

Supplementary materials

Supplementary Figures

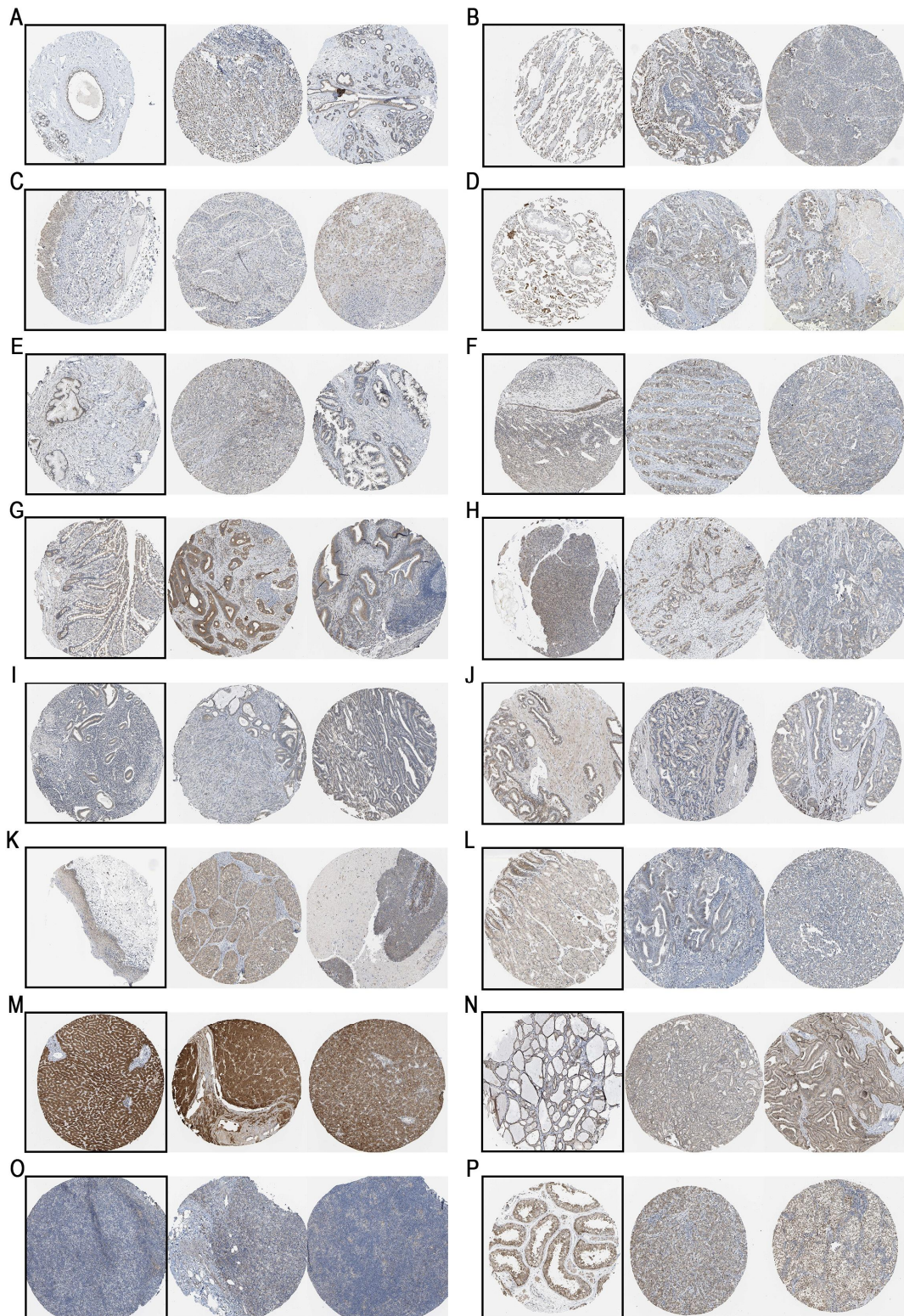


Figure S1 Immunohistochemical Staining of 16 Normal Tissues and Tumor Tissues from the

HPA Database. **(A)** BRAC, **(B)** LUAD, **(C)** BLCA, **(D)** LUSC, **(E)** CESC, **(F)** OV, **(G)** COAD, **(H)** PAAD, **(I)** UCEC, **(J)** PARD, **(K)** HNSC, **(L)** STAD, **(M)** LIHC, **(N)** THCA, **(O)** DLBC, **(P)** TGCT. Black boxes denote normal tissues, while unboxed images represent tumor tissues.

