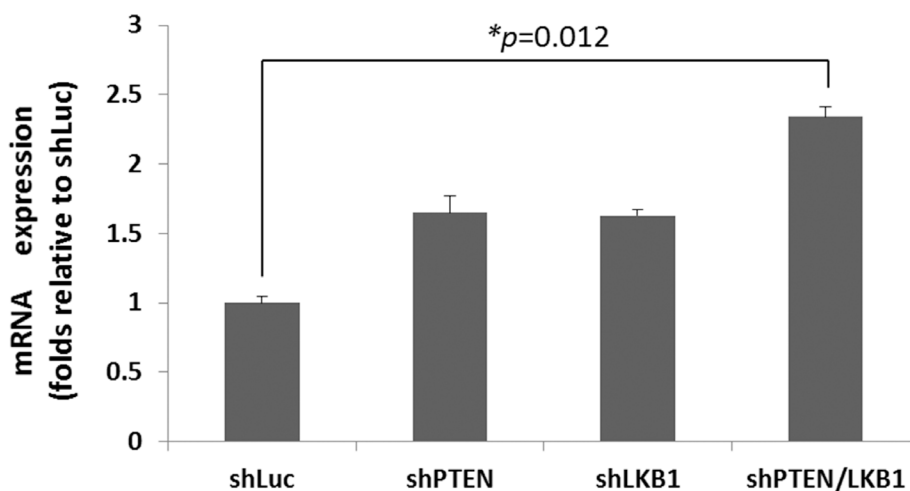


The regulatory role of aberrant Phosphatase and Tensin Homologue and Liver Kinase B1 on AKT/mTOR/c-Myc axis in pancreatic neuroendocrine tumors

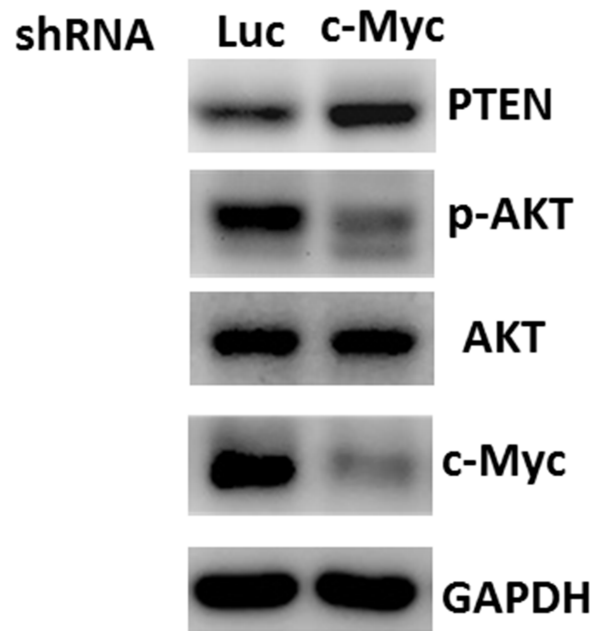
SUPPLEMENTARY MATERIALS



*, QGP-1/shLuc vs QGP-1/shPTEN/LKB1, $P=0.012$

Supplementary Figure 1: The mRNA expression of QGP-1/shLuc, QGP-1/shPTEN, QGP-1 shLKB1 and QGP-1/shPTEN/LKB1.

QGP-1



Supplementary Figure 2: The Protein expression of PTEN, AKT, c-Myc and phosphorylated AKT in QGP-1 cells with or without knockdown of c-Myc

Supplementary Table 1: The demographics and expression status of PTEN, LKB1, and c-Myc in pNET patients

| Case No. | Sex | Age | Grade | Stage | PTEN | LKB1 | c-Myc | Survival |
|----------|-----|-----|-------|-------|----------|--------|---------|----------|
| 1 | F | 80 | 2 | IB | C*, 1+ | C*, 1+ | N**, 2+ | alive |
| 2 | M | 53 | 1 | IA | C, 1+ | C, 2+ | N, 2+ | dead |
| 3 | M | 45 | 2 | IV | C, 1+ | C, 2+ | N, 2+ | alive |
| 4 | M | 67 | 1 | IA | C, 1+ | C, 2+ | N, 2+ | alive |
| 5 | M | 52 | 2 | IV | C, 2+ | C, 3+ | N, 2+ | alive |
| 6 | M | 54 | 1 | IV | C, 2+ | C, 2+ | N, 2+ | alive |
| 7 | F | 47 | 1 | IA | C, 1+ | C, 1+ | N, 1+ | alive |
| 8 | M | 71 | 1 | IIB | C, 1+ | C, 2+ | N, 2+ | alive |
| 9 | M | 42 | 2 | IV | Negative | C, 1+ | N, 2+ | alive |
| 10 | M | 34 | 2 | IV | C, 1+ | C, 2+ | N, 3+ | alive |
| 11 | M | 61 | 2 | IV | C, 3+ | C, 3+ | N, 3+ | alive |
| 12 | F | 62 | 1 | IV | C, 1+ | C, 2+ | N, 2+ | alive |
| 13 | M | 45 | 1 | IB | C, 2+ | C, 3+ | N, 1+ | alive |
| 14 | F | 54 | 1 | IB | C, 2+ | C, 3+ | N, 2+ | alive |
| 15 | M | 48 | 1 | IB | C, 2+ | C, 3+ | N, 3+ | dead |
| 16 | F | 73 | 1 | IIA | C, 2+ | C, 1+ | N, 1+ | alive |
| 17 | M | 73 | 1 | IA | C, 1+ | C, 1+ | N, 3+ | alive |
| 18 | M | 21 | 2 | IA | C, 3+ | C, 3+ | N, 3+ | alive |
| 19 | F | 62 | 1 | IA | C, 3+ | C, 3+ | N, 2+ | alive |
| 20 | F | 39 | 1 | IA | C, 3+ | C, 3+ | N, 2+ | alive |
| 21 | M | 32 | 2 | IV | C, 2+ | C, 2+ | N, 1+ | alive |

