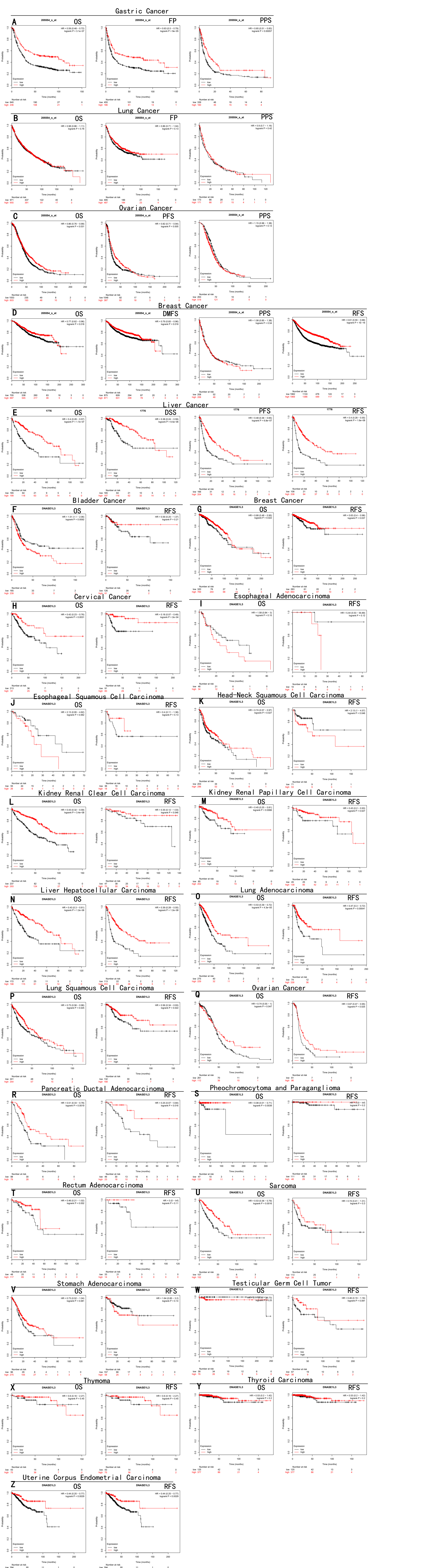
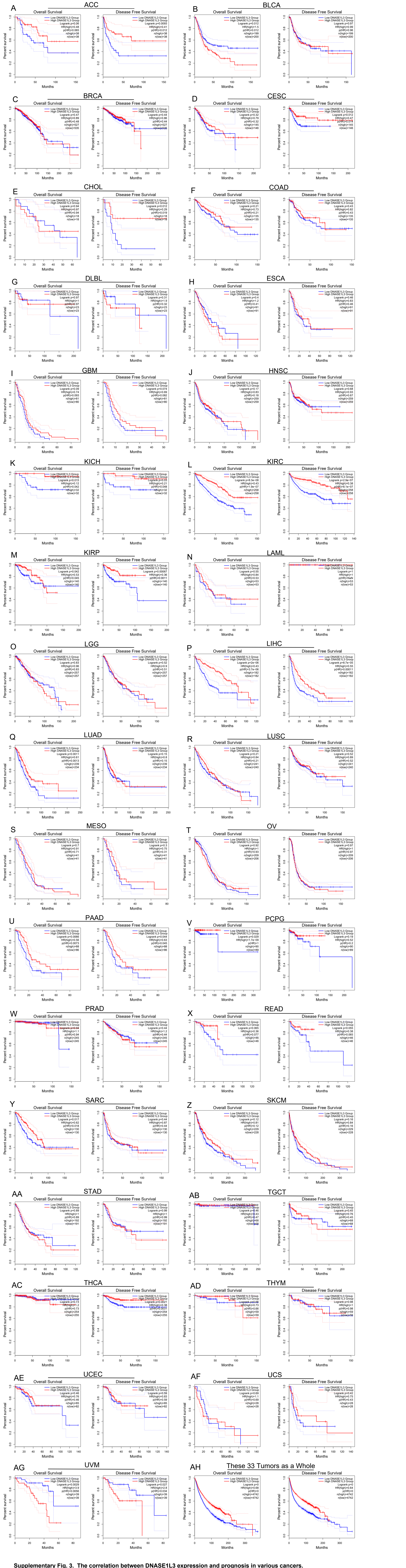


Supplementary Fig. 1. Correlation between DNASE1L3 expression and various cancers in Prognoscan Database. The expression of DNASE1L3 were found in one or more cohorts, which showed significant correlation with prognosis of related cancer type, including blood, breast, colorectal, head and neck cancer, lung adenocarcinoma, ovarian, melanoma. The following targets were used to evaluate the prognosis, OS: overall survival, DSS: disease specific survival, RFS: relapse free survival, DMFS: disease metastasis free survival.

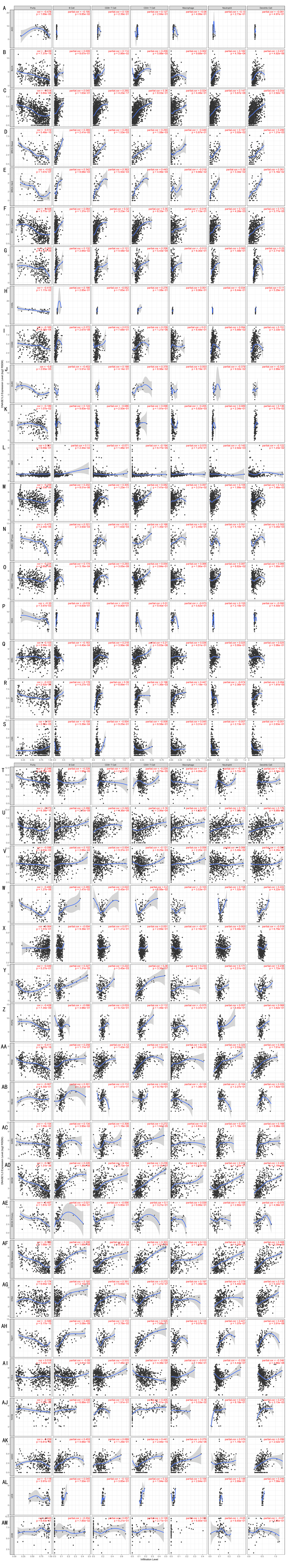


Supplementary Fig. 2. Correlation between DNASE1L3 expression and various cancers in Kaplan-Meier Plotter Database. All the correlation between DNASE1L3 expression and various cancers in Kaplan-Meier Plotter Database were analyzed, and the data for A-D (gastric, lung, ovarian and breast cancer respectively) came from gene array in Kaplan-Meier Plotter, the data for E-Z came from RNA Sequencing in Kaplan-Meier Plotter. OS: overall survival, RFS: relapse free survival, DMFS: distant metastasis free survival, FP: first progress, DSS: disease specific survival, PPS: post-progression survival, PFS: progression free survival.