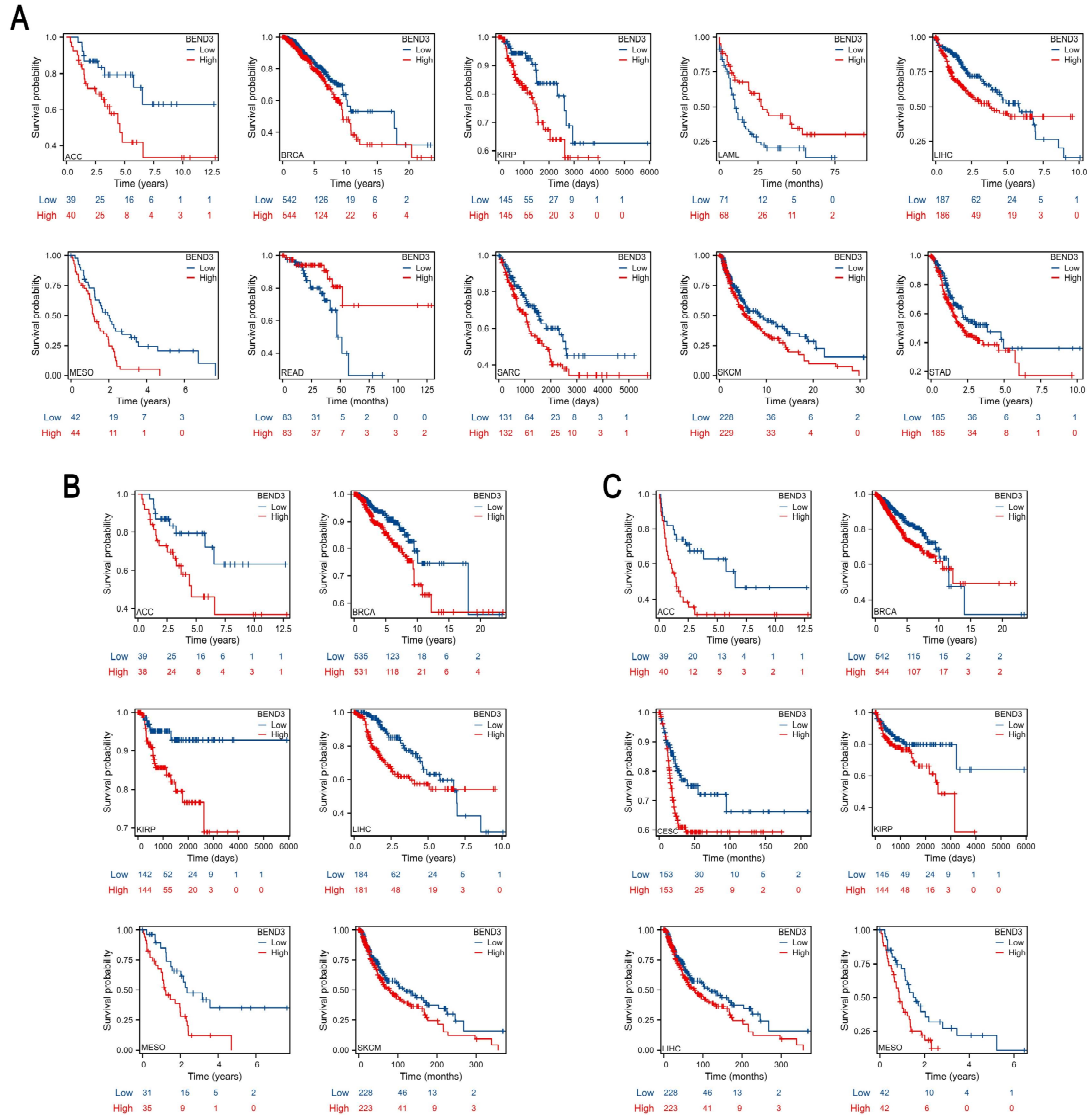


Figure S2 Kaplan-Meier (KM) Curves Showing the Detailed Association Between BEND3 Expression and Prognosis in Cancer Patients. **(A)** OS in ACC (HR=2.52, $p=0.023$), BRCA (HR=1.41, $p=0.037$), KIRP (HR=2.02, $p=0.026$), LAML (HR=0.37, $p=0.020$), LIHC (HR=1.48, $p=0.027$), MESO (HR=2.09, $p=0.603$), READ (HR=0.37, $p=0.020$), SARC (HR=1.51, $p=0.045$), SKCM (HR=1.38, $p=0.019$) and STAD (HR=1.39, $p=0.049$). **(B)** DSS in ACC (HR=2.34, $p=0.040$), BRCA (HR=1.76, $p=0.012$), KIRP (HR=3.15, $p=0.009$), LIHC (HR=1.92, $p=0.004$), MESO (HR=2.6, $p=0.003$) and SKCM (HR=1.34, $p=0.047$). **(C)** PFS in

ACC (HR=2.28, $p=0.012$), BRCA (HR=1.49, $p=0.018$), CESC (HR=1.74, $p=0.023$), KIRP (HR=1.55, $p=0.032$), LIHC (HR=1.55, $p=0.004$) and MESO (HR=1.85, $p=0.024$).

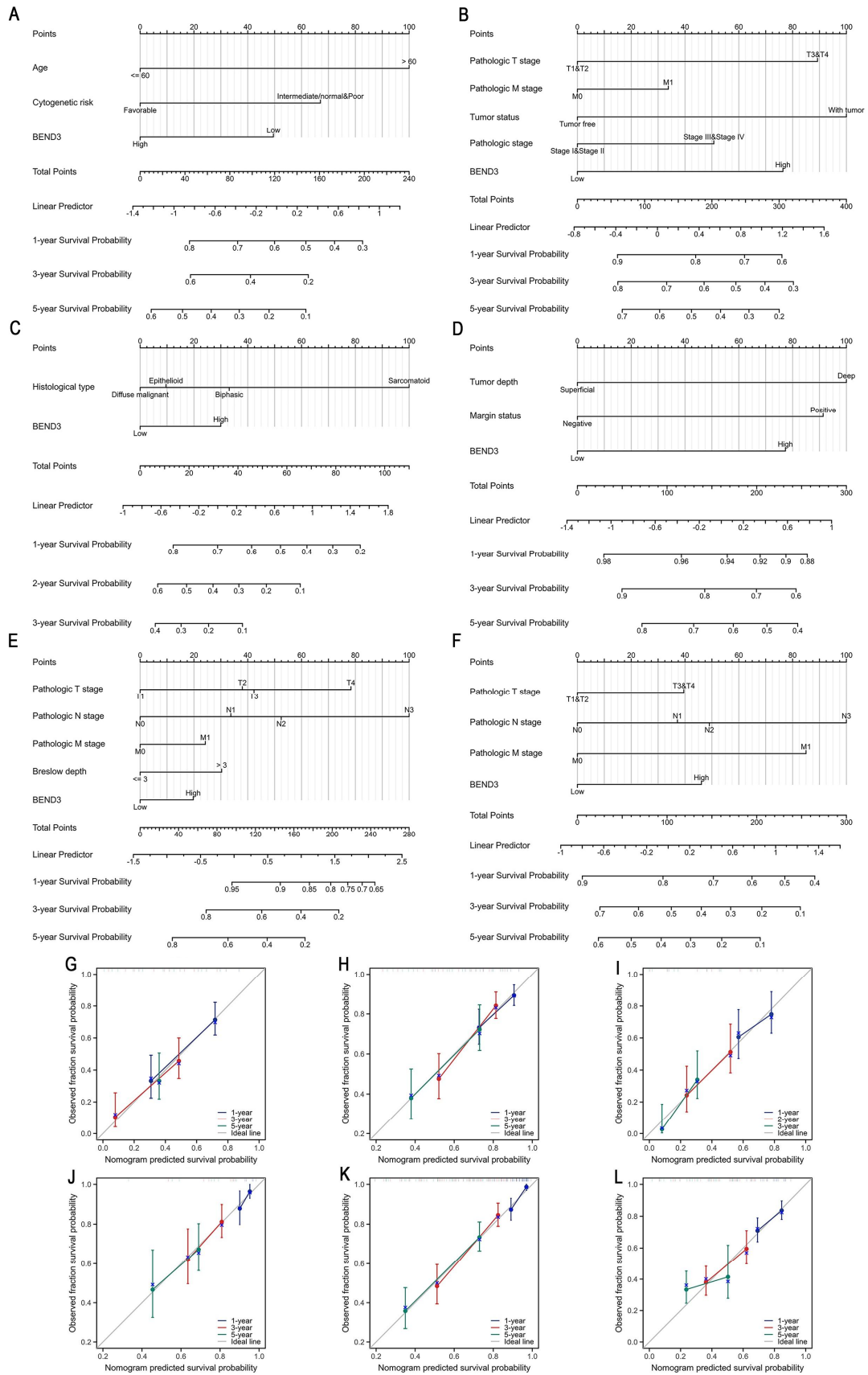


Figure S3 Nomograms and Calibration Curves Predicting Patient OS in 6 Cancers.

