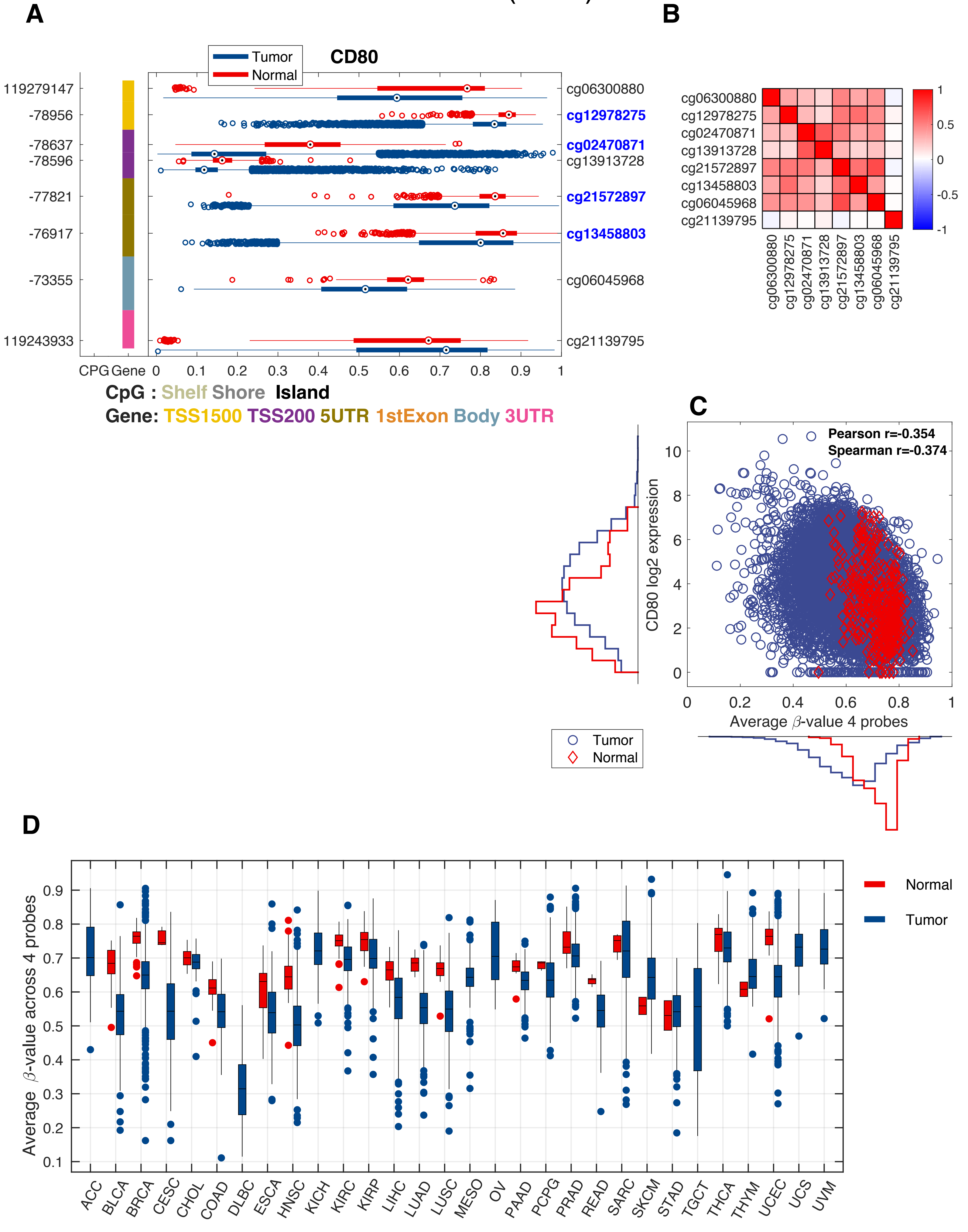
Supplementary Figure 9

CD86 (B7-2)



