## Supplementary



Figure S1 Study flow chart for our analysis.


Figure S2 Establishment of the risk signature integrating the mutated genes. (A,B) OS; (C,D) PFS. The coefficients estimated by the Lasso regression method are presented. Each curve in the ( $\mathrm{A}, \mathrm{C}$ ) represents the path of a lasso coefficient against the L1-norm (the penalty term for lasso) when $\lambda$ changes. A coefficient that becomes non-zero when $\lambda$ changes enters the LASSO regression model. (B,D) The coefficients estimated by the Lasso regression method are presented. OS, overall survival; PFS, progression free survival; LASSO, least absolute shrinkage and selection operator.

Table S1 Gene mutation type, frequency and risk score formula included in the analysis

| Genes | Point mutation | Splice site | Total | Frequency (\%) | Coefficient (OS risk score) | Coefficient (PFS risk score) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ADCY8 | 19 | 0 | 19 | 6.1 | -0.35 | - |
| ALK | 5 | 0 | 5 | 1.6 | 0.07 | 0.27 |
| ARID1A | 12 | 4 | 16 | 5.1 | 0.13 | -0.48 |
| CDK8 | 6 | 0 | 6 | 1.9 | 0.26 | 0.58 |
| DICER1 | 14 | 1 | 15 | 4.8 | -0.25 | - |
| EPC1 | 5 | 0 | 5 | 1.6 | 0.027 | - |
| ERBB2 | 7 | 0 | 7 | 2.2 | 0.07 | - |
| MED12 | 11 | 0 | 11 | 3.5 | 0.11 | - |
| TSC1 | 8 | 0 | 8 | 2.6 | 0.43 | - |
| MAP3K13 | 10 | 0 | 10 | 3.2 | - | -0.91 |
| BAP1 | 3 | 2 | 5 | 1.6 | - | -0.75 |
| NCOR1 | 12 | 0 | 12 | 3.8 | - | -0.21 |
| TSHR | 9 | 0 | 9 | 2.9 | - | -0.17 |
| CS | 4 | 0 | 4 | 1.3 | - | -0.17 |
| PMS1 | 3 | 0 | 3 | 1.0 | - | 0.036 |
| MSH2 | 4 | 0 | 4 | 1.3 | - | 0.043 |
| BCR | 11 | 0 | 11 | 3.5 | - | 0.095 |
| MLL2 | 58 | 14 | 72 | 23.1 | - | 0.14 |
| EPC1 | 5 | 0 | 5 | 1.6 | - | 0.19 |
| PMS2 | 5 | 0 | 5 | 1.6 | - | 0.20 |
| LAMA2 | 22 | 0 | 22 | 7.1 | - | 0.22 |
| AP3B2 | 6 | 0 | 6 | 1.9 | - | 0.30 |
| PTCH1 | 11 | 6 | 17 | 5.4 | - | 0.34 |
| ERCC5 | 7 | 0 | 7 | 2.2 | - | 0.42 |
| FANCF | 5 | 0 | 5 | 1.6 | - | 0.44 |
| PIK3CA | 21 | 1 | 22 | 7.1 | - | 0.47 |
| PDZRN4 | 7 | 0 | 7 | 2.2 | - | 0.56 |

Risk score $=$ sum up genes (coefficient*0/1); mutation $=1$, wild type $=0$. For example: OS risk score $=-0.35^{*}$ ADCY8 $+0.07^{\star}$ ALK $+\ldots$ $+0.43^{*}$ TSC1 .

Table S2 Cutoff values based on X-title in OS and PFS analysis

|  | Overall survival (OS) |  |  |  |  | Progression free survival (PFS) |  |  |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Pt No. | Events | Range |  | Pt No. | Events | Range |  |
| Low risk | 38 | 13 | -0.38 thru -0.13 |  | 207 | 117 | -0.91 thru 0.00 |  |
| High risk | 274 | 155 | 0 thru 0.46 |  | 105 | 78 | 0.04 thru 1.19 |  |
| Chi-Square |  | 9.15 |  |  | 30.44 |  |  |  |
| P value |  | 0.002 |  |  | $<0.001$ |  |  |  |



Figure S3 Verification of the risk model in the public database. (A) Comparison of survival curves of high-risk and low-risk groups in ICGC data. (B) Risk score model verified in TCGA data. ICGC, International Cancer Genome Consortium; TCGA, The Cancer Genome Atlas.