Nomograms of **(A)** LAML, **(B)** LIHC, **(C)** MESO, **(D)** SARC, **(E)** SKCM and **(F)** STAD. Calibration curves of **(G)** LAML, **(H)** LIHC, **(I)** MESO, **(J)** SARC, **(K)** SKCM and **(L)** STAD.

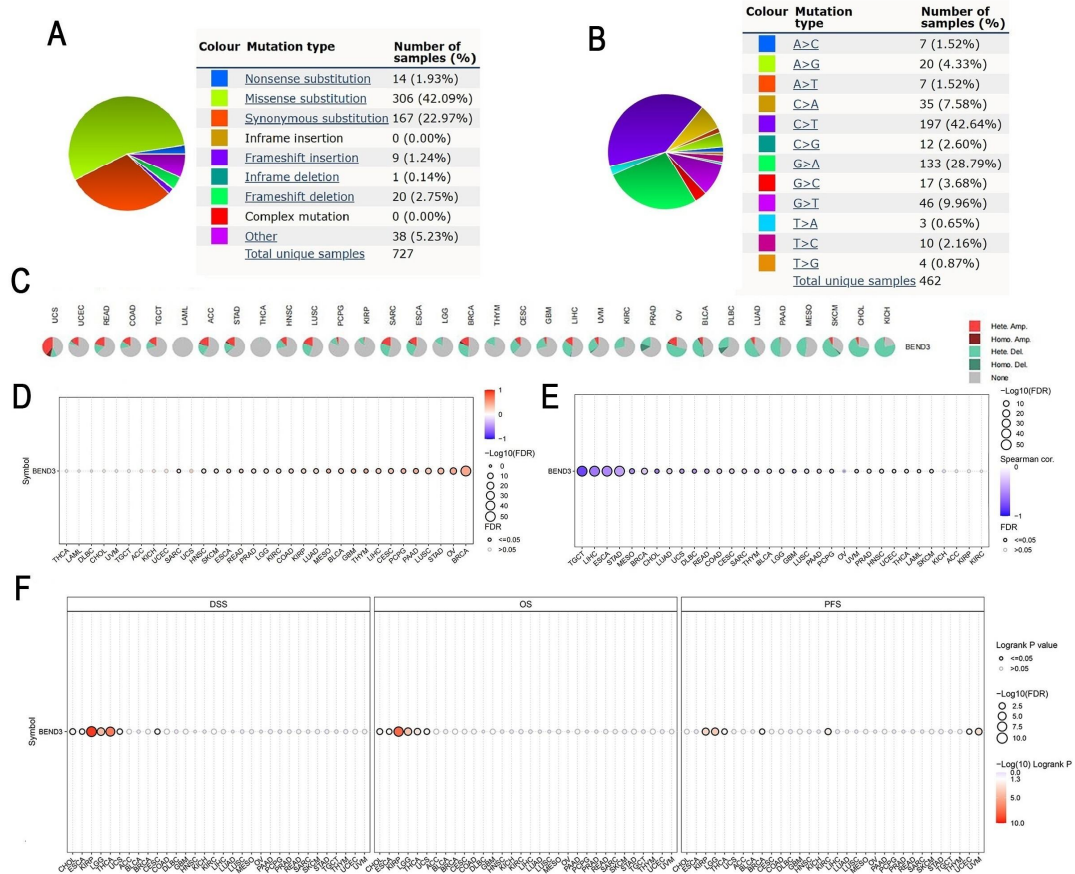


Figure S4 Mutation analysis and epigenetic methylation analysis of BEND3. **(A)** The main mutation types of BEND3. **(B)** The main types of SNVs in BEND3. **(C)** Percentage of BEND3 CNVs in each cancer. **(D)** Correlation between BEND3 mRNA expression and CNVs. **(E)** Correlation between BEND3 mRNA expression and methylation. **(F)** Effect of BEND3 CNVs on prognosis in cancer patients.

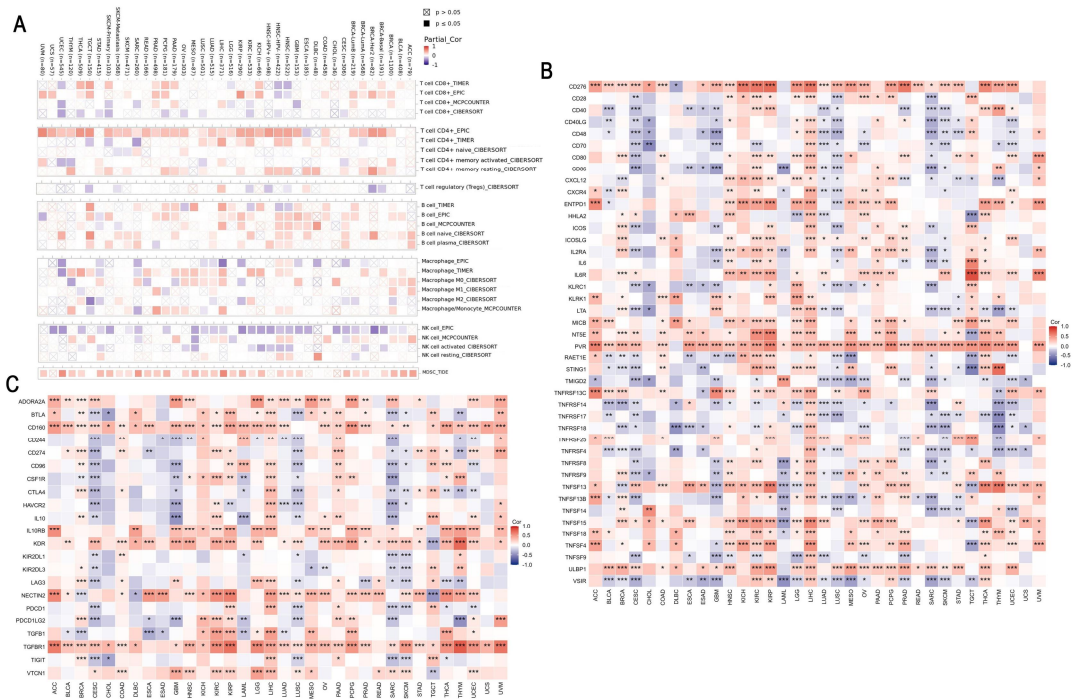


Figure S5 (A) Correlation analysis of BEND3 expression with multiple immune cell infiltrates in pan-carcinogenesis. **(B)** Co-expression of BEND3 with immune activating genes. **(C)** Co-expression of BEND3 with immune suppressive genes. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