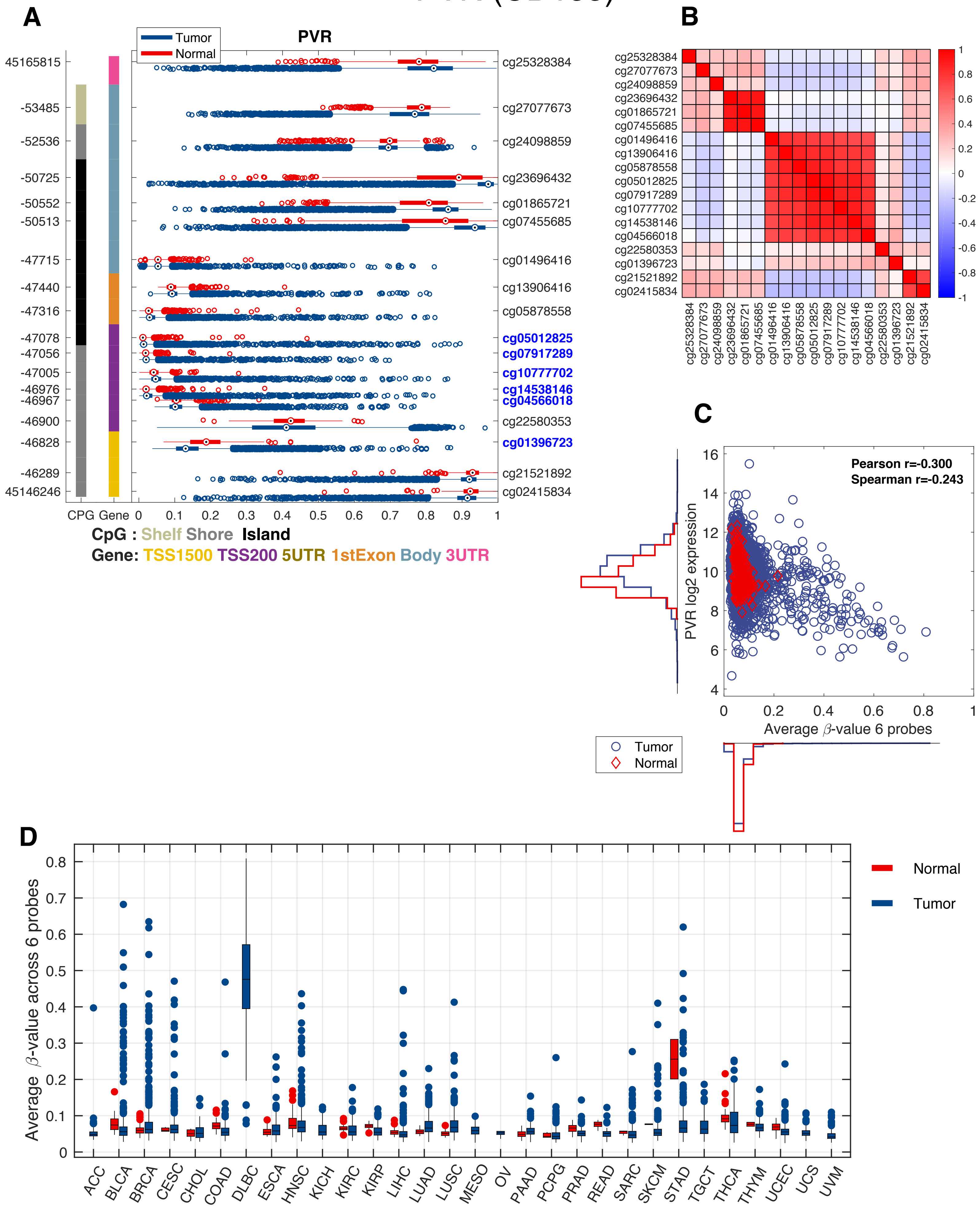
Supplementary Figure 10

CD80 (B7-1)



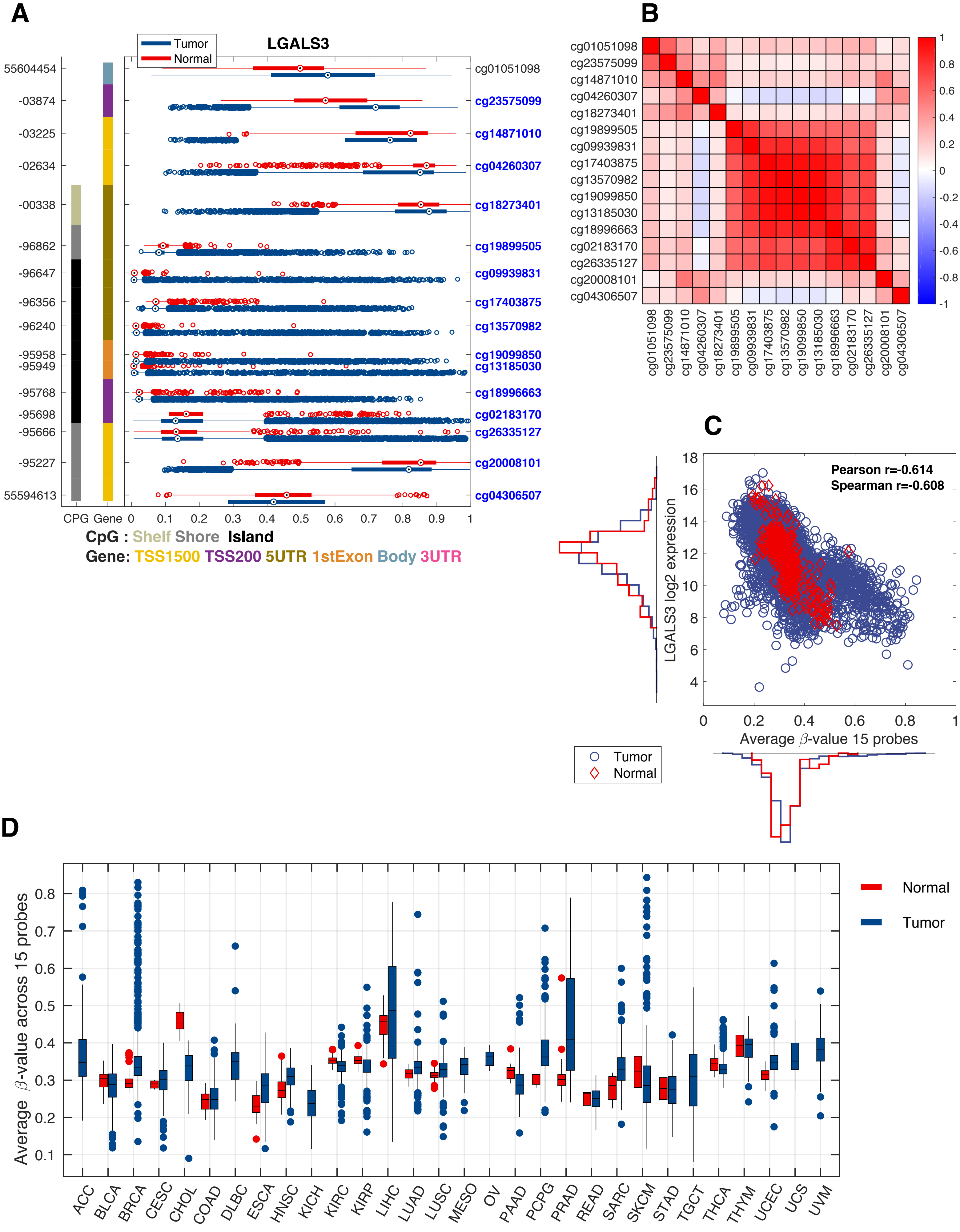
Supplementary Figure 11

PVR (CD155)