Table S3 Difference of gene expression in prediction model

| Tag | logFold change | t | P.Value | adj.P.Value |
| :---: | :---: | :---: | :---: | :---: |
| MSH2 | 0.955421434 | 12.973787 | $3.55 \mathrm{E}-27$ | 9.23E-26 |
| PDZRN4 | -2.797635282 | -12.703337 | $2.29 \mathrm{E}-26$ | $2.97 \mathrm{E}-25$ |
| PMS2 | 0.577708425 | 9.8023191 | $2.97 \mathrm{E}-18$ | $2.58 \mathrm{E}-17$ |
| MAP3K13 | 0.683298236 | 8.47407183 | $1.10 \mathrm{E}-14$ | 7.17E-14 |
| PIK3CA | 0.546798828 | 8.04385861 | $1.44 \mathrm{E}-13$ | 7.49E-13 |
| ERBB2 | -0.940390979 | -6.5502086 | $6.60 \mathrm{E}-10$ | $2.86 \mathrm{E}-09$ |
| LAMA2 | -0.921598582 | -6.2652714 | $2.97 \mathrm{E}-09$ | $1.10 \mathrm{E}-08$ |
| EPC1 | -0.277881644 | -4.8392592 | $2.91 \mathrm{E}-06$ | $9.47 \mathrm{E}-06$ |
| PMS1 | 0.305496453 | 4.63025238 | $7.24 \mathrm{E}-06$ | $1.93 \mathrm{E}-05$ |
| CDK8 | -0.234367933 | -4.6243013 | $7.43 \mathrm{E}-06$ | 1.93E-05 |
| ALK | -0.590100126 | -3.9464695 | 0.000116 | 0.00027418 |
| FANCF | 0.3410801 | 3.89951657 | 0.00013869 | 0.00030049 |
| AP3B2 | 0.705142481 | 3.65231723 | 0.00034605 | 0.00069211 |
| ERCC5 | -0.21241243 | -3.4774067 | 0.00064328 | 0.00119466 |
| PTCH1 | 0.383879766 | 2.837049 | 0.0051087 | 0.00874771 |
| TSHR | 0.419768959 | 2.81949044 | 0.00538321 | 0.00874771 |
| CS | -0.141265076 | -2.4226395 | 0.01646118 | 0.02517592 |
| NCOR1 | -0.077996044 | -1.9835203 | 0.04892388 | 0.07066783 |
| ARID1A | 0.09669169 | 1.77274301 | 0.0780671 | 0.10682867 |
| MED12 | 0.076218753 | 1.32440151 | 0.18715238 | 0.24329809 |
| ADCY8 | 0.390736396 | 0.88031764 | 0.38176388 | 0.4511755 |
| DICER1 | -0.051965895 | -1.1366515 | 0.25728809 | 0.31854716 |
| BAP1 | 0.048765511 | 0.75285616 | 0.45258049 | 0.51161272 |
| TSC1 | -0.023436271 | -0.5002885 | 0.61752071 | 0.66898077 |
| BCR | -0.037372671 | -0.4154559 | 0.67833352 | 0.70546686 |
| MLL2 | -0.018561492 | -0.3088409 | 0.75782179 | 0.75782179 |



Figure S4 The expression of genes in PFS prediction model. PFS, progression free survival.


Figure S5 ROC plots of the Lasso regression model. (A) Comparison of the prognostic value for the gene-mutation-based model and TNM stage in OS; (B) comparison of the prognostic value for the gene-mutation-based model and TNM stage in OS for ICGC data; (C) comparison of the prognostic value for the gene-mutation-based model and TNM stage in PFS. The green dashed line represents the ROC curve of the gene mutation model. The blue line represents the ROC curve of TNM stage. The red line represents the combination of the gene mutation model and TNM stage. ROC, Receiver Operating Characteristic; OS, overall survival; PFS, progression free survival; ICGC, International Cancer Genome Consortium.

