Supplementary Fig. 1

Expression profiles of circRNA in hypoxia-induced PC cells.

a QRT-PCR confirmed the expression of top 10 upregulated circRNAs under hypoxia in MIA PaCa-2 cells. b QRT-PCR analysis of the relative expression of circRNF13 in PC cells compared with normal pancreatic ductal epithelial cells (HPDE6-c7). c IHC analysis of circRNF13 expression in PC tissues of T, N, M and AJCC stages. Data represent at least three independent experiments and present as means ± SD. *P < 0.05, **P < 0.01.

Supplementary Fig. 2
**CircRNF13 is hypoxia-inducible.**

a QRT-PCR analysis of circRNF13 level in SW-1990 cells under hypoxia. b QRT-PCR analysis of circRNF13 level after HIF-1α knockdown. Data represent at least three independent experiments and present as means ± SD. *P < 0.05, **P < 0.01.

**Supplementary Fig. 3**

a CircRNF13 overexpression and knockdown efficiency was determined by qRT-PCR. b Ki-67 and CD31 expression in tumor tissues of circRNF13 knockdown group and control group (scale bar: 100 μm, magnification: 200 x). Data represent at least three independent experiments and present as means ± SD. ***P < 0.001.
Supplementary Fig. 4

CircRNF13 promotes PC metastasis in vivo.

a, c Representative bioluminescence images of mice 8 weeks after tail vein injection of SW-1990/circRNF13 and MIA PaCa-2/sh-circRNF13 cells. b, d Representative images of metastatic nodes in the lungs and HE staining of the lung tissues of respective groups. e, f Representative liver images and HE staining of the liver tissues of respective groups. Data represent at least three
independent experiments and present as means ± SD. *P < 0.05, **P < 0.01.

Supplementary Fig. 5

CircRNF13 silence suppresses the tumor-promoting effects of
hypoxia in PC cells.

a Colony formation assay was used to analyze the effect of circRNF13 silence on the hypoxia induced cell proliferation. b, c Transwell and wound healing assays were conducted to detect the migration and invasion abilities. d, e ECAR after glucose (GLU) treatment indicated the glycolysis rate. ECAR after oligomycin (OLI) treatment indicated glycolytic capacity. f, g OCR before oligomycin treatment indicated basal respiration. OCR after FCCP treatment indicated maximum respiration capacity. Data represent at least three independent experiments and present as means ± SD. *P < 0.05, **P < 0.01.

Supplementary Fig. 6

CircRNF13 promotes PC cell progression by sponging miR-654-3p.
a Cell invasion ability was detected in circRNF13 overexpressing SW-1990 cells transfected with miR-654-3p mimics or mimics NC. b Cell proliferation ability was determined in circRNF13 knockdown MIA PaCa-2 cells transfected with miR-654-3p inhibitor or inhibitor NC. Data represent at least three independent experiments and present as means ± SD. *P < 0.05, **P < 0.01.
CircRNF13 accelerates the PC malignant process through PDK3.

a Knockdown of PDK3 impaired cell migration ability in SW-1990 cells (scale
bar: 20 μm). b Knockdown of PDK3 impaired tube formation ability. c ECAR and OCR in SW-1990 cells were measured by the Seahorse XF96 extracellular Flux analyzer. d Cell colony formation ability of circRNF13-overexpressing SW-1990 cells transfected with PDK3 siRNAs or their corresponding controls. e Representative images of the cell migration ability of circRNF13-overexpressing SW-1990 cells transfected with PDK3 siRNAs or their corresponding control (scale bar: 20 μm). f Cell invasion ability of circRNF13-overexpressing SW-1990 cells transfected with PDK3 siRNAs or their corresponding control (scale bar: 100 μm). g Representative IHC images of PDK3 expression in T2 vs T4, N0 vs N1 and AJJC IIA vs IV. Data represent at least three independent experiments and present as means ± SD. *P < 0.05, **P < 0.01.
**Supplementary Table 1.** The relationship of circRNF13 and clinicopathologic parameters in 90 PC patients

| Variables          | No.  | circRNF13 expression |
|--------------------|------|----------------------|
|                    | (n=90) | high (n=62) | low (n=28) | P       |
| Gender             |       |               |           |
| Male               | 58    | 38            | 20        | 0.352   |
| Female             | 32    | 24            | 8         |         |
| Age (years)        |       |               |           |
| ≤60                | 40    | 25            | 15        | 0.242   |
| >60                | 50    | 37            | 13        |         |
| Pathologic grade   |       |               |           |
| Low                | 33    | 22            | 11        | 0.729   |
| Middle-High        | 57    | 40            | 17        |         |
| T stage            |       |               |           |
| T1-T2              | 51    | 28            | 23        | **0.001** |
| T3-T4              | 39    | 34            | 5         |         |
| N stage            |       |               |           |
| N0                 | 43    | 21            | 22        | < **0.0001** |
| N1-N2              | 47    | 41            | 6         |         |
| M stage            |       |               |           |
| M0                 | 73    | 46            | 27        | **0.01** |
| M1                 | 17    | 16            | 1         |         |
| AJCC stage         |       |               |           |
| 0-IIA              | 36    | 15            | 21        | < **0.0001** |
| IIB-IV             | 54    | 47            | 7         |         |
**Supplementary Table 2.** The relationship of PDK3 and clinicopathologic parameters in 90 PC patients

| Variables                | No. PDK3 expression |  |  |  |  |
|--------------------------|---------------------|---|---|---|---|
|                          | (n=90)              | high | low | P  |
|                          | (n=67)              | (n=23) |     |   |
| Gender                   |                     |     |     |   |   |
| Male                     | 58                  | 40  | 18  | 0.108 |
| Female                   | 32                  | 27  | 5   |     |
| Age (years)              |                     |     |     |   |   |
| ≤60                      | 40                  | 28  | 12  | 0.387 |
| >60                      | 50                  | 39  | 11  |     |
| Pathologic grade         |                     |     |     |   |   |
| Low                      | 33                  | 22  | 11  | 0.198 |
| Middle-High              | 57                  | 45  | 12  |     |
| T stage                  |                     |     |     |   |   |
| T1-T2                    | 51                  | 32  | 19  | **0.004** |
| T3-T4                    | 39                  | 35  | 4   |     |
| N stage                  |                     |     |     |   |   |
| N0                       | 43                  | 25  | 18  | **0.0007** |
| N1-N2                    | 47                  | 42  | 5   |     |
| M stage                  |                     |     |     |   |   |
| M0                       | 73                  | 52  | 21  | 0.2193 |
| M1                       | 17                  | 15  | 2   |     |
| AJCC stage               |                     |     |     |   |   |
| 0-IIA                    | 36                  | 21  | 15  | **0.0042** |
| IIB-IV                   | 54                  | 46  | 8   |     |