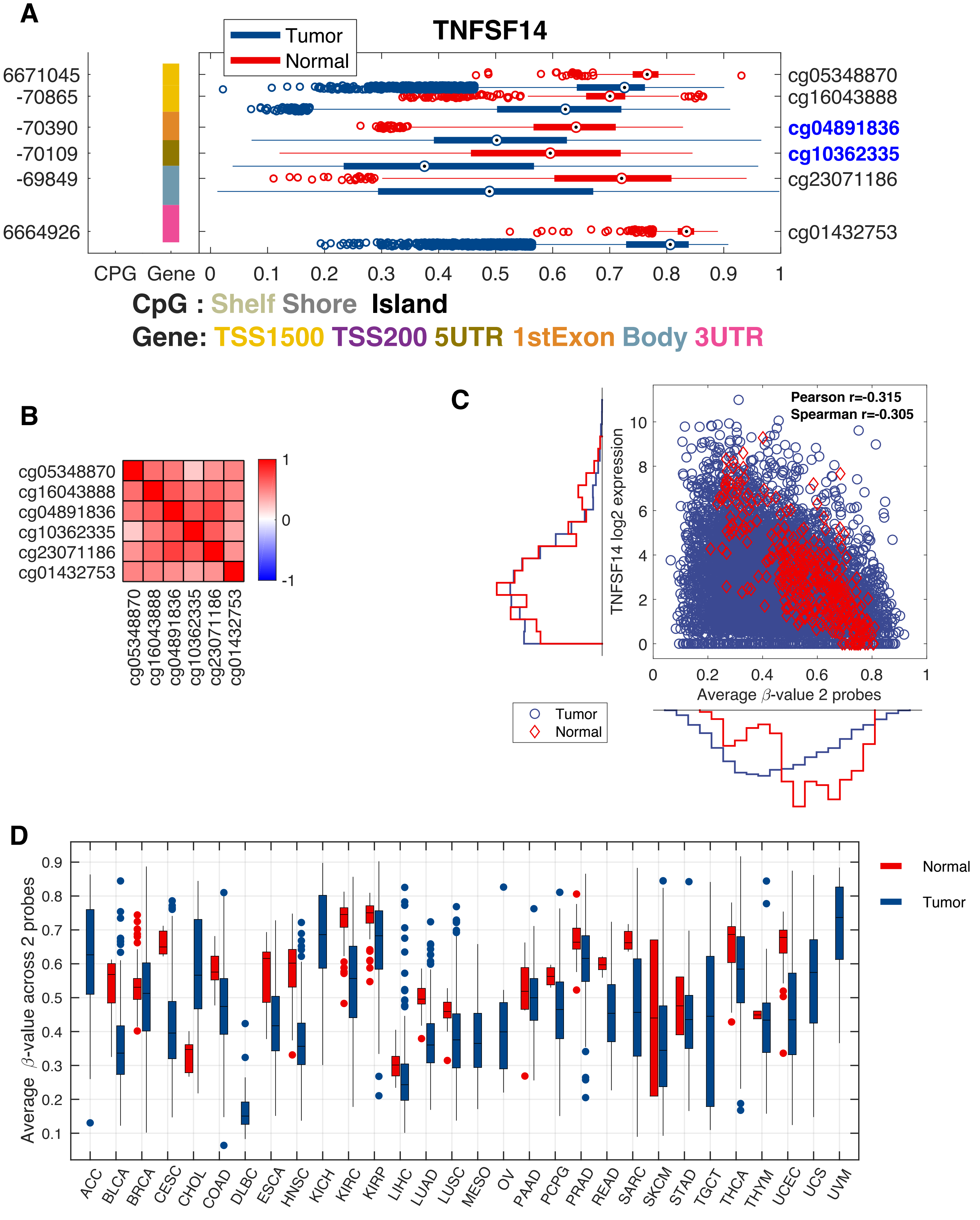
Supplementary Figure 12

LGALS3 (Galectin 3)



