

Figure S1

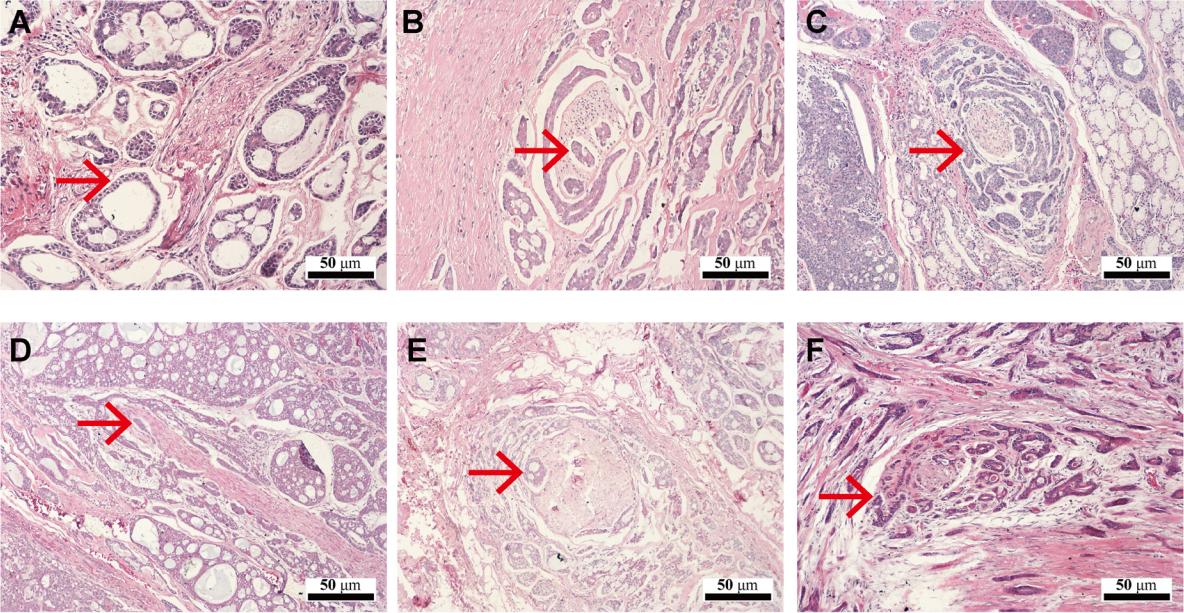
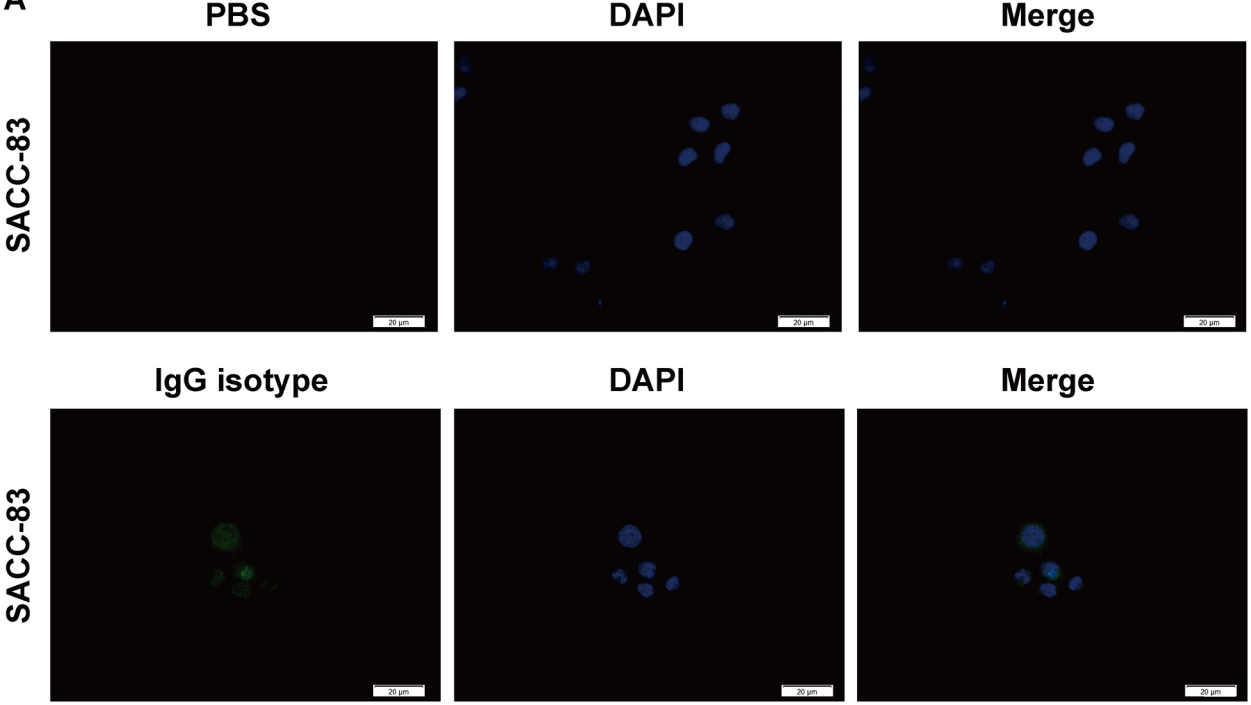