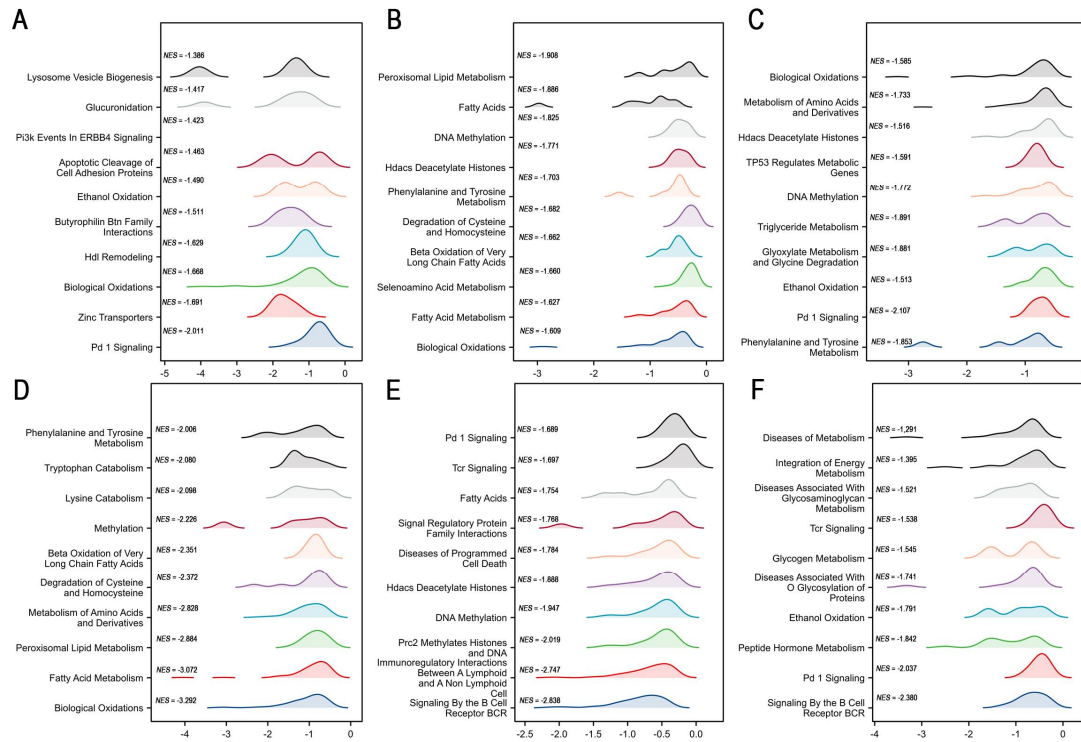


Figure S6 Functional enrichment analysis of BEND3 in six types of cancer. In **(A)** ACC, **(B)** BRCA, **(C)** KIRP, **(D)** LIHC, **(E)** READ, and **(F)** STAD, the top ten pathways are negatively correlated with BEND3 expression.