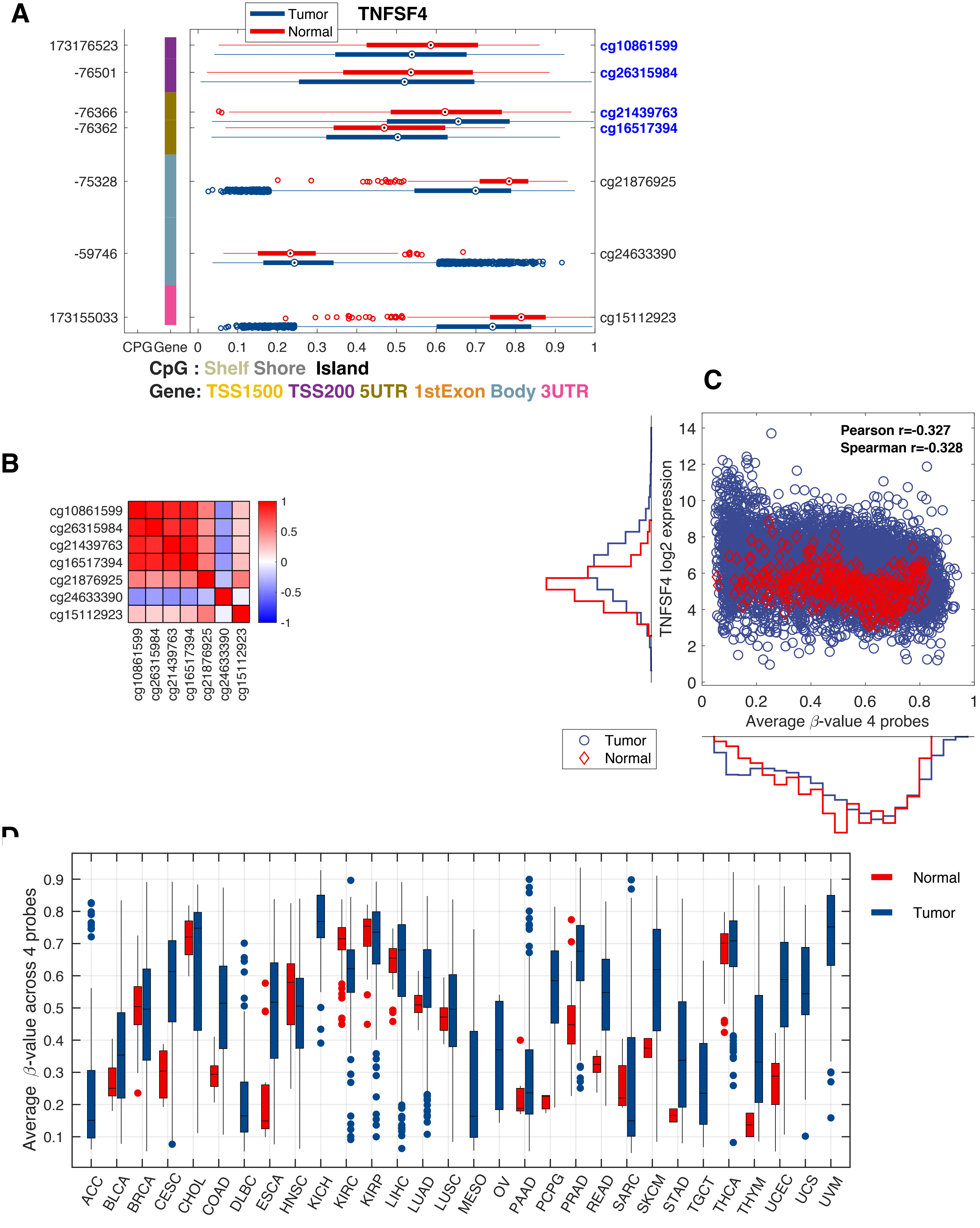
Supplementary Figure 13

TNFSF14 (LIGHT)