Figure S2

A



B

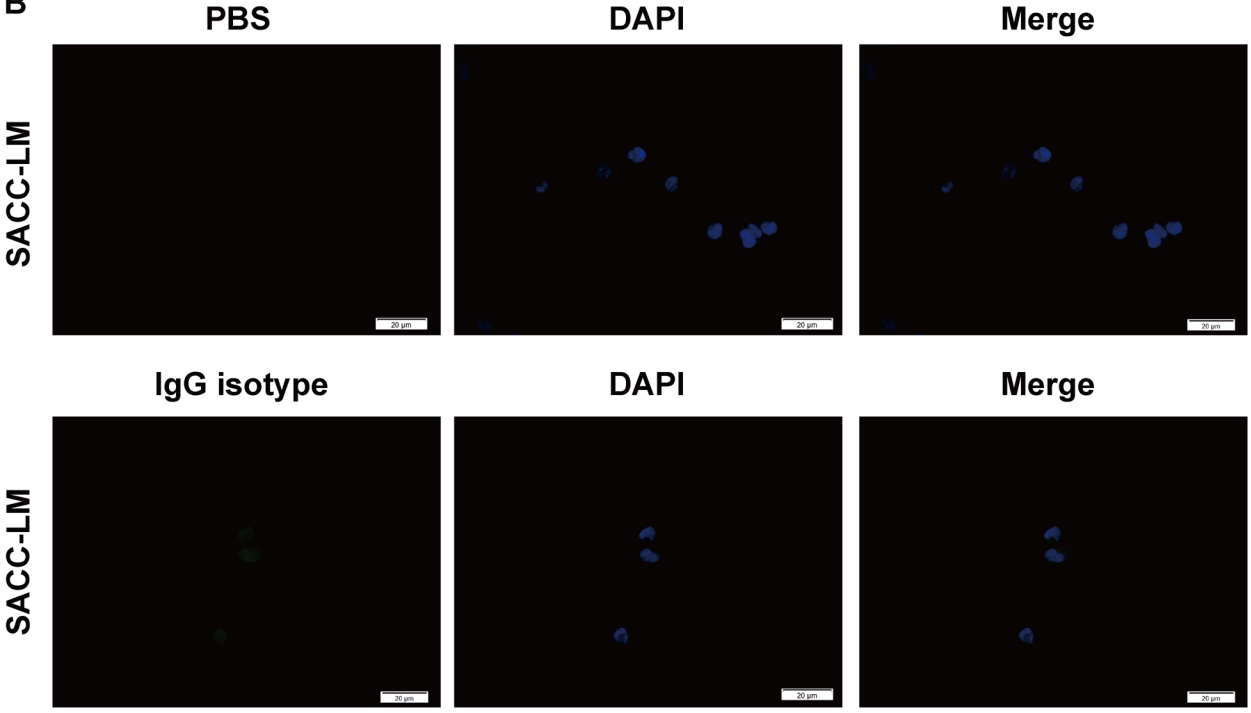


Figure S3

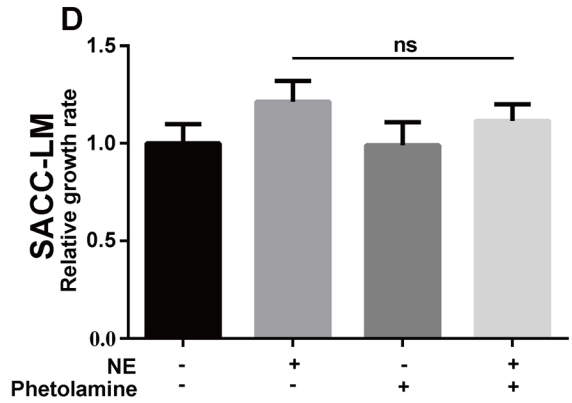
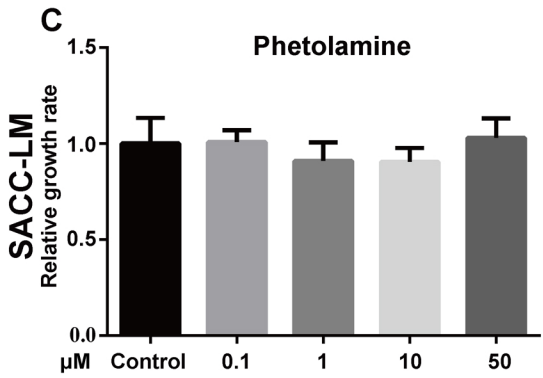
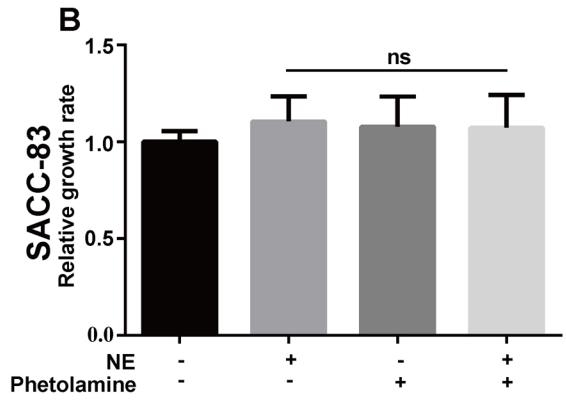