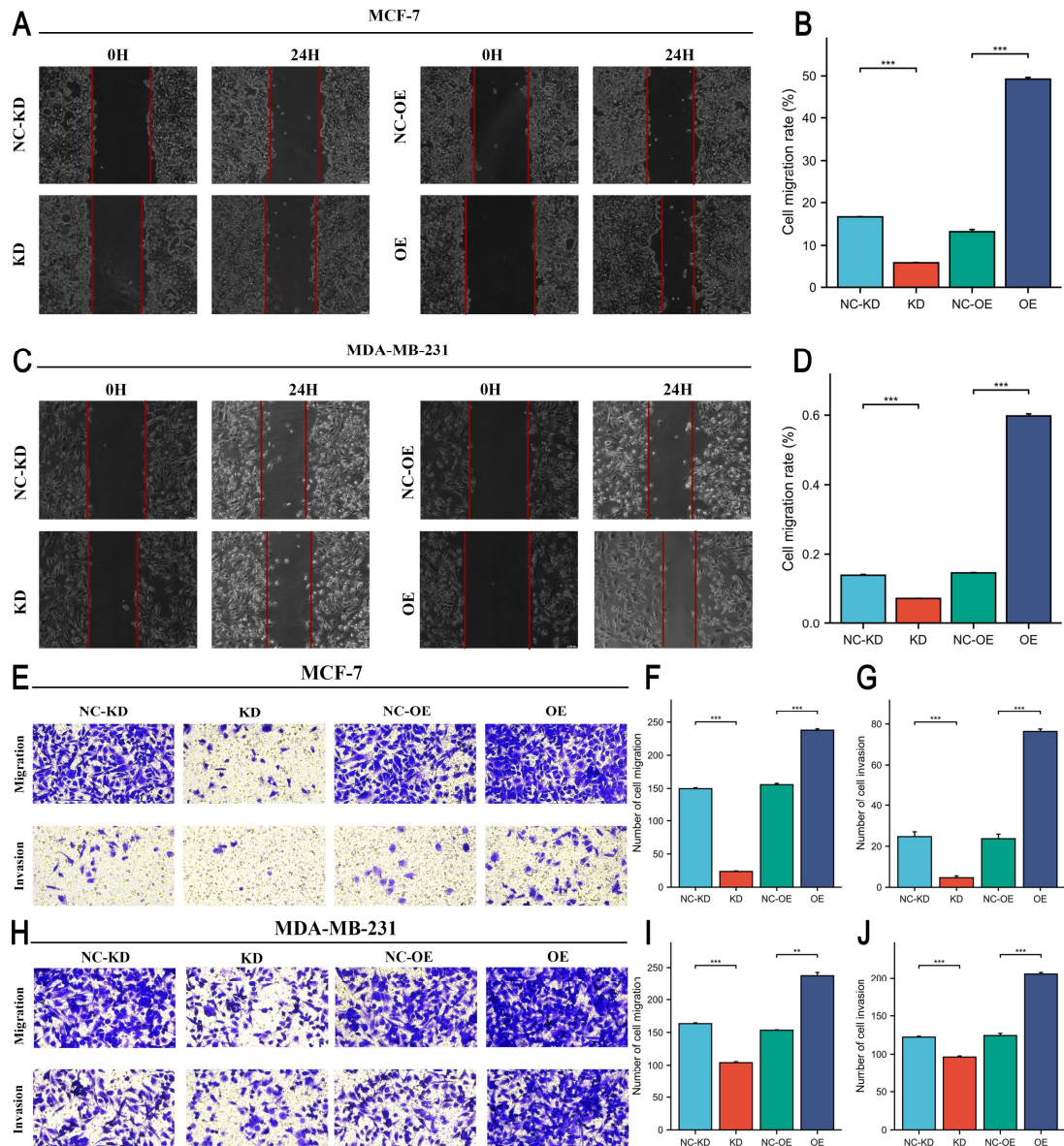


Figure S7 The Cell wound scratch assay results at 0h and 24h, along with their statistical analysis for the BEND3 NC-KD, KD, NC-OE, and OE using the (A-B) MCF-7 and (C-D) MDA-MB-231 cell lines ($p < 0.001$). The outcomes of the Transwell migration and invasion experiments, along with their statistical analyses in (E-G) MCF-7 and (H-J) MDA-MB-231 cell lines ($p < 0.001$). ** $p < 0.01$, *** $p < 0.001$.

Supplementary Table S1. Sequence information of the shRNA used

| Name | Targeting sequence (5'→3') |
|------------|----------------------------|
| sh-BEND3-1 | GCAAGAAGCTGGACAAGAA |

| | |
|------------|-----------------------|
| sh-BEND3-2 | GCAGTTTGTCTGAAGAAT |
| sh-BEND3-3 | GGACGAAGAGCTGATCAAG |
| BEND3-OE-F | AGGCGGCGGAGGCGGAG |
| BEND3-OE-R | GCCGGTGTAGTTGTTGATGA |
| BEND3-F | CAGGAGTGC GTTCTACAACG |
| BEND3-R | TGCTGGTGGTGTGTTGTAG |
| GAPDH-F | GAAGGTGAAGGTTCGGAGTC |
| GAPDH-R | GAAGATGGTGATGGGATTT |

Supplementary Table S2. Results of univariate and multivariate Cox analysis of clinical parameters in **(A)** ACC, **(B)** BRCA, **(C)** KIRP, **(D)** READ, **(E)** LAML, **(F)** LIHC, **(G)** MESO, **(H)** SARC, **(I)** SKCM and **(J)** STAD, Bold values indicate statistical significance at $p < 0.05$.

Supplementary Table S2A. ACC

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|--------------------|----------|-------------------------|-------------------|------------------------|---------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Pathologic T stage | 77 | | | | |
| T1&T2 | 51 | Reference | | Reference | |
| T3&T4 | 26 | 10.286 (3.976 - 26.608) | < 0.001 | 7.409 (0.901 - 60.900) | 0.062 |
| Clinical M stage | 77 | | | | |
| M0 | 62 | Reference | | Reference | |
| M1 | 15 | 6.150 (2.710 - 13.959) | < 0.001 | 0.261 (0.044 - 1.546) | 0.139 |
| Pathologic stage | 77 | | | | |
| Stage I&Stage II | 46 | Reference | | Reference | |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|-------------------------|----------|-------------------------|-------------------|-------------------------|-------------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Stage III&Stage IV | 31 | 6.476 (2.706 - 15.498) | < 0.001 | 0.905 (0.099 - 8.297) | 0.930 |
| Primary therapy outcome | 67 | | | | |
| PR&CR | 47 | Reference | | Reference | |
| PD&SD | 20 | 15.754 (5.017 - 49.472) | < 0.001 | 15.825 (3.298 - 75.933) | < 0.001 |
| BEND3 | 79 | | | | |
| Low | 39 | Reference | | Reference | |
| High | 40 | 2.518 (1.136 - 5.582) | 0.023 | 3.241 (0.739 - 14.217) | 0.119 |

Bold values indicate statistical significance at $p < 0.05$.

Supplementary Table S2B. BRCA

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|--------------------|----------|-----------------------|--------------|-----------------------|---------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Pathologic T stage | 1,083 | | | | |
| T1&T2 | 908 | Reference | | Reference | |
| T3&T4 | 175 | 1.588 (1.096 - 2.301) | 0.014 | 0.952 (0.526 - 1.722) | 0.871 |
| Pathologic N stage | 1,067 | | | | |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|--------------------|----------|-----------------------|----------------|------------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| N0 | 516 | Reference | | Reference | |
| N1 | 358 | 1.947 (1.322 - 2.865) | < 0.001 | 1.162 (0.656 - 2.059) | 0.606 |
| N2 | 116 | 2.522 (1.484 - 4.287) | < 0.001 | 1.798 (0.629 - 5.141) | 0.273 |
| N3 | 77 | 4.191 (2.318 - 7.580) | < 0.001 | 3.932 (1.395 - 11.078) | 0.010 |
| Pathologic M stage | 925 | | | | |
| M0 | 905 | Reference | | Reference | |
| M1 | 20 | 4.266 (2.474 - 7.354) | < 0.001 | 2.752 (1.150 - 6.590) | 0.023 |
| Pathologic stage | 1,062 | | | | |
| Stage I | 181 | Reference | | Reference | |
| Stage II | 619 | 1.703 (0.989 - 2.933) | 0.055 | 1.772 (0.834 - 3.766) | 0.137 |
| Stage III&Stage IV | 262 | 3.566 (2.042 - 6.228) | < 0.001 | 2.513 (0.755 - 8.367) | 0.133 |
| Menopause status | 975 | | | | |
| Pre&Peri | 270 | Reference | | Reference | |
| Post | 705 | 2.336 (1.421 - 3.840) | < 0.001 | 2.317 (1.362 - 3.939) | 0.002 |
| Anatomic neoplasm | 1,086 | | | | |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|-----------------|----------|-----------------------|--------------|-----------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| subdivisions | | | | | |
| Left | 566 | Reference | | | |
| Right | 520 | 0.770 (0.557 - 1.063) | 0.112 | | |
| BEND3 | | | | | |
| Low | 542 | Reference | | Reference | |
| High | 544 | 1.412 (1.021 - 1.951) | 0.037 | 1.591 (1.045 - 2.421) | 0.030 |

Bold values indicate statistical significance at $p < 0.05$.