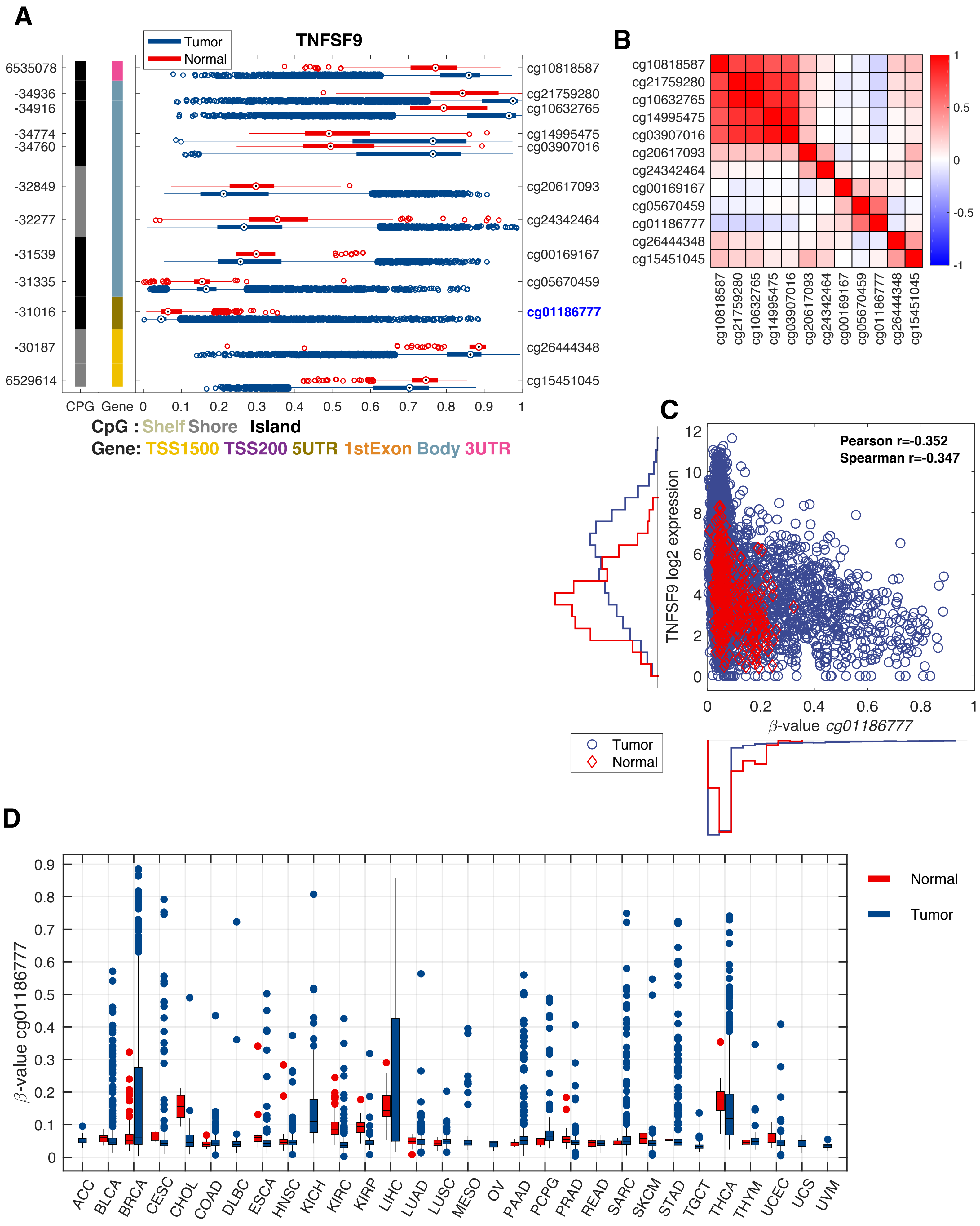
Supplementary Figure 14

TNFSF4 (OX40L)



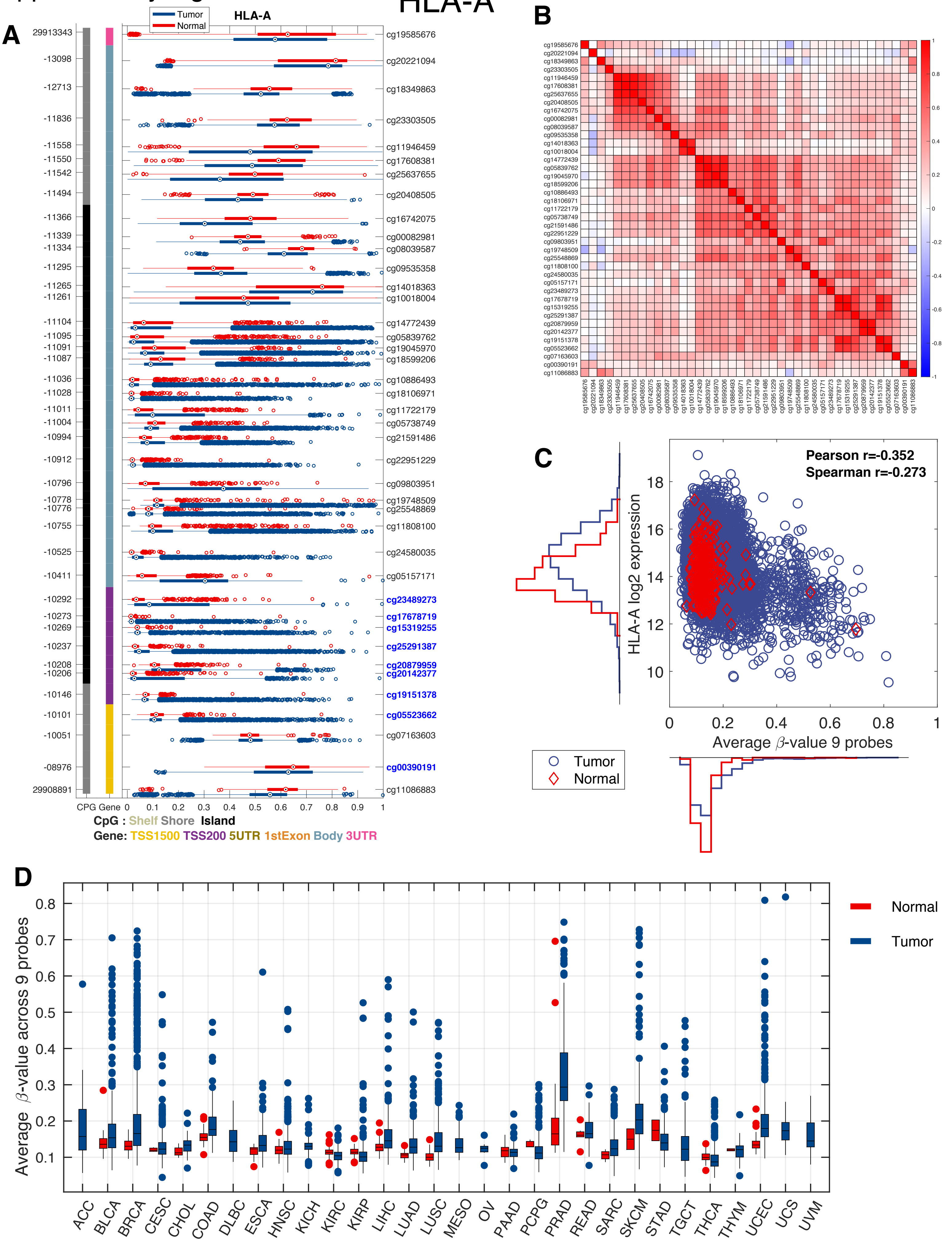
Supplementary Figure 15

TNFSF9 (CD173L)