Supplementary Fig. 3. The correlation between DNASE1L3 expression and prognosis in various cancers.

The correlation between DNASE1L3 expression and prognosis in various cancers. Overall survival (OS) and disease free survival (DFS) curves were generated by comparing the high (50%) and low (50%) expression of DNASE1L3 in 33 types of cancers, respectively and totally, including A: Adrenocortical carcinoma (ACC), B: Bladder Urothelial Carcinoma (BLCA), C: Breast invasive carcinoma (BRCA), D: Cervical squamous cell carcinoma and endocervical adenocarcinoma (CESC), E: Cholangio carcinoma (CHOL), F: Colon adenocarcinoma (COAD), G: Lymphoid Neoplasm Diffuse B-cell Lymphoma (DLBL), H: Esophageal carcinoma (ESCA), I: Glioblastoma multiforme (GBM), J: Head and Neck squamous cell carcinoma (HNSC), K: Kidney Chromophobe (KICH), L: Kidney renal clear cell carcinoma (KIRC), M: Kidney renal papillary cell carcinoma (KIRP), N: Acute Myeloid Leukemia (LAML), O: Brain Lower Grade Glioma (LGG), P: Liver hepatocellular carcinoma (LIHC), Q: Lung adenocarcinoma (LUAD), R: Lung squamous cell carcinoma (LUSC), S: Mesothelioma (MESO), T: Ovarian serous cystadenocarcinoma (OV), U: Pancreatic adenocarcinoma (PAAD), V: Pheochromocytoma and Paraganglioma (PCPG), W: Prostate adenocarcinoma (PRAD), X: Rectum adenocarcinoma (READ), Y: Sarcoma (SARC), Z: Skin Cutaneous Melanoma (SKCM), AA: Stomach adenocarcinoma (STAD), AB: Testicular Germ Cell Tumors (TGCT), AC: Thyroid carcinoma (THCA), AD: Thyroid Cancer (THYM), AE: Uterine Endometrial Carcinoma (UCEC), AF: Uterine Endometrial Carcinoma (UCS), AG: Uveal Melanoma (UVM), AH: These 33 tumors as a whole.



Supplementary Figure. 4 The correlation between DANSE1L3 expression and immune infiltration levels in all cancers in TIMER. ACC: adrenocortical carcinoma (**A**); BLCA: bladder urothelial carcinoma(**B**); BRCA: breast invasive carcinoma(**C, D, E,F**); CESC: cervical squamous cell carcinoma and endocervical adenocarcinoma(**G**); CHOL: cholangio carcinoma(**H**); COAD: colon adenocarcinoma(**I**); DLBC: lymphoid neoplasm diffuse large B-cell lymphoma(**J**); ESCA: esophageal carcinoma(**K**); GBM: glioblastoma multiforme(**L**); HNSC: head and neck squamous cell carcinoma(**M, N,O**); KICH: kidney chromophobe(**P**); KIRC: kidney renal clear cell carcinoma(**Q**); KIRP: kidney renal papillary cell carcinoma(**R**); LGG: brain lower grade glioma(**S**); LIHC: liver hepatocellular carcinoma(**T**); LUAD: lung adenocarcinoma(**U**); LUSC: lung squamous cell carcinoma(**V**); MESO: mesothelioma(**W**); OV: ovarian serous cystadenocarcinoma(**X**); PAAD: pancreatic adenocarcinoma(**Y**); PCPG: pheochromocytoma and paraganglioma(**Z**); PRAD: prostate adenocarcinoma(**AA**); READ: rectum adenocarcinoma(**AB**); SARC: sarcoma(**AC**); SKCM: skin cutaneous melanoma(**AD, AE,AF**); STAD: stomach adenocarcinoma(**AG**); TGCT: testicular germ cell tumors(**AH**); THCA: thyroid carcinoma(**AI**); THYM: thymoma(**AJ**); UCEC: uterine corpus endometrial carcinoma(**AK**); UCS: uterine carcinosarcoma(**AL**); UVM: uveal melanoma(**AM**).

Supplementary Table 1. DNASE1L3 expression in tumors and normal tissues in OncoMine database.