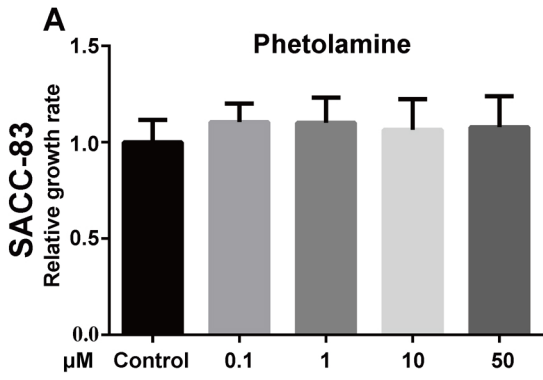


Figure S4

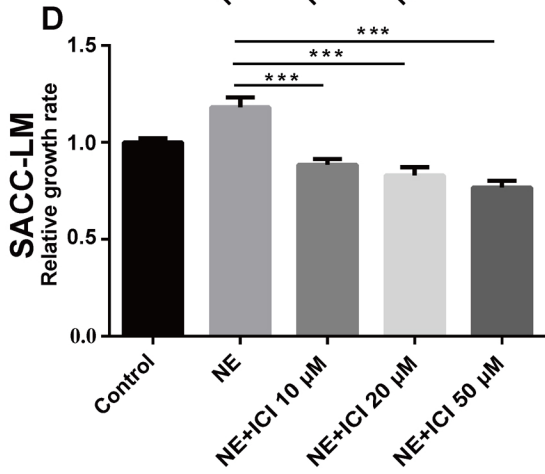
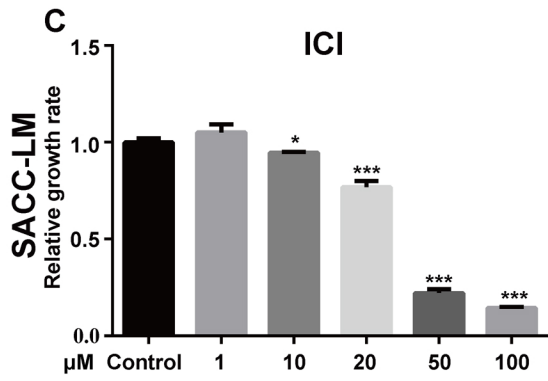
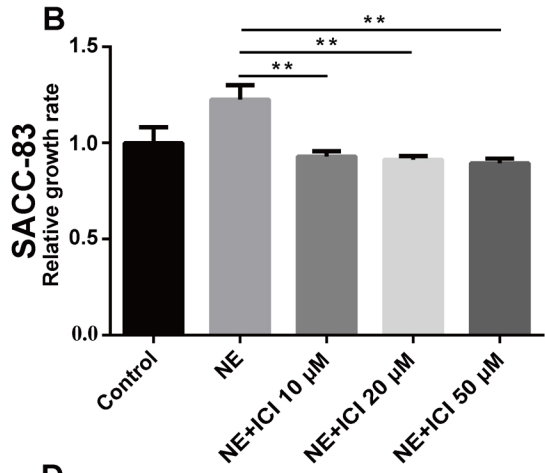
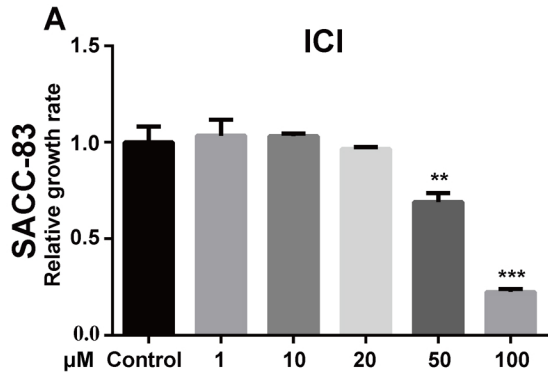


Figure S5