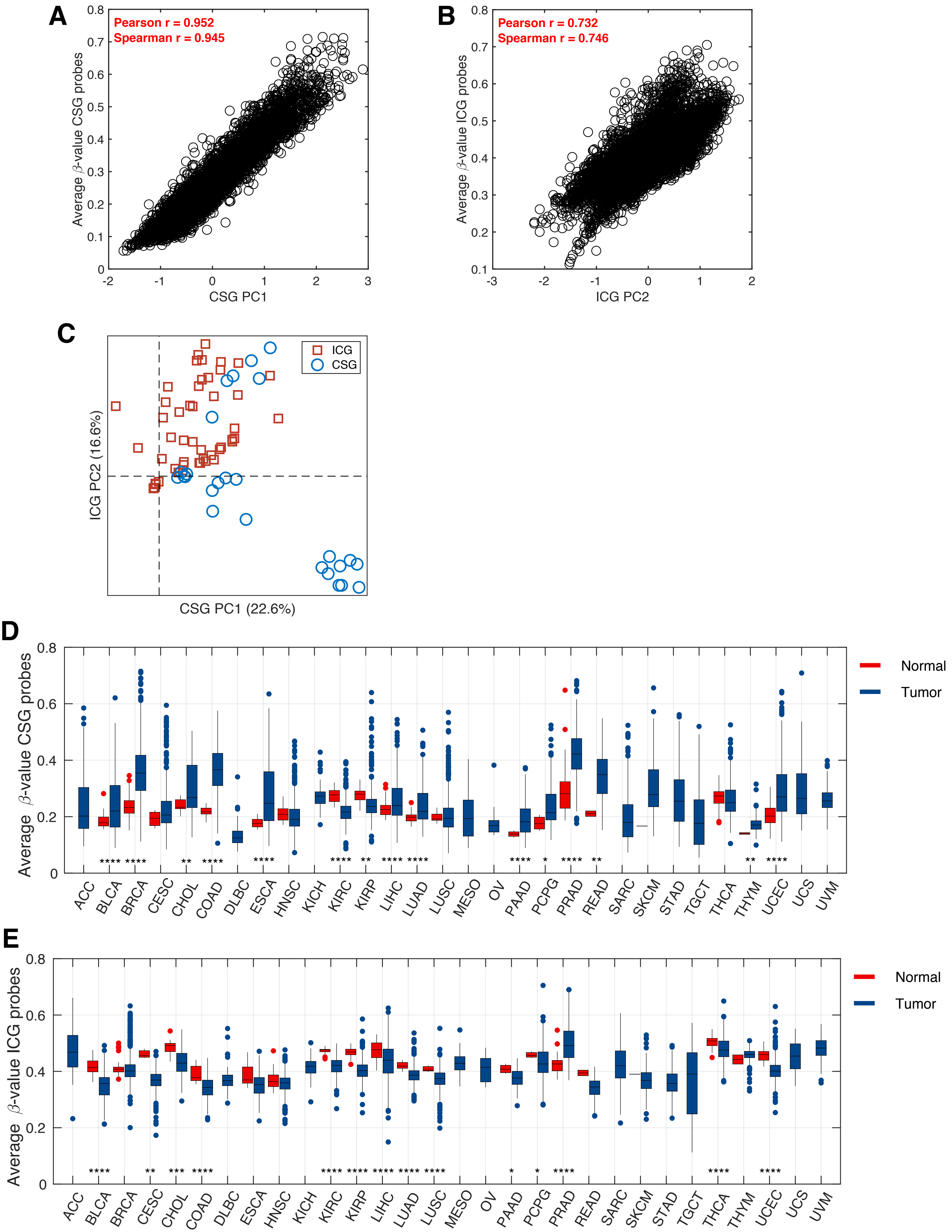


Supplementary Figure 16

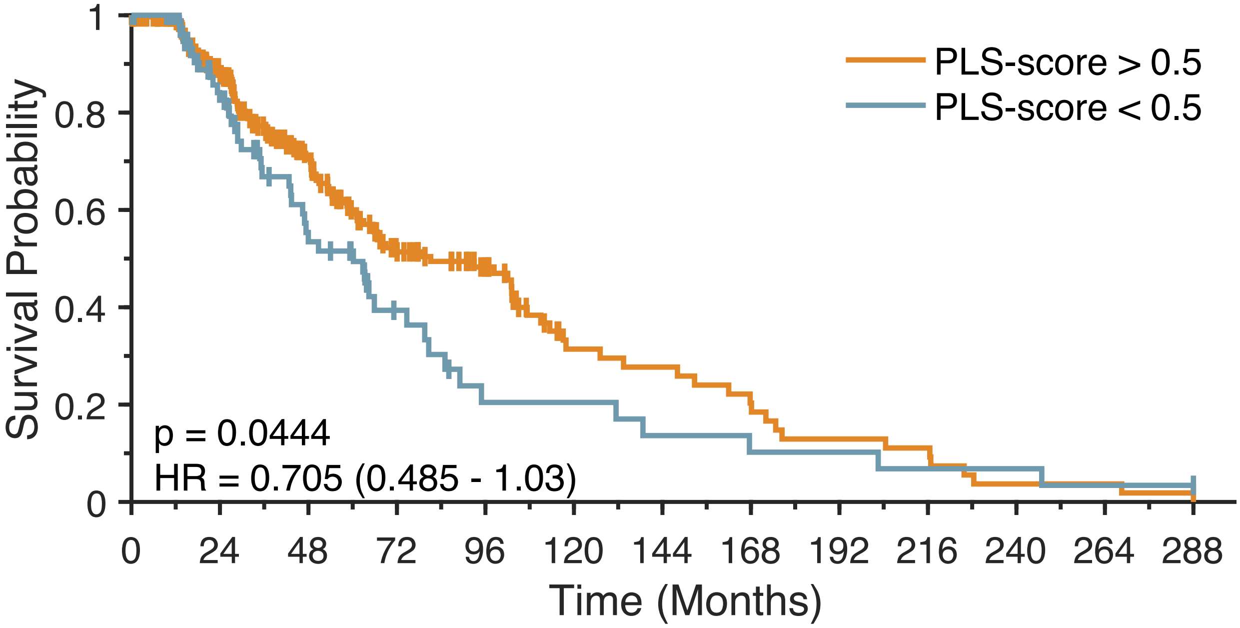
HLA-A



Supplementary Figure 17



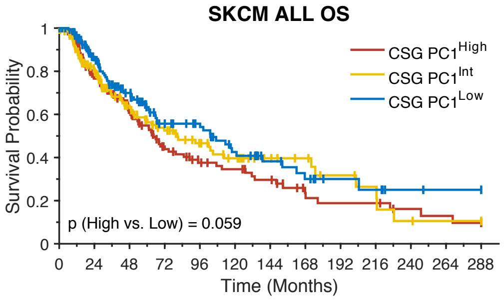
Supplementary Figure 18



PLS-Score > 0.5	300	190	118	62	41	18	16	12	8	7	3	3	2
PLS-Score < 0.5	85	53	28	13	6	6	4	3	3	2	2	1	1

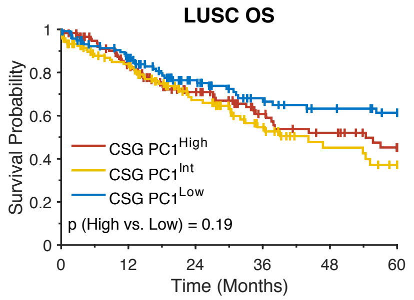
Supplementary Figure 19

A



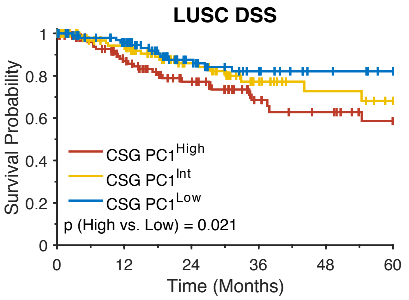
PC1^{High}	152	93	63	38	27	23	18	10	8	8	5	4	3
PC1^{Int}	153	94	60	41	30	22	15	12	8	6	3	2	2
PC1^{Low}	152	103	70	42	36	24	15	11	6	5	2	1	1