| Cancer | Cancer type | P-value | t-Test | Fold change | Rank (Top%) | Sample | Reference (PMID) |
|--|--|--------------------------|----------|-------------|-------------|--------|------------------|
| Breast Cancer | Invasive Ductal Breast Carcinoma Stroma | 1.85E-04 | -4.429 | -3.051 | 2% | 66 | 19187537 |
| | Invasive Ductal Breast Carcinoma | 2.42E-37 | -20.816 | -8.874 | 2% | 593 | TCGA |
| | Invasive Breast Carcinoma | 8.63E-18 | -9.924 | -5.312 | 5% | 593 | TCGA |
| | Invasive Lobular Breast Carcinoma | 3.16E-11 | -7.966 | -4.378 | 5% | 593 | TCGA |
| | Mucinous Breast Carcinoma | 9.33E-04 | -6.985 | -5.794 | 6% | 593 | TCGA |
| | Invasive Breast Carcinoma | 3.10E-08 | -7.26 | -2.194 | 4% | 2,136 | 22522925 |
| | Tubular Breast Carcinoma | 2.88E-26 | -12.294 | -2.072 | 4% | 2,136 | 22522925 |
| | Mucinous Breast Carcinoma | 1.02E-15 | -9.491 | -2.037 | 7% | 2,136 | 22522925 |
| | Invasive Ductal Breast Carcinoma | 1.65E-39 | -17.657 | -2.201 | 8% | 2,136 | 22522925 |
| Cervical Cancer | Cervical Squamous Cell Carcinoma | 6.26E-08 | -6.111 | -3.216 | 2% | 66 | 18506748 |
| Colorectal Cancer | Colon Adenocarcinoma | 2.36E-26 | -14.133 | -4.535 | 1% | 237 | TCGA |
| | Rectal Adenocarcinoma | 4.45E-18 | -11.06 | -5.583 | 4% | 237 | TCGA |
| | Colon Mucinous Adenocarcinoma | 2.95E-09 | -8.998 | -11.905 | 7% | 237 | TCGA |
| | Cecum Adenocarcinoma | 5.54E-10 | -8.791 | -4.706 | 8% | 237 | TCGA |
| | Colon Adenocarcinoma | 4.30E-10 | -7.473 | -2.492 | 2% | 123 | 17640062 |
| | Colon Carcinoma | 1.32E-07 | -9.898 | -7.401 | 4% | 40 | 20957034 |
| | Colon Adenoma | 9.59E-08 | -6.079 | -2.138 | 4% | 64 | 18171984 |
| | Rectosigmoid Adenocarcinoma | 7.80E-05 | -5.653 | -2.758 | 5% | 105 | 17615082 |
| | Colon Mucinous Adenocarcinoma | 2.25E-05 | -6.541 | -3.11 | 5% | 105 | 17615082 |
| | Cecum Adenocarcinoma | 3.74E-05 | -6.031 | -2.848 | 6% | 105 | 17615082 |
| | Colon Adenocarcinoma | 1.18E-04 | -7.857 | -3.055 | 10% | 105 | 17615082 |
| | Colorectal Carcinoma | 2.38E-08 | -6.409 | -3.91 | 6% | 105 | 20957034 |
| | Rectal Adenocarcinoma | 7.62E-18 | -10.705 | -4.195 | 8% | 130 | 20725992 |
| | Colorectal Carcinoma | 3.26E-07 | -7.847 | -5.761 | 8% | 82 | 20143136 |
| | Esophageal Cancer | Esophageal Adeocarcinoma | 9.10E-17 | -10.738 | -4.142 | 4% | 118 |
| Barrett's Esophagus | | 1.34E-08 | -8.124 | -4.964 | 9% | 118 | 21152079 |
| Esophageal Squamous Cell Carcinoma | | 5.24E-06 | -5.802 | -4.633 | 8% | 34 | 20955586 |
| Gastric Cancer | Gastric Mixed Adenocarcinoma | 4.06E-07 | -7.565 | -3.146 | 1% | 90 | 21447720 |
| | Diffuse Gastric Adenocarcinoma | 1.38E-09 | -7.285 | -2.813 | 1% | 90 | 21447720 |
| | Gastric Intestinal Type Adenocarcinoma | 3.52E-04 | -3.817 | -2.069 | 5% | 90 | 21447720 |
| Head and Neck Cancer | Tongue Squamous Cell Carcinoma | 3.79E-06 | -5.522 | -4.299 | 1% | 38 | 18254958 |
| | Nasopharyngeal Carcinoma | 3.26E-06 | -5.717 | -2.629 | 1% | 41 | 16912175 |
| | Head and Neck Squamous Cell Carcinoma | 1.39E-12 | -11.411 | -6.99 | 3% | 54 | 14729608 |
| | Oral Cavity Squamous Cell Carcinoma | 1.99E-12 | -9.539 | -3.928 | 3% | 79 | 21853135 |
| Kidney Cancer | Non-Hereditary Clear Cell Renal Cell Carcinoma | 9.65E-09 | -7.744 | -4.903 | 2% | 70 | 19470766 |
| | Hereditary Clear Cell Renal Cell Carcinoma | 1.01E-06 | -6.103 | -3.269 | 6% | 70 | 19470766 |
| | Papillary Renal Cell Carcinoma | 2.61E-06 | -6.553 | -2.311 | 11% | 92 | 16115910 |
| Leukemia | Renal Pelvis Urothelial Carcinoma | 1.96E-04 | -5.389 | -2.526 | 14% | 92 | 16115910 |
| Liver Cancer | Hepatocellular Carcinoma | 9.30E-16 | -12.255 | -10.303 | 1% | 75 | 17393520 |
| | Hepatocellular Carcinoma | 6.15E-17 | -17.011 | -12.378 | 1% | 43 | 21159642 |
| | Hepatocellular Carcinoma | 6.67E-97 | -28.108 | -7.653 | 1% | 445 | 21159642 |
| | Hepatocellular Carcinoma | 1.49E-36 | -16.14 | -8.386 | 1% | 197 | 12058060 |
| Lung Cancer | Lung Adenocarcinoma | 1.38E-10 | -7.756 | -2.655 | 2% | 66 | 17540040 |
| | Lung Adenocarcinoma | 8.62E-28 | -17.797 | -5.22 | 2% | 116 | 22613842 |
| | Lung Adenocarcinoma | 1.33E-17 | -10.536 | -5.127 | 2% | 156 | 20421987 |
| | Squamous Cell Lung Carcinoma | 5.93E-12 | -8.858 | -4.709 | 8% | 156 | 20421987 |
| | Large Cell Lung Carcinoma | 1.18E-05 | -5.305 | -4.559 | 14% | 156 | 20421987 |
| | Lung Adenocarcinoma | 4.60E-22 | -13.452 | -2.469 | 2% | 107 | 18297132 |
| | Lung Adenocarcinoma | 1.64E-13 | -9.937 | -5.326 | 2% | 50 | 22726390 |
| | Lung Adenocarcinoma | 1.28E-09 | -8.944 | -3.914 | 7% | 246 | 22080568 |
| | Lymphoma | Follicular Lymphoma | 6.92E-10 | 7.44 | 3.523 | 8% | 136 |
| Angioimmunoblastic T Cell Lymphoma | | 6.91E-04 | 5.07 | 10.218 | 17% | 60 | 17304354 |
| Unspecified Peripheral T Cell Lymphoma | | 4.92E-04 | 3.548 | 2.388 | 27% | 60 | 17304354 |
| Ovarian Cancer | Ovarian Serous Adenocarcinoma | 6.60E-11 | -9.63 | -39.6 | 4% | 53 | 19486012 |
| Pancreatic Cancer | Pancreatitis | 2.40E-04 | -5.862 | -2.077 | 3% | 27 | 12750293 |

| | | | | | | | |
|---------------|--|----------|--------|--------|----|----|----------|
| Sarcoma | Pancreatic Adenocarcinoma | 4.64E-06 | -7.006 | -2.57 | 3% | 27 | 12750293 |
| | Synovial Sarcoma | 6.90E-05 | -4.956 | -5.298 | 2% | 54 | 15994966 |
| Other Cancers | Malignant Fibrous Histiocytoma | 3.76E-04 | -4.103 | -3.996 | 4% | 54 | 15994966 |
| | Pleural Malignant Mesothelioma | 1.69E-06 | -6.67 | -2.234 | 2% | 54 | 15920167 |
| | Pleural Malignant Fibrous Histiocytoma | 3.76E-04 | -4.103 | -3.996 | 4% | 54 | 15994966 |