*C, cytoplasm; **N, nucleus.

Supplementary Table 2: The correlation between PTEN, LKB1, or c-Myc with clinical characteristics

| | PTEN | | <i>P</i> * | LKB1 | | <i>P</i> * | c-Myc | | <i>P</i> * |
|----------|--------------|--------------|------------|--------------|--------------|------------|--------------|--------------|------------|
| | Low | High | | Low | High | | Low | High | |
| | <i>N</i> (%) | <i>N</i> (%) | | <i>N</i> (%) | <i>N</i> (%) | | <i>N</i> (%) | <i>N</i> (%) | |
| Sex | | | | | | | | | |
| F | 3 (30.0) | 4 (36.4) | 1 | 3 (60.0) | 4 (25.0) | 0.28 | 2 (50.0) | 5 (29.4) | 0.57 |
| M | 7 (70.0) | 7 (63.6) | | 2 (40.0) | 12 (70.0) | | 2 (50.0) | 12 (70.6) | |
| Age | | | | | | | | | |
| < 60 | 5 (50.0) | 8 (72.7) | 0.39 | 2 (40.0) | 11 (68.8) | 0.33 | 3 (75.0) | 10 (58.8) | 1 |
| >= 60 | 5 (50.0) | 3 (27.3) | | 3 (60.0) | 5 (31.2) | | 1 (25.0) | 7 (41.2) | |
| Grade | | | | | | | | | |
| I | 6 (60.0) | 7 (63.6) | 1 | 3 (60.0) | 10 (62.5) | 1 | 3 (75.0) | 10 (58.8) | 1 |
| II | 4 (40.0) | 4 (36.4) | | 2 (40.0) | 6 (37.5) | | 1 (25.0) | 7 (41.2) | |
| Stage | | | | | | | | | |
| I + II | 6 (60.0) | 7 (63.6) | 1 | 4 (80.0) | 9 (56.3) | 0.61 | 3 (75.0) | 10 (58.8) | 1 |
| IV | 4 (40.0) | 4 (36.4) | | 1 (20.0) | 7 (43.7) | | 1 (25.0) | 7 (41.2) | |
| Survival | | | | | | | | | |
| No | 1 (10.0) | 1 (9.1) | 1 | 0 (0.0) | 2 (12.5) | 1 | 0 (0.0) | 2 (11.8) | 1 |
| Yes | 9 (90.0) | 10 (90.9) | | 5 (100.0) | 14 (87.5) | | 4 (100.0) | 15 (88.2) | |

*The *P* value was generated by Fisher's Exact Test.

Supplementary Table 3: The correlation among PTEN, LKB1 and c-Myc expression in pNETs

| | PTEN | | <i>P</i> * |
|-------|--------------|--------------|------------|
| | Low | High | |
| | <i>N</i> (%) | <i>N</i> (%) | |
| LKB1 | | | |
| Low | 4 (40.0) | 1 (9.1) | 0.15 |
| High | 6 (60.0) | 10 (90.9) | |
| c-Myc | | | |
| Low | 1 (10.0) | 3 (27.3) | 0.59 |
| High | 9 (90.0) | 8 (72.7) | |
| | LKB1 | | <i>P</i> * |
| | Low | High | |
| | <i>N</i> (%) | <i>N</i> (%) | |
| c-Myc | | | |
| Low | 2 (40.0) | 2 (12.5) | 0.23 |
| High | 3 (60.0) | 14 (87.5) | |

**P* was generated by Fisher's Exact Test

Supplementary Table 4: The demographics, expression status of PTEN, LKB1, and c-Myc and response to everolimus in pNET patients

| case No. | sex | age | Grade | stage | PTEN | LKB1 | c-Myc | survival | response to everolimus |
|-----------------|------------|------------|--------------|--------------|-------------|-------------|--------------|-----------------|-------------------------------|
| 3 | M | 45 | II | IV | 1+ | 2+ | 2+ | alive | yes |
| 6 | M | 54 | I | IV | 2+ | 2+ | 2+ | alive | yes |
| 10 | M | 34 | II | IV | 1+ | 2+ | 3+ | alive | no |
| 11 | M | 61 | II | IV | 3+ | 3+ | 3+ | alive | no |
| 12 | F | 62 | I | IV | 1+ | 2+ | 2+ | alive | yes |