B



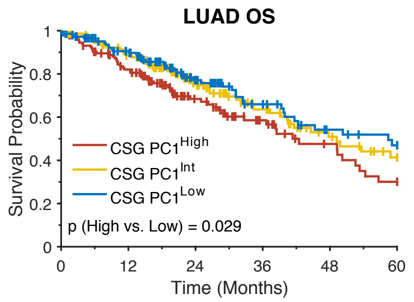
PC1^{High}	119	87	59	37	29	20
PC1^{Int}	119	88	51	29	17	12
PC1^{Low}	119	93	61	44	36	31

C



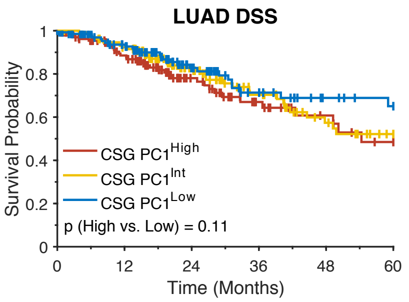
PC1^{High}	105	74	48	27	21	14
PC1^{Int}	105	79	47	24	16	12
PC1^{Low}	105	84	52	38	30	26

D



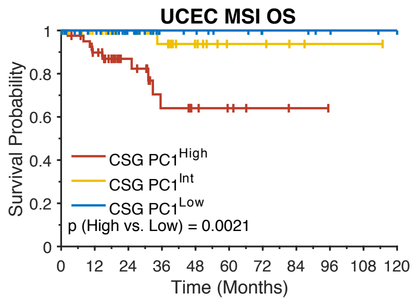
PC1^{High}	148	110	55	31	20	13
PC1^{Int}	147	119	68	41	24	15
PC1^{Low}	148	116	60	38	25	20

E



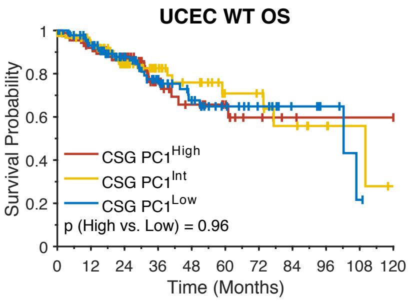
PC1^{High}	138	103	49	26	17	11
PC1^{Int}	139	117	65	39	23	14
PC1^{Low}	138	108	55	33	22	18