Supplementary Table 2A The correlation between immune molecular sets and DNASE1L3 in various cancers

| Discription | Geng markers | HNSC(n=520) | | | | KIRP(n=290) | | | | LIHC (n=371) | | | |
|------------------------|----------------|-------------|-------|--------|-------|-------------|-------|--------|-------|--------------|-------|--------|-------|
| | | None | | Purity | | None | | Purity | | None | | Purity | |
| | | Cor | P | Cor | P | Cor | P | Cor | P | Cor | P | Cor | P |
| CD8+T cell | CD8A | 0.370 | **** | 0.314 | **** | 0.320 | **** | 0.283 | **** | 0.168 | ** | 0.088 | 0.101 |
| | CD8B | 0.352 | **** | 0.303 | **** | 0.338 | **** | 0.292 | **** | 0.132 | * | 0.058 | 0.284 |
| T cell (genenral) | CD3D | 0.440 | **** | 0.385 | **** | 0.374 | **** | 0.334 | **** | 0.017 | 0.745 | 0.133 | * |
| | CD3E | 0.422 | **** | 0.361 | **** | 0.364 | **** | 0.313 | **** | 0.150 | ** | 0.029 | 0.588 |
| | CD2 | 0.395 | **** | 0.335 | **** | 0.352 | **** | 0.306 | **** | 0.115 | * | 0.003 | 0.959 |
| B cell | CD19 | 0.362 | **** | 0.313 | **** | 0.166 | ** | 0.146 | * | 0.044 | 0.401 | 0.039 | 0.472 |
| | CD79A | 0.366 | **** | 0.324 | **** | 0.231 | **** | 0.207 | *** | 0.171 | *** | 0.075 | 0.164 |
| Monocyte | CD86 | 0.143 | ** | 0.048 | 0.286 | 0.373 | **** | 0.359 | **** | 0.022 | 0.677 | 0.138 | * |
| TAM | CD115(CSF1R) | 0.217 | **** | 0.120 | ** | 0.284 | **** | 0.269 | **** | 0.119 | * | 0.025 | 0.641 |
| | CCL2 | 0.139 | ** | 0.047 | 0.300 | 0.284 | **** | 0.253 | **** | 0.197 | *** | 0.079 | 0.141 |
| MI Macrophage | CD68 | 0.093 | * | 0.040 | 0.376 | 0.254 | **** | 0.216 | *** | 0.023 | 0.666 | 0.142 | ** |
| | IL10 | 0.169 | *** | 0.073 | 0.107 | 0.403 | **** | 0.403 | **** | 0.034 | 0.519 | 0.108 | * |
| | INOS(NOS2) | 0.100 | * | 0.114 | * | 0.081 | 0.168 | 0.055 | 0.375 | 0.185 | *** | 0.173 | ** |
| M2 Macrophage | IRF5 | 0.214 | **** | 0.207 | **** | 0.114 | 0.054 | 0.092 | 0.141 | 0.109 | * | 0.130 | * |
| | COX2(PTGS2) | 0.075 | 0.085 | 0.052 | 0.250 | 0.176 | ** | 0.179 | ** | 0.146 | ** | 0.005 | 0.924 |
| | CD163 | 0.069 | 0.116 | 0.021 | 0.640 | 0.359 | **** | 0.372 | **** | 0.240 | **** | 0.143 | ** |
| Neutrophils | VSIG4 | 0.031 | 0.480 | 0.053 | 0.239 | 0.306 | **** | 0.313 | **** | 0.084 | 0.106 | 0.053 | 0.329 |
| | MS4A4A | 0.111 | * | 0.022 | 0.629 | 0.472 | **** | 0.468 | **** | 0.180 | *** | 0.053 | 0.329 |
| | CD66b(CEACAM8) | 0.096 | * | 0.081 | 0.071 | 0.053 | 0.365 | 0.019 | 0.760 | 0.019 | 0.721 | 0.014 | 0.794 |
| Natural killer cell | CD11b(ITGAM) | 0.128 | ** | 0.068 | 0.134 | 0.213 | *** | 0.209 | *** | 0.237 | **** | 0.371 | **** |
| | CCR7 | 0.386 | **** | 0.320 | 0.000 | 0.354 | **** | 0.362 | **** | 0.290 | **** | 0.186 | *** |
| | KIR2DL1 | 0.152 | *** | 0.130 | ** | 0.012 | 0.839 | 0.024 | 0.697 | 0.140 | ** | 0.137 | * |
| Dendritic cell | KIR2DL3 | 0.147 | *** | 0.116 | ** | 0.006 | 0.918 | 0.001 | 0.989 | 0.018 | 0.727 | 0.009 | 0.874 |
| | KIR2DL4 | 0.310 | **** | 0.271 | **** | 0.120 | * | 0.112 | 0.072 | 0.019 | 0.719 | 0.003 | 0.960 |
| | KIR3DL1 | 0.161 | *** | 0.124 | ** | 0.160 | ** | 0.152 | * | 0.114 | * | 0.096 | 0.074 |
| | KIR3DL2 | 0.228 | **** | 0.192 | **** | 0.059 | 0.319 | 0.043 | 0.491 | 0.147 | ** | 0.122 | * |
| | KIR3DL3 | 0.113 | ** | 0.079 | 0.081 | 0.005 | 0.937 | 0.023 | 0.711 | 0.040 | 0.442 | 0.028 | 0.603 |
| | KIR2DS4 | 0.137 | ** | 0.084 | 0.063 | 0.053 | 0.371 | 0.041 | 0.510 | 0.166 | ** | 0.174 | ** |
| | HLA-DPB1 | 0.356 | **** | 0.289 | **** | 0.501 | **** | 0.491 | **** | 0.167 | ** | 0.061 | 0.255 |
| | HLA-DQB1 | 0.248 | **** | 0.192 | **** | 0.357 | **** | 0.305 | **** | 0.132 | * | 0.032 | 0.555 |
| Dendritic cell | HLA-DRA | 0.344 | **** | 0.271 | **** | 0.484 | **** | 0.476 | **** | 0.135 | ** | 0.022 | 0.678 |
| | HLA-DPA1 | 0.342 | **** | 0.271 | **** | 0.467 | **** | 0.464 | **** | 0.161 | ** | 0.045 | 0.401 |
| | BDCA-1(CD11C) | 0.321 | **** | 0.252 | **** | 0.254 | **** | 0.242 | **** | 0.372 | 0.000 | 0.303 | **** |