Supplementary Table S2C. KIRP

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|--------------------|----------|-----------------------|---------|-----------------------|---------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Sex | | | | | |
| Female | 77 | Reference | | | |
| Male | 213 | 0.630 (0.327 - 1.213) | 0.167 | | |
| Laterality | | | | | |
| Left | 160 | Reference | | | |
| Right | 127 | 0.725 (0.387 - 1.357) | 0.315 | | |
| Pathologic T stage | | | | | |
| T1&T2 | 226 | Reference | | Reference | |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|-------------------------|----------|------------------------|-------------------|------------------------|-------------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| T3&T4 | 62 | 4.874 (2.658 - 8.937) | < 0.001 | 0.650 (0.172 - 2.458) | 0.525 |
| Age | 288 | | | | |
| <= 60 | 135 | Reference | | | |
| > 60 | 153 | 0.969 (0.533 - 1.762) | 0.917 | | |
| Primary therapy outcome | 199 | | | | |
| PR&CR | 187 | Reference | | Reference | |
| PD&SD | 12 | 6.168 (2.572 - 14.792) | < 0.001 | 3.123 (1.070 - 9.122) | 0.037 |
| Pathologic stage | 260 | | | | |
| Stage I&Stage II | 193 | Reference | | Reference | |
| Stage III&Stage IV | 67 | 6.261 (3.252 - 12.052) | < 0.001 | 8.277 (2.363 - 28.993) | < 0.001 |
| BEND3 | 290 | | | | |
| Low | 145 | Reference | | Reference | |
| High | 145 | 2.018 (1.087 - 3.745) | 0.026 | 2.966 (1.140 - 7.721) | 0.026 |

Bold values indicate statistical significance at $p < 0.05$.

Supplementary Table S2D. READ

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|-----------------|----------|-----------------------|---------|-----------------------|---------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|--------------------|----------|-----------------------|--------------|------------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Pathologic T stage | 164 | | | | |
| T1&T2 | 37 | Reference | | | |
| T3&T4 | 127 | 1.408 (0.476 - 4.159) | 0.536 | | |
| Pathologic N stage | 162 | | | | |
| N0 | 84 | Reference | | Reference | |
| N1 | 45 | 2.400 (0.834 - 6.906) | 0.105 | 1.210 (0.337 - 4.343) | 0.770 |
| N2 | 33 | 3.683 (1.390 - 9.762) | 0.009 | 4.348 (1.424 - 13.270) | 0.010 |
| Pathologic M stage | 149 | | | | |
| M0 | 126 | Reference | | Reference | |
| M1 | 23 | 3.412 (1.424 - 8.174) | 0.006 | 2.703 (1.004 - 7.273) | 0.049 |
| Age | 166 | | | | |
| <= 65 | 82 | Reference | | Reference | |
| > 65 | 84 | 3.843 (1.535 - 9.622) | 0.004 | 6.530 (2.112 - 20.188) | 0.001 |
| BMI | 73 | | | | |
| <= 25 | 20 | Reference | | | |
| > 25 | 53 | 1.218 (0.341 - 4.351) | 0.762 | | |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|-----------------|----------|-----------------------|--------------|-----------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Sex | 166 | | | | |
| Female | 75 | Reference | | | |
| Male | 91 | 0.916 (0.422 - 1.988) | 0.824 | | |
| CEA level | 112 | | | | |
| <= 5 | 65 | Reference | | | |
| > 5 | 47 | 1.453 (0.489 - 4.316) | 0.501 | | |
| BEND3 | 166 | | | | |
| Low | 83 | Reference | | Reference | |
| High | 83 | 0.369 (0.160 - 0.854) | 0.020 | 0.366 (0.142 - 0.945) | 0.038 |

Bold values indicate statistical significance at $p < 0.05$.

Supplementary Table S2E. LAML

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|------------------|----------|-----------------------|-------------------|-----------------------|-------------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Age | 139 | | | | |
| <= 60 | 78 | Reference | | Reference | |
| > 60 | 61 | 3.321 (2.156 - 5.116) | < 0.001 | 2.978 (1.907 - 4.649) | < 0.001 |
| Cytogenetic risk | 137 | | | | |
| Favorable | 30 | Reference | | Reference | |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|--------------------------|----------|-----------------------|-------------------|-----------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Intermediate/normal&Poor | 107 | 3.184 (1.637 - 6.193) | < 0.001 | 2.078 (1.037 - 4.164) | 0.039 |
| BEND3 | 139 | | | | |
| Low | 71 | Reference | | Reference | |
| High | 68 | 0.521 (0.339 - 0.802) | 0.003 | 0.582 (0.372 - 0.913) | 0.018 |

Bold values indicate statistical significance at $p < 0.05$.

Supplementary Table S2F. LIHC

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|--------------------|----------|-----------------------|-------------------|-----------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Pathologic T stage | 370 | | | | |
| T1&T2 | 277 | Reference | | Reference | |
| T3&T4 | 93 | 2.598 (1.826 - 3.697) | < 0.001 | 1.874 (1.076 - 3.264) | 0.026 |
| Pathologic N stage | 258 | | | | |
| N0 | 254 | Reference | | | |
| N1 | 4 | 2.029 (0.497 - 8.281) | 0.324 | | |
| Pathologic M stage | 272 | | | | |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|--------------------------------|----------|------------------------|-------------------|-----------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| M0 | 268 | Reference | | Reference | |
| M1 | 4 | 4.077 (1.281 - 12.973) | 0.017 | 1.266 (0.301 - 5.326) | 0.748 |
| Tumor status | 354 | | | | |
| Tumor free | 202 | Reference | | Reference | |
| With tumor | 152 | 2.317 (1.590 - 3.376) | < 0.001 | 1.830 (1.142 - 2.932) | 0.012 |
| BMI | 336 | | | | |
| <= 25 | 177 | Reference | | | |
| > 25 | 159 | 0.798 (0.550 - 1.158) | 0.235 | | |
| Age | 373 | | | | |
| <= 60 | 177 | Reference | | | |
| > 60 | 196 | 1.205 (0.850 - 1.708) | 0.295 | | |
| Pathologic stage | 349 | | | | |
| Stage I | 173 | Reference | | Reference | |
| Stage II&Stage III&Stage IV | 176 | 2.090 (1.429 - 3.055) | < 0.001 | 1.586 (0.867 - 2.901) | 0.134 |
| BEND3 | 373 | | | | |
| Low | 187 | Reference | | Reference | |
| High | 186 | 1.478 (1.045 - 2.090) | 0.027 | 1.599 (1.012 - 2.526) | 0.044 |

Bold values indicate statistical significance at $p < 0.05$.