F



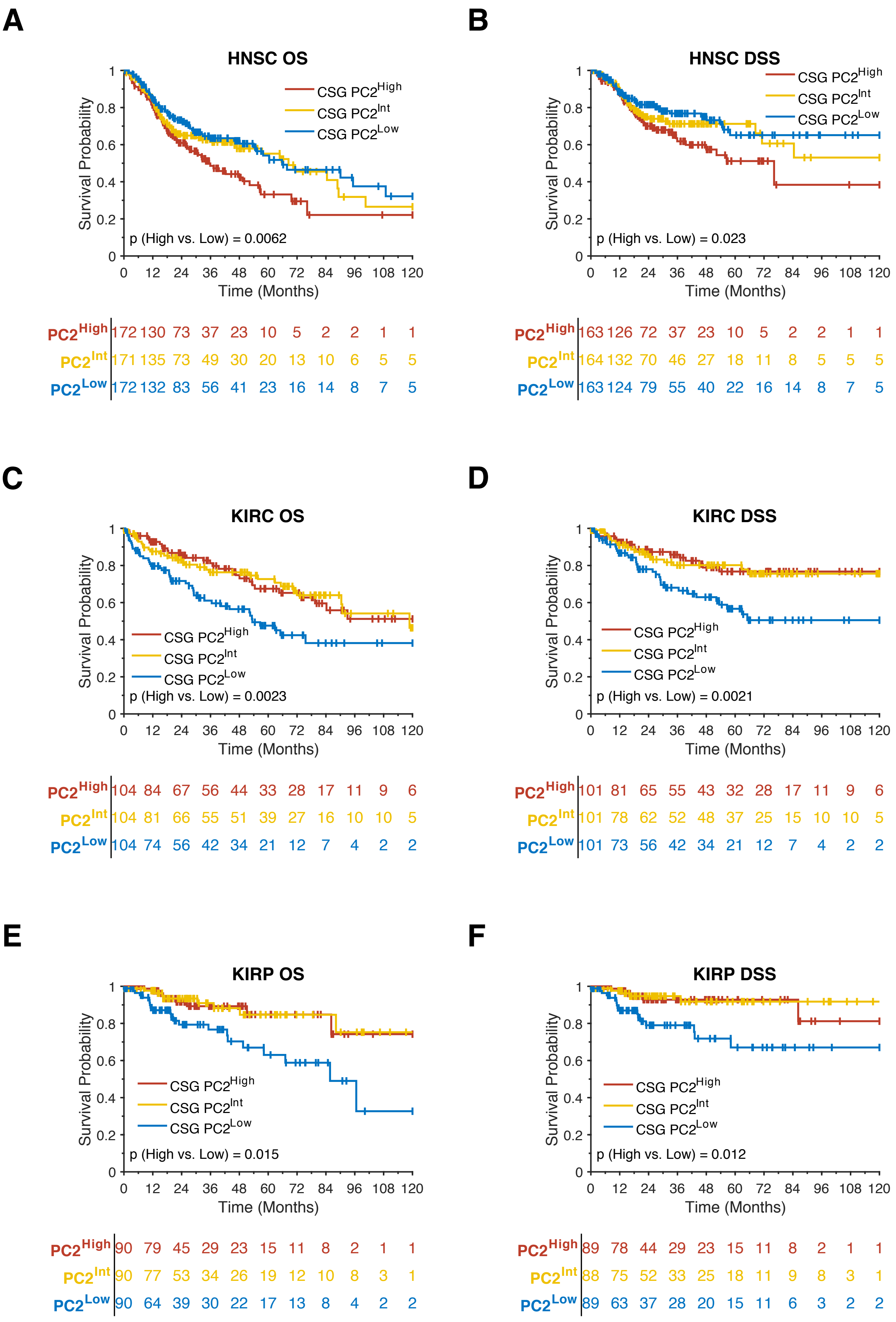
PC1^{High}	43	33	19	10	6	4	2	1	0	0	0
PC1^{Int}	43	35	22	15	9	4	4	2	1	1	0
PC1^{Low}	43	34	22	12	11	8	5	5	3	2	1

G



PC1^{High}	95	78	50	27	17	12	6	3	2	2	2
PC1^{Int}	96	79	51	31	23	13	12	8	5	3	1
PC1^{Low}	95	78	55	39	26	17	12	7	4	1	0

Supplementary Figure 20



A

PC2^{High}	172	130	73	37	23	10	5	2	2	1	1
PC2^{Int}	171	135	73	49	30	20	13	10	6	5	5
PC2^{Low}	172	132	83	56	41	23	16	14	8	7	5

B

PC2^{High}	163	126	72	37	23	10	5	2	2	1	1
PC2^{Int}	164	132	70	46	27	18	11	8	5	5	5
PC2^{Low}	163	124	79	55	40	22	16	14	8	7	5

C

PC2^{High}	104	84	67	56	44	33	28	17	11	9	6
PC2^{Int}	104	81	66	55	51	39	27	16	10	10	5
PC2^{Low}	104	74	56	42	34	21	12	7	4	2	2

D

PC2^{High}	101	81	65	55	43	32	28	17	11	9	6
PC2^{Int}	101	78	62	52	48	37	25	15	10	10	5
PC2^{Low}	101	73	56	42	34	21	12	7	4	2	2

E

PC2^{High}	90	79	45	29	23	15	11	8	2	1	1
PC2^{Int}	90	77	53	34	26	19	12	10	8	3	1
PC2^{Low}	90	64	39	30	22	17	13	8	4	2	2

F

PC2^{High}	89	78	44	29	23	15	11	8	2	1	1
PC2^{Int}	88	75	52	33	25	18	11	9	8	3	1
PC2^{Low}	89	63	37	28	20	15	11	6	3	2	2