| | | | | | | | | | | | | | |
|-------------------|----------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | BDCA4(NRP1) | 0.002 | 0.956 | 0.082 | 0.069 | 0.180 | ** | 0.205 | *** | 0.027 | 0.606 | 0.021 | 0.695 |
| Th1 | CD11c(ITGAX) | 0.206 | **** | 0.130 | ** | 0.290 | **** | 0.265 | **** | 0.030 | 0.570 | 0.187 | *** |
| | T-bet(TBX21) | 0.341 | **** | 0.289 | **** | 0.392 | **** | 0.352 | **** | 0.298 | **** | 0.225 | **** |
| | STAT1 | 0.191 | **** | 0.136 | ** | 0.165 | ** | 0.171 | ** | 0.036 | 0.493 | 0.097 | 0.071 |
| | STAT4 | 0.198 | **** | 0.127 | ** | 0.073 | 0.218 | 0.066 | 0.290 | 0.025 | 0.627 | 0.046 | 0.394 |
| | IFN- γ (IFNG) | 0.294 | **** | 0.245 | **** | 0.016 | 0.780 | 0.002 | 0.975 | 0.021 | 0.687 | 0.088 | 0.101 |
| | TNF- α (TNF) | 0.098 | * | 0.054 | 0.231 | 0.166 | ** | 0.152 | * | 0.007 | 0.895 | 0.148 | ** |
| Th2 | GATA3 | 0.180 | **** | 0.134 | ** | 0.210 | *** | 0.203 | ** | 0.078 | 0.135 | 0.050 | 0.356 |
| | STAT5A | 0.289 | **** | 0.228 | **** | 0.355 | **** | 0.320 | **** | 0.129 | * | 0.068 | 0.208 |
| | STAT6 | 0.104 | * | 0.111 | * | 0.052 | 0.379 | 0.030 | 0.632 | 0.186 | *** | 0.195 | *** |
| | IL13 | 0.182 | **** | 0.133 | ** | 0.006 | 0.919 | 0.026 | 0.675 | 0.023 | 0.653 | 0.029 | 0.595 |
| Tfh | BCL6 | 0.022 | 0.617 | 0.066 | 0.142 | 0.287 | **** | 0.320 | **** | 0.058 | 0.264 | 0.037 | 0.499 |
| | IL21 | 0.262 | **** | 0.226 | **** | 0.042 | 0.475 | 0.058 | 0.356 | 0.012 | 0.812 | 0.050 | 0.353 |
| Th17 | STAT3 | 0.218 | **** | 0.183 | **** | 0.135 | * | 0.186 | ** | 0.001 | 0.990 | 0.084 | 0.120 |
| Treg | IL17A | 0.242 | **** | 0.211 | **** | 0.007 | 0.910 | 0.009 | 0.882 | 0.018 | 0.727 | 0.008 | 0.881 |
| | FOXP3 | 0.319 | **** | 0.255 | **** | 0.060 | 0.307 | 0.039 | 0.538 | 0.136 | ** | 0.057 | 0.294 |
| | CCR8 | 0.242 | **** | 0.173 | ** | 0.098 | 0.095 | 0.075 | 0.229 | 0.110 | * | 0.214 | **** |
| | STAT5B | 0.058 | 0.189 | 0.009 | 0.843 | 0.084 | 0.154 | 0.129 | * | 0.239 | **** | 0.283 | **** |
| T cell exhaustion | TGF- β (TGFB1) | 0.110 | * | 0.148 | *** | 0.074 | 0.210 | 0.054 | 0.388 | 0.057 | 0.269 | 0.170 | ** |
| | PD-1(PDCD1) | 0.358 | **** | 0.306 | **** | 0.145 | * | 0.118 | 0.058 | 0.057 | 0.270 | 0.159 | ** |
| | CTLA4 | 0.319 | **** | 0.257 | **** | 0.234 | **** | 0.220 | *** | 0.101 | 0.053 | 0.222 | **** |
| | LAG3 | 0.328 | **** | 0.285 | **** | 0.178 | ** | 0.149 | * | 0.063 | 0.224 | 0.036 | 0.510 |
| | TIM-3(HAVCR2) | 0.210 | **** | 0.131 | ** | 0.362 | **** | 0.365 | **** | 0.081 | 0.120 | 0.265 | **** |
| | GZMB | 0.330 | **** | 0.282 | **** | 0.170 | ** | 0.153 | * | 0.255 | **** | 0.199 | **** |

TAM: tumor-associated macrophage; Th: T helper cell; Tfh: Follicular helper T cell; Treg: regulatory T cell; Cor, R value of Spearman's correlation; None, correlation without adjustment. Purity, correlation adjusted by purity. Red fonts stands for P value with adjustment. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; **** $P < 0.0001$.

