

**Supplement 1. Demographic characteristics of patients with papillary thyroid carcinoma.**

Characteristics	Number (%)
Age (years)	
Mean at diagnosis (range)	49.58 ± 11.08 (24–74)
<55	133 (64.9)
≥55	72 (35.1)
Sex	
Female	162 (79.0)
Male	43 (21.0)
Tumor size (mm)	
Mean (range)	6.6 ± 2.1 (1–10)
<5 mm	38 (18.5)
≥5 mm	167 (81.5)
Tumor extension	
Confinement to thyroid parenchyma	126 (61.5)
Extrathyroid extension	79 (38.5)
Cervical lymph node metastasis	
Absent	145 (70.7)
Present	60 (29.3)
Resection margin	
Clear	184 (89.8)
Closed	7 (3.4)
Involved	14 (6.8)
Sirt4 expression	
Negative	86 (42.0)
Positive	119 (58.0)

**Supplement 2. Sirt4 inhibits cell proliferation in TPC-1 (A-C) and SNU-790 (D-F) cells.**

(A) Expression levels of sirtuins in TPC-1 cells. (B) CCK-8 assay and (C) clonogenic assay of Sirt4-overexpressing and shSirt4-transfected TPC-1 cells compared with the controls. (D) Expression levels of sirtuins in SNU-790 cells. (E) CCK-8 assay and (F) clonogenic assay of Sirt4-overexpressing and shSirt4-transfected SNU-790 cells compared with the controls.

CCK-8, Cell Counting Kit-8.

**Supplement 3. Sirt4 promote cell apoptosis by modulating ROS levels in TPC-1 (A-D) and SNU-790 (E-H) cells.**

(A,B) The percentage of apoptotic cells in Sirt4-upregulated and -downregulated TPC-1 cells. (C) Differences in total ROS levels upon regulation of Sirt4 expression. (D) Changes in MitoSox Red levels and the intensity of MTDR by regulating Sirt4 expression in TPC-1 cells. (E-H) These findings were consistent with results from SNU-790 cells.

**Supplement 4. Sirt4 regulates the invasion and migration of TPC-1 and SNU-790 cells.**

(A-D) Results of invasion, migration, and wound healing assays of Sirt4-upregulation and downregulation in TPC-1 cells compared with the controls. (E-H) These results were consistent with results from SNU-790 cells. (I) Modulation of EMT-related proteins by Sirt4 expression in three human thyroid cancer cell lines, B-CPAP, TPC-1, and SNU-790.

**Supplement 5. Uncropped western blots cited in Figures and Supplement figures.**