

**Supplementary Figure1.** **Comparison of molecular structures between curcumin and L48H37.** (A) The molecular structure of curcumin and L48H37. (B) The three-dimensional structure of curcumin and L48H37.



**Supplementary Figure2. SiRNA knockdown of the ATF-4 gene in SW1990 and Aspc-1 cell lines.** (A-B) ATF4 mRNA and protein levels in SW1990 and ASPC-1 cells transfected with control or ATF4-targeting siRNA. Data were expressed as mean±SEM. A: bP <0.01 vs siCTRL group. B: aP <0.05 vs siCTRL group. bP<0.01 vs siCTRL group.



**Supplementary Figure3. The basal level of KMT2D in pancreatic cancer cell lines and lentivirus-mediated KMT2D-shRNA or Control-shRNA in SW1990 and Aspc-1 cells.** (A) Basal level of KMT2D mRNA in SW1990, MIA PaCa2, ASPC-1 and PANC-1 cells. Data were expressed as mean±SEM. bP <0.01 vs SW1990 group. cP <0.05 vs MIA PaCa-2 group. fP <0.01 vs Aspc-1 group. (B-C) KMT2D mRNA and protein levels in control and KMT2D-knockdown SW1990 and ASPC-1 cells. Data were expressed as mean±SEM. bP <0.01 vs shCTRL group.



**Supplementary Figure4.** (A) The heat map of the top 200 DEGs between the normal and KMT2D-silenced PDAC cell lines; red indicates up-regulation and blue indicates down-regulation. (B) Pearson correlation analysis of the relationship between KMT2D methylation degree and KMT2D mRNA expression levels conducted using program R. (C) Pearson correlation analysis of the relationship between KMT2D methylation degree and the methylated sites.

**TableS1** Correlation analysis between KMT2D gene expression and clinicopathological features of patients with PDAC

| Parameters | No. | KMT2D expression  High（％） Low（％） | |  | P |
| --- | --- | --- | --- | --- | --- |
| **Age(years)**  ≤60  >60 | 33  73 | 16(48.5)  37(50.7) | 17(51.5)  36(49.3) | 0.044 | 0.834 |
| **Gender**  Male  Female | 60  46 | 34(56.7)  19(41.3) | 26(43.3)  27(58.7) | 2.458 | 0.117 |
| **Grade**  G1  G2  G3/G4 | 11  61  34 | 6(54.5)  24(39.3)  23(67.6) | 5(45.5)  37(60.7)  11(32.4) | 7.097 | 0.029\* |
| **T stage**  T1/T2  T3/T4 | 17  89 | 7 (41.2)  46(51.7) | 10(58.8)  43(48.3) | 0.631 | 0.427 |
| **N stage**  N0 | 26 | 10(38.5) | 16(61.5) | 1.835 | 0.176 |
| N1/X | 80 | 43(53.8) | 37(46.3) |  |  |
| **M stage**  M0 | 60 | 31(51.7) | 29(48.3) | 0.154 | 0.695 |
| M1/X | 46 | 22(47.8) | 24(52.2) |  |  |
| **AJCC stage**  Stage I  Stage II | 10  93 | 3(30.0)  48(51.6) | 7(70.0)  45(48.4) | 2.042 | 0.484 |
| Stage III | 3 | 2(66.7) | 1(33.3) |  |  |
| **Location** |  |  |  |  |  |
| Head  Body  Tail  Other | 87  7  8  4 | 45(51.7)  2(28.6)  4(50.0)  2(50.0) | 42(48.3)  5(71.4)  4(50.0)  2(50.0) | 1.507 | 0.762 |
| **Surgical margin** |  |  |  |  |  |
| R0  R1/2/X | 65  41 | 35(53.8)  18(43.9) | 30(46.2)  23(56.1) | 0.994 | 0.319 |
| **Alcohol consumption**  No | 33 | 14(42.4) | 19(57.6) | 1.100 | 0.294 |
| Yes | 73 | 39(53.4) | 34(46.6) |  |  |
| **History of diabetes** |  |  |  |  |  |
| No  Yes | 75  31 | 34(45.3)  19(61.3) | 41(54.7)  12(38.7) | 2.234 | 0.135 |
| **History of chronic pancreatitis** |  |  |  |  |  |
| No  Yes | 96  10 | 48(50.0)  5(50.0) | 48(50.0)  5(50.0) | 0.000 | 1.000\* |
| **History of malignant tumor** |  |  |  |  |  |
| No  Yes | 96  10 | 46(47.9)  7(70.0) | 50(52.1)  3(30.0) | 1.767 | 0.184 |

\*P<0.05