Supplementary Table 2B The correlation between immune molecular sets and DNASE1L3 in various cancers

| Discription | Geng markers | Sarcoma SARC (n=259) | | | | Skin Cutaneous Melanoma SKCM (n=103) | | | | Uterine Corpus Endometrial Carcinoma UCEC (n=545) | | | |
|---------------------|--------------|-------------------------|------|--------|------|---|------|--------|------|---|------|--------|------|
| | | None | | Purity | | None | | Purity | | None | | Purity | |
| | | Cor | P | Cor | P | Cor | P | Cor | P | Cor | P | Cor | P |
| CD8+T cell | CD8A | 0.371 | **** | 0.328 | **** | 0.503 | **** | 0.244 | **** | 0.460 | **** | 0.435 | **** |
| | CD8B | 0.431 | **** | 0.401 | **** | 0.543 | **** | 0.298 | **** | 0.374 | **** | 0.348 | **** |
| T cell (genenal) | CD3D | 0.437 | **** | 0.409 | **** | 0.650 | **** | 0.441 | **** | 0.557 | **** | 0.558 | **** |
| | CD3E | 0.445 | **** | 0.416 | **** | 0.652 | **** | 0.447 | **** | 0.575 | **** | 0.573 | **** |
| | CD2 | 0.454 | **** | 0.426 | **** | 0.604 | **** | 0.369 | **** | 0.523 | **** | 0.523 | **** |
| B cell | CD19 | 0.260 | **** | 0.217 | **** | 0.603 | **** | 0.455 | **** | 0.398 | **** | 0.373 | **** |
| | CD79A | 0.365 | **** | 0.322 | **** | 0.585 | **** | 0.404 | **** | 0.483 | **** | 0.426 | **** |
| Monocyte | CD86 | 0.263 | **** | 0.199 | ** | 0.474 | **** | 0.195 | **** | 0.433 | **** | 0.432 | **** |
| | CD115(CSF1R) | 0.320 | **** | 0.275 | **** | 0.437 | **** | 0.182 | **** | 0.456 | **** | 0.420 | **** |
| TAM | CCL2 | 0.308 | **** | 0.260 | **** | 0.431 | **** | 0.195 | **** | 0.274 | **** | 0.315 | **** |

| | | | | | | | | | | | | | |
|---------------------|----------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | CD68 | 0.193 | ** | 0.109 | 0.088 | 0.294 | **** | 0.041 | 0.386 | 0.350 | **** | 0.301 | **** |
| | IL10 | 0.168 | ** | 0.071 | 0.267 | 0.310 | **** | 0.037 | 0.433 | 0.112 | ** | 0.098 | 0.094 |
| MI | | | | | | | | | | | | | |
| Macrophage | INOS(NOS2) | 0.178 | ** | 0.157 | * | 0.095 | * | 0.091 | 0.051 | 0.184 | **** | 0.166 | ** |
| | IRF5 | 0.307 | **** | 0.249 | **** | 0.475 | **** | 0.225 | **** | 0.232 | **** | 0.206 | *** |
| | | - | | - | | | | - | | - | | - | |
| M2 | COX2(PTGS2) | 0.035 | 0.572 | 0.006 | 0.924 | 0.002 | 0.960 | 0.106 | * | 0.128 | ** | 0.107 | 0.067 |
| Macrophage | CD163 | 0.248 | **** | 0.181 | ** | 0.276 | **** | 0.006 | 0.893 | 0.218 | **** | 0.172 | ** |
| | | | | | | | | - | | | | | |
| | VSIG4 | 0.203 | ** | 0.126 | 0.050 | 0.218 | **** | 0.049 | 0.295 | 0.263 | **** | 0.188 | ** |
| | MS4A4A | 0.354 | **** | 0.322 | **** | 0.393 | **** | 0.138 | ** | 0.385 | **** | 0.337 | **** |
| | | | | | | | | - | | | | | |
| Neutrophils | CD66b(CEACAM8) | 0.005 | 0.933 | 0.009 | 0.888 | 0.023 | 0.621 | 0.002 | 0.963 | 0.093 | * | 0.077 | 0.191 |
| | CD11b(ITGAM) | 0.253 | **** | 0.190 | ** | 0.322 | **** | 0.083 | 0.077 | 0.398 | **** | 0.384 | **** |
| | CCR7 | 0.566 | **** | 0.543 | **** | 0.738 | **** | 0.591 | **** | 0.578 | **** | 0.553 | **** |
| Natural killer cell | | | | | | | | | | | | | |
| | KIR2DL1 | 0.216 | *** | 0.181 | ** | 0.220 | **** | 0.055 | 0.242 | 0.254 | **** | 0.203 | *** |
| | KIR2DL3 | 0.327 | **** | 0.295 | **** | 0.357 | **** | 0.132 | ** | 0.221 | **** | 0.204 | *** |
| | KIR2DL4 | 0.213 | *** | 0.155 | * | 0.409 | **** | 0.170 | *** | 0.284 | **** | 0.270 | **** |
| | KIR3DL1 | 0.359 | **** | 0.333 | **** | 0.400 | **** | 0.208 | **** | 0.299 | **** | 0.285 | **** |
| | KIR3DL2 | 0.278 | **** | 0.269 | **** | 0.465 | **** | 0.271 | **** | 0.245 | **** | 0.271 | **** |
| | KIR3DL3 | 0.169 | ** | 0.165 | ** | 0.118 | * | 0.062 | 0.183 | 0.222 | **** | 0.229 | **** |
| | KIR2DS4 | 0.223 | ** | 0.200 | ** | 0.316 | **** | 0.172 | ** | 0.275 | **** | 0.290 | **** |
| Dendritic cell | HLA-DPB1 | 0.363 | **** | 0.324 | **** | 0.543 | **** | 0.287 | **** | 0.448 | **** | 0.441 | **** |
| | HLA-DQB1 | 0.289 | **** | 0.239 | ** | 0.514 | **** | 0.266 | **** | 0.333 | **** | 0.343 | **** |
| | HLA-DRA | 0.341 | **** | 0.297 | **** | 0.524 | **** | 0.254 | **** | 0.344 | **** | 0.338 | **** |
| | HLA-DPA1 | 0.367 | **** | 0.329 | **** | 0.510 | **** | 0.264 | **** | 0.426 | **** | 0.427 | **** |
| | BDCA-1(CD1C) | 0.565 | **** | 0.549 | **** | 0.720 | **** | 0.601 | **** | 0.534 | **** | 0.519 | **** |
| | BDCA4(NRP1) | 0.078 | 0.207 | 0.040 | 0.536 | 0.177 | ** | 0.005 | 0.907 | 0.237 | **** | 0.173 | ** |
| | CD11c(ITGAX) | 0.192 | ** | 0.135 | * | 0.442 | **** | 0.192 | ** | 0.508 | **** | 0.480 | **** |
| Th1 | T-bet(TBX21) | 0.482 | **** | 0.458 | **** | 0.550 | **** | 0.305 | ** | 0.498 | **** | 0.499 | **** |
| | STAT1 | 0.261 | **** | 0.215 | ** | 0.280 | **** | 0.044 | 0.351 | 0.058 | 0.178 | 0.075 | 0.201 |
| | STAT4 | 0.441 | **** | 0.418 | **** | 0.575 | **** | 0.367 | **** | 0.507 | **** | 0.500 | **** |
| | IFN- γ (IFNG) | 0.303 | **** | 0.253 | **** | 0.408 | **** | 0.133 | ** | 0.252 | **** | 0.249 | **** |
| | TNF- α (TNF) | 0.146 | * | 0.094 | 0.143 | 0.522 | **** | 0.296 | **** | 0.050 | 0.245 | 0.044 | 0.458 |
| Th2 | GATA3 | 0.098 | 0.116 | 0.041 | 0.520 | 0.620 | **** | 0.410 | **** | 0.352 | **** | 0.328 | **** |
| | STAT5A | 0.385 | **** | 0.360 | **** | 0.233 | **** | 0.230 | **** | 0.299 | **** | 0.247 | **** |
| | STAT6 | 0.336 | **** | 0.358 | **** | 0.143 | ** | 0.149 | ** | 0.156 | ** | 0.172 | ** |
| | IL13 | 0.183 | ** | 0.167 | ** | 0.181 | **** | 0.090 | 0.053 | 0.153 | ** | 0.205 | ** |
| Tfh | BCL6 | 0.210 | *** | 0.212 | ** | 0.259 | **** | 0.133 | ** | 0.054 | 0.204 | 0.064 | 0.273 |
| | IL21 | 0.194 | ** | 0.132 | * | 0.346 | **** | 0.177 | ** | 0.080 | 0.063 | 0.081 | 0.169 |
| Th17 | STAT3 | 0.233 | *** | 0.256 | **** | 0.134 | ** | 0.025 | 0.592 | 0.040 | 0.352 | 0.037 | 0.525 |
| | | - | | - | | | | - | | | | | |
| Treg | IL17A | 0.024 | 0.699 | 0.045 | 0.480 | 0.002 | 0.969 | 0.061 | 0.194 | 0.034 | 0.433 | 0.053 | 0.367 |
| | FOXP3 | 0.218 | ** | 0.162 | * | 0.651 | **** | 0.471 | **** | 0.416 | **** | 0.443 | **** |
| | CCR8 | 0.279 | **** | 0.236 | ** | 0.517 | **** | 0.311 | **** | 0.246 | **** | 0.253 | **** |
| | STAT5B | 0.315 | **** | 0.405 | **** | 0.190 | **** | 0.188 | **** | 0.254 | **** | 0.217 | ** |
| | | - | | - | | | | - | | | | | |
| T cell exhaustion | TGF- β (TGFB1) | 0.007 | 0.910 | 0.095 | 0.141 | 0.264 | **** | 0.039 | 0.411 | 0.318 | **** | 0.289 | **** |
| | PD-1(PDCD1) | 0.291 | **** | 0.235 | ** | 0.524 | **** | 0.274 | **** | 0.399 | **** | 0.383 | **** |
| | CTLA4 | 0.293 | **** | 0.242 | ** | 0.333 | **** | 0.091 | 0.051 | 0.451 | **** | 0.425 | **** |
| | LAG3 | 0.192 | ** | 0.143 | * | 0.458 | **** | 0.192 | **** | 0.362 | **** | 0.361 | **** |
| | TIM-3(HAVCR2) | 0.198 | ** | 0.118 | 0.065 | 0.426 | **** | 0.111 | * | 0.421 | **** | 0.394 | **** |
| | GZMB | 0.304 | **** | 0.262 | **** | 0.543 | **** | 0.290 | **** | 0.301 | **** | 0.294 | **** |