Supplementary Table S2G. MESO

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|--------------------|----------|-----------------------|---------|-----------------------|---------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Pathologic T stage | 84 | | | | |
| T1 | 14 | Reference | | | |
| T2 | 25 | 0.977 (0.470 - 2.032) | 0.950 | | |
| T3 | 32 | 1.056 (0.519 - 2.149) | 0.880 | | |
| T4 | 13 | 0.775 (0.327 - 1.838) | 0.563 | | |
| Pathologic M stage | 60 | | | | |
| M0 | 57 | Reference | | | |
| M1 | 3 | 1.856 (0.441 - 7.817) | 0.399 | | |
| Pathologic stage | 86 | | | | |
| Stage I&Stage II | 26 | Reference | | | |
| Stage III&Stage IV | 60 | 0.993 (0.588 - 1.675) | 0.978 | | |
| Sex | 86 | | | | |
| Female | 16 | Reference | | | |
| Male | 70 | 0.888 (0.494 - 1.595) | 0.691 | | |
| Age | 86 | | | | |
| <= 65 | 46 | Reference | | | |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|---------------------------|----------|------------------------|--------------|------------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| > 65 | 40 | 1.325 (0.826 - 2.125) | 0.243 | | |
| Histological type | 86 | | | | |
| Biphasic | 23 | Reference | | Reference | |
| Diffuse malignant | 5 | 0.575 (0.215 - 1.540) | 0.271 | 0.425 (0.155 - 1.163) | 0.096 |
| Epithelioid | 57 | 0.497 (0.293 - 0.842) | 0.009 | 0.545 (0.321 - 0.926) | 0.025 |
| Sarcomatoid | 1 | 3.418 (0.438 - 26.654) | 0.241 | 5.625 (0.697 - 45.410) | 0.105 |
| Residual tumor | 35 | | | | |
| R0 | 17 | Reference | | | |
| R1&R2 | 18 | 1.086 (0.522 - 2.259) | 0.824 | | |
| History asbestos exposure | 69 | | | | |
| No | 14 | Reference | | | |
| Yes | 55 | 0.988 (0.520 - 1.879) | 0.972 | | |
| Radiation therapy | 85 | | | | |
| No | 60 | Reference | | | |
| Yes | 25 | 0.682 (0.403 - 1.155) | 0.155 | | |
| BEND3 | 86 | | | | |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|-----------------|----------|-----------------------|--------------|-----------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Low | 42 | Reference | | Reference | |
| High | 44 | 2.088 (1.286 - 3.389) | 0.003 | 2.169 (1.306 - 3.600) | 0.003 |

Bold values indicate statistical significance at $p < 0.05$.

Supplementary Table S2H. SARC

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|-------------------|----------|-----------------------|--------------|-----------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Margin status | 213 | | | | |
| Negative | 139 | Reference | | Reference | |
| Positive | 74 | 1.957 (1.215 - 3.151) | 0.006 | 2.102 (1.209 - 3.655) | 0.008 |
| Tumor depth | 209 | | | | |
| Superficial | 21 | Reference | | Reference | |
| Deep | 188 | 2.888 (0.910 - 9.168) | 0.072 | 2.259 (0.534 - 9.550) | 0.268 |
| Radiation therapy | 257 | | | | |
| No | 179 | Reference | | | |
| Yes | 78 | 0.864 (0.557 - 1.339) | 0.513 | | |
| Sex | 263 | | | | |
| Female | 144 | Reference | | | |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|-----------------|----------|-----------------------|--------------|-----------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Male | 119 | 0.905 (0.607 - 1.349) | 0.623 | | |
| Age | 263 | | | | |
| <= 60 | 130 | Reference | | | |
| > 60 | 133 | 1.285 (0.864 - 1.911) | 0.216 | | |
| BEND3 | 263 | | | | |
| Low | 131 | Reference | | Reference | |
| High | 132 | 1.509 (1.008 - 2.260) | 0.045 | 1.875 (1.066 - 3.301) | 0.029 |

Bold values indicate statistical significance at $p < 0.05$.

Supplementary Table S2I. SKCM

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|--------------------|----------|-----------------------|-------------------|-----------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Pathologic T stage | 362 | | | | |
| T1 | 42 | Reference | | Reference | |
| T2 | 77 | 1.523 (0.826 - 2.806) | 0.178 | 1.722 (0.875 - 3.388) | 0.116 |
| T3 | 90 | 2.135 (1.179 - 3.867) | 0.012 | 1.832 (0.909 - 3.694) | 0.091 |
| T4 | 153 | 3.780 (2.109 - 6.776) | < 0.001 | 3.069 (1.312 - 7.181) | 0.010 |
| Pathologic N stage | 403 | | | | |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|--------------------|----------|-----------------------|-------------------|-----------------------|-------------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| N0 | 225 | Reference | | Reference | |
| N1 | 73 | 1.503 (1.018 - 2.220) | 0.040 | 1.620 (1.043 - 2.515) | 0.032 |
| N2 | 49 | 1.540 (0.977 - 2.429) | 0.063 | 2.117 (1.212 - 3.699) | 0.008 |
| N3 | 56 | 2.744 (1.777 - 4.236) | < 0.001 | 4.181 (2.442 - 7.157) | < 0.001 |
| Pathologic M stage | 431 | | | | |
| M0 | 407 | Reference | | Reference | |
| M1 | 24 | 1.902 (1.032 - 3.506) | 0.039 | 1.414 (0.546 - 3.663) | 0.475 |
| Breslow depth | 356 | | | | |
| <= 3 | 181 | Reference | | Reference | |
| > 3 | 175 | 2.665 (1.948 - 3.644) | < 0.001 | 1.543 (0.866 - 2.748) | 0.141 |
| BEND3 | 457 | | | | |
| Low | 228 | Reference | | Reference | |
| High | 229 | 1.384 (1.054 - 1.818) | 0.019 | 1.326 (0.951 - 1.850) | 0.096 |

Bold values indicate statistical significance at $p < 0.05$.

Supplementary Table S2J. STAD

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|-----------------|----------|-----------------------|---------|-----------------------|---------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|--------------------|----------|-----------------------|-------------------|-----------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Pathologic T stage | 362 | | | | |
| T1&T2 | 96 | Reference | | Reference | |
| T3&T4 | 266 | 1.719 (1.131 - 2.612) | 0.011 | 1.391 (0.877 - 2.208) | 0.161 |
| Pathologic N stage | 352 | | | | |
| N0 | 107 | Reference | | Reference | |
| N1 | 97 | 1.629 (1.001 - 2.649) | 0.049 | 1.364 (0.809 - 2.300) | 0.244 |
| N2 | 74 | 1.655 (0.979 - 2.797) | 0.060 | 1.506 (0.872 - 2.601) | 0.142 |
| N3 | 74 | 2.709 (1.669 - 4.396) | < 0.001 | 2.303 (1.371 - 3.869) | 0.002 |
| Pathologic M stage | 352 | | | | |
| M0 | 327 | Reference | | Reference | |
| M1 | 25 | 2.254 (1.295 - 3.924) | 0.004 | 2.031 (1.142 - 3.611) | 0.016 |
| Histologic grade | 361 | | | | |
| G1 | 10 | Reference | | | |
| G2 | 134 | 1.648 (0.400 - 6.787) | 0.489 | | |
| G3 | 217 | 2.174 (0.535 - 8.832) | 0.278 | | |
| Sex | 370 | | | | |

| Characteristics | Total(N) | Univariate analysis | | Multivariate analysis | |
|-----------------|----------|-----------------------|--------------|-----------------------|--------------|
| | | Hazard ratio (95% CI) | P value | Hazard ratio (95% CI) | P value |
| Female | 133 | Reference | | | |
| Male | 237 | 1.267 (0.891 - 1.804) | 0.188 | | |
| BEND3 | 370 | | | | |
| Low | 185 | Reference | | Reference | |
| High | 185 | 1.395 (1.001 - 1.943) | 0.049 | 1.469 (1.033 - 2.088) | 0.032 |