TAM: tumor-associated macrophage; Th: T helper cell; Tfh: Follicular helper T cell; Treg: regulatory T cell; Cor, R value of Spearman's correlation; None, correlation without adjustment. Purity, correlation adjusted by purity. Red fonts stands for P value with adjustment. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; **** $P < 0.0001$.

Supplementary Table 3A Correlation analysis between DNASE1L3 and immune cells in tumor/normal tissue of TCGA through GEPIA2

| Description | Gene Markers | HNSC | | | | KIRP | | | | LIHC | | | |
|-------------------|---------------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|
| | | Tumor | | Normal | | Tumor | | Normal | | Tumor | | Normal | |
| | | R | P | R | P | R | P | R | P | R | P | R | P |
| DCs | HLA-DPB1 | 0.320 | **** | 0.250 | 0.110 | 0.470 | **** | 0.092 | 0.620 | 0.130 | ** | 0.440 | ** |
| | HLA-DQB1 | 0.160 | *** | 0.280 | 0.070 | 0.260 | **** | 0.088 | 0.630 | 0.430 | * | 0.015 | 0.920 |
| | HLA-DRA | 0.330 | **** | 0.160 | 0.300 | 0.470 | **** | 0.067 | 0.710 | 0.110 | * | 0.470 | *** |
| | HLA-DPA1 | 0.330 | **** | 0.170 | 0.260 | 0.430 | **** | 0.300 | 0.092 | 0.140 | ** | 0.450 | ** |
| | BDCA-1(CD1C) | 0.320 | **** | 0.420 | ** | 0.270 | **** | 0.160 | 0.390 | 0.350 | **** | 0.240 | 0.088 |
| | BDCA4(NRP1) | 0.061 | 0.160 | 0.057 | 0.710 | 0.005 | 0.930 | 0.230 | 0.200 | 0.041 | 0.430 | 0.230 | 0.100 |
| | CD11c(ITGAX) | 0.190 | **** | 0.001 | 1.000 | 0.230 | *** | 0.040 | 0.830 | 0.019 | 0.710 | 0.290 | * |
| T cell exhaustion | PD-1(PDCD1) | 0.310 | **** | 0.330 | * | 0.100 | 0.083 | 0.380 | * | 0.064 | 0.220 | 0.210 | 0.150 |
| | CTLA4 | 0.290 | **** | 0.400 | ** | 0.190 | ** | 0.310 | 0.086 | 0.130 | ** | 0.100 | 0.490 |
| | LAG3 | 0.280 | **** | 0.350 | * | 0.140 | * | 0.081 | 0.660 | 0.001 | 0.980 | 0.380 | ** |
| | TIM-3(HAVCR2) | 0.200 | **** | 0.090 | 0.560 | 0.300 | **** | 0.210 | 0.240 | 0.095 | 0.069 | 0.550 | **** |
| | GZMB | 0.270 | **** | 0.380 | * | 0.110 | 0.062 | 0.250 | 0.160 | 0.180 | *** | 0.390 | ** |

HNSC: Head and neck squamous cell carcinoma; KIRP Kidney renal papillary cell carcinoma; LIHC Liver hepatocellular carcinoma; DCs: dendritic cells; Tumor: correlation analysis between DNASE1L3 and immune cell markers in tumor tissue of TCGA through GEPIA2; Normal: correlation analysis between DNASE1L3 and immune cell markers in normal tissue of TCGA through GEPIA2.

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; **** $P < 0.0001$.

Supplementary Table 3B Correlation analysis between DNASE1L3 and immune cells in tumor/normal tissue of TCGA through GEPIA2

| Description | Gene Markers | SARC | | | | SKCM | | | | UCEC | | | |
|-------------------|---------------|-------|-------|--------|----|-------|------|--------|---|-------|------|--------|-------|
| | | Tumor | | Normal | | Tumor | | Normal | | Tumor | | Normal | |
| | | R | P | R | P | R | P | R | P | R | P | R | P |
| DCs | HLA-DPB1 | 0.360 | **** | -1 | 1 | 0.510 | **** | N | N | 0.370 | **** | 0.250 | 0.400 |
| | HLA-DQB1 | 0.250 | **** | -1 | 1 | 0.450 | **** | N | N | 0.200 | ** | 0.210 | 0.490 |
| | HLA-DRA | 0.340 | **** | 1 | 1 | 0.500 | **** | N | N | 0.260 | *** | 0.220 | 0.470 |
| | HLA-DPA1 | 0.370 | **** | -1 | 1 | 0.480 | **** | N | N | 0.350 | **** | 0.190 | 0.530 |
| | BDCA-1(CD1C) | 0.570 | **** | -1 | 1 | 0.700 | **** | N | N | 0.500 | **** | 0.470 | 0.110 |
| | BDCA4(NRP1) | 0.077 | 0.220 | 1 | 1 | 0.150 | ** | N | N | 0.290 | **** | 0.660 | * |
| | CD11c(ITGAX) | 0.170 | ** | 1 | -1 | 0.370 | **** | N | N | 0.350 | **** | 0.210 | 0.480 |
| T cell exhaustion | PD-1(PDCD1) | 0.260 | **** | 1 | 1 | 0.510 | **** | N | N | 0.380 | **** | 0.033 | 0.910 |
| | CTLA4 | 0.260 | **** | -1 | 1 | 0.300 | **** | N | N | 0.430 | **** | 0.150 | 0.620 |
| | LAG3 | 0.150 | * | -1 | 1 | 0.440 | **** | N | N | 0.360 | **** | 0.320 | 0.290 |
| | TIM-3(HAVCR2) | 0.190 | ** | 1 | 1 | 0.400 | **** | N | N | 0.410 | **** | 0.033 | 0.920 |
| | GZMB | 0.270 | **** | -1 | 1 | 0.530 | **** | N | N | 0.290 | *** | 0.200 | 0.520 |

SARC: Sarcoma; STAD: stomach adenocarcinoma; SKCM: Skin Cutaneous Melanoma; UCEC Uterine Corpus Endometrial Carcinoma; DCs: dendritic cells; Tumor: correlation analysis between DNASE1L3 and immune cell markers in tumor tissue of TCGA through GEPIA2; Normal: correlation analysis between DNASE1L3 and immune cell markers in normal tissue of TCGA through GEPIA2; N: No results got from GEPIA2.

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$; **** $P < 0.0001$.

Supplementary Table 4. Clinicopathologic features in our HCC cohorts.

| Clinicopathologic parameters | No. of Specimens | |
|------------------------------|------------------|-------|
| | qPCR | IHC |
| Sex | 22 | 9 |
| Female | 4 | 1 |
| Male | 18 | 8 |
| Age | 22 | 9 |
| ≤50 | 8 | 3 |
| >50 | 14 | 6 |
| Average | 56 | 54.22 |
| Drink | 22 | 9 |
| Yes | 8 | 4 |
| No | 14 | 5 |
| AFP | 22 | 9 |
| ≤20 ng/ml | 8 | 3 |
| 20-300 ng/ml | 6 | 3 |
| ≥300 ng/ml | 8 | 3 |
| Tumor size | 22 | 9 |
| ≤3 cm | 2 | 1 |
| 3-5 cm | 6 | 1 |
| >5 cm | 14 | 7 |
| Tumor number | 22 | 9 |
| =1 | 18 | 7 |
| >1 | 4 | 2 |
| Vascular invasion | 22 | 9 |
| Yes | 16 | 6 |
| No | 6 | 3 |
| Grade | 22 | 9 |
| I | 5 | 3 |
| II | 9 | 4 |
| III | 6 | 2 |
| IV | 2 | 0 |

HCC: Hepatocellular carcinoma

Supplementary Table 5. Clinicopathologic features in our LAUD cohort.

| Clinicopathologic parameters | No. of Specimens |
|------------------------------|------------------|
| Sex | 20 |
| Female | 12 |
| Male | 8 |
| Age | 20 |
| Average | 65 |
| ≤50 | 1 |
| >50 | 19 |
| CEA | 20 |
| ≤10ng/ml | 11 |
| 10-100 ng/ml | 7 |
| ≥100 ng/ml | 2 |
| Tumor number | 20 |
| =1 | 19 |
| >1 | 1 |
| Vascular invasion | 20 |
| Yes | 7 |
| No | 13 |
| Grade | 20 |
| I | 8 |
| II | 8 |
| III | 6 |

LUAD: Lung adenocarcinoma