Bold values indicate statistical significance at $p < 0.05$.

Supplementary Table S3. List of the top 50 genes associated with BEND3

| Gene Symbol | Gene ID | PCC |
|-------------|-----------------|-------|
| CHRD | ENSP00000204604 | 0.172 |
| CERK | ENSP00000216264 | 0.163 |
| DDX39A | ENSP00000242776 | 0.292 |
| H4C6 | ENSP00000244537 | 0.292 |
| SP110 | ENSP00000258381 | 0.163 |
| TRIM37 | ENSP00000262294 | 0.166 |
| TRAF4 | ENSP00000262395 | 0.202 |
| FAM160A2 | ENSP00000265978 | 0.166 |
| RIOK2 | ENSP00000283109 | 0.237 |
| SMARCA5 | ENSP00000283131 | 0.292 |
| FAM81A | ENSP00000288228 | 0.166 |
| POC1A | ENSP00000296484 | 0.162 |
| VIRMA | ENSP00000297591 | 0.292 |
| NOL6 | ENSP00000297990 | 0.164 |
| PIWIL4 | ENSP00000299001 | 0.174 |
| RNF169 | ENSP00000299563 | 0.292 |
| SLFN5 | ENSP00000299977 | 0.164 |

| | | |
|----------|-----------------|-------|
| MORN4 | ENSP00000307636 | 0.308 |
| RRP7A | ENSP00000321449 | 0.164 |
| DENND5A | ENSP00000328524 | 0.166 |
| ERCC6L | ENSP00000334675 | 0.9 |
| RBPJ | ENSP00000345206 | 0.164 |
| DPY30 | ENSP00000345837 | 0.161 |
| SMARCAD1 | ENSP00000351947 | 0.295 |
| USP21 | ENSP00000356981 | 0.42 |
| MKI67 | ENSP00000357643 | 0.292 |
| HDAC1 | ENSP00000362649 | 0.225 |
| FOXP3 | ENSP00000365380 | 0.167 |
| MDC1 | ENSP00000365588 | 0.439 |
| MAP7D2 | ENSP00000368964 | 0.241 |
| SUMO1 | ENSP00000376077 | 0.292 |
| CIT | ENSP00000376306 | 0.292 |
| ZNF785 | ENSP00000378642 | 0.242 |
| TRPS1 | ENSP00000379065 | 0.303 |
| TULP3 | ENSP00000380321 | 0.292 |
| GATAD2A | ENSP00000384899 | 0.165 |
| NFATC1 | ENSP00000389377 | 0.166 |
| HSBP1 | ENSP00000392896 | 0.164 |
| KANSL3 | ENSP00000396749 | 0.164 |
| TNIK | ENSP00000399511 | 0.411 |
| SUMO3 | ENSP00000409666 | 0.292 |
| CFAP97 | ENSP00000409964 | 0.166 |
| CPSF1 | ENSP00000484669 | 0.241 |
| HDAC2 | ENSP00000430432 | 0.195 |
| YTHDC1 | ENSP00000463982 | 0.292 |
| CHD4 | ENSP00000440542 | 0.292 |
| ZFHX3 | ENSP00000493252 | 0.423 |
| BAZ2A | ENSP00000446880 | 0.292 |

Supplementary Table S4. GO terms and KEGG pathways enriched in the analysis

| ONTOLOGY | Description | GeneRatio | pvalue | p.adjust | qvalue |
|----------|---|-----------|-------------|-------------|-------------|
| BP | histone modification | 13/47 | 1.51512E-10 | 1.67724E-07 | 1.3684E-07 |
| BP | chromatin remodeling | 9/47 | 1.69132E-08 | 4.68071E-06 | 3.81881E-06 |
| BP | protein deacetylation | 7/47 | 1.63851E-08 | 4.68071E-06 | 3.81881E-06 |
| BP | methylation | 7/47 | 3.82184E-05 | 0.003846157 | 0.003137929 |
| BP | peptidyl-lysine modification | 7/47 | 4.97661E-05 | 0.004237778 | 0.003457437 |
| CC | transcription regulator complex | 7/46 | 0.000123308 | 0.0017109 | 0.001119508 |
| CC | nuclear chromosome | 6/46 | 1.47556E-05 | 0.000327575 | 0.000214345 |
| CC | heterochromatin | 4/46 | 2.05535E-05 | 0.000380239 | 0.000248805 |
| CC | histone deacetylase complex | 4/46 | 2.4334E-05 | 0.000385868 | 0.000252488 |
| CC | methyltransferase complex | 3/46 | 0.00131389 | 0.008578929 | 0.005613524 |
| MF | DNA-binding transcription factor binding | 7/45 | 0.000132452 | 0.001694798 | 0.001102835 |
| MF | ATP-dependent activity, acting on DNA | 4/45 | 0.000115421 | 0.001694798 | 0.001102835 |
| MF | histone deacetylase binding | 4/45 | 0.00025083 | 0.002380089 | 0.001548766 |
| MF | ubiquitin-like protein ligase binding | 4/45 | 0.007377383 | 0.028982575 | 0.018859475 |
| MF | NF-kappaB binding | 3/45 | 5.84743E-05 | 0.001286435 | 0.000837106 |
| KEGG | Viral carcinogenesis | 5/21 | 0.000136181 | 0.006945232 | 0.004873847 |
| KEGG | Notch signaling pathway | 3/21 | 0.000434718 | 0.011085318 | 0.00777917 |
| KEGG | Ribosome biogenesis in eukaryotes | 3/21 | 0.002584532 | 0.043937044 | 0.030833014 |
| KEGG | Th1 and Th2 cell differentiation | 2/21 | 0.022954994 | 0.097558726 | 0.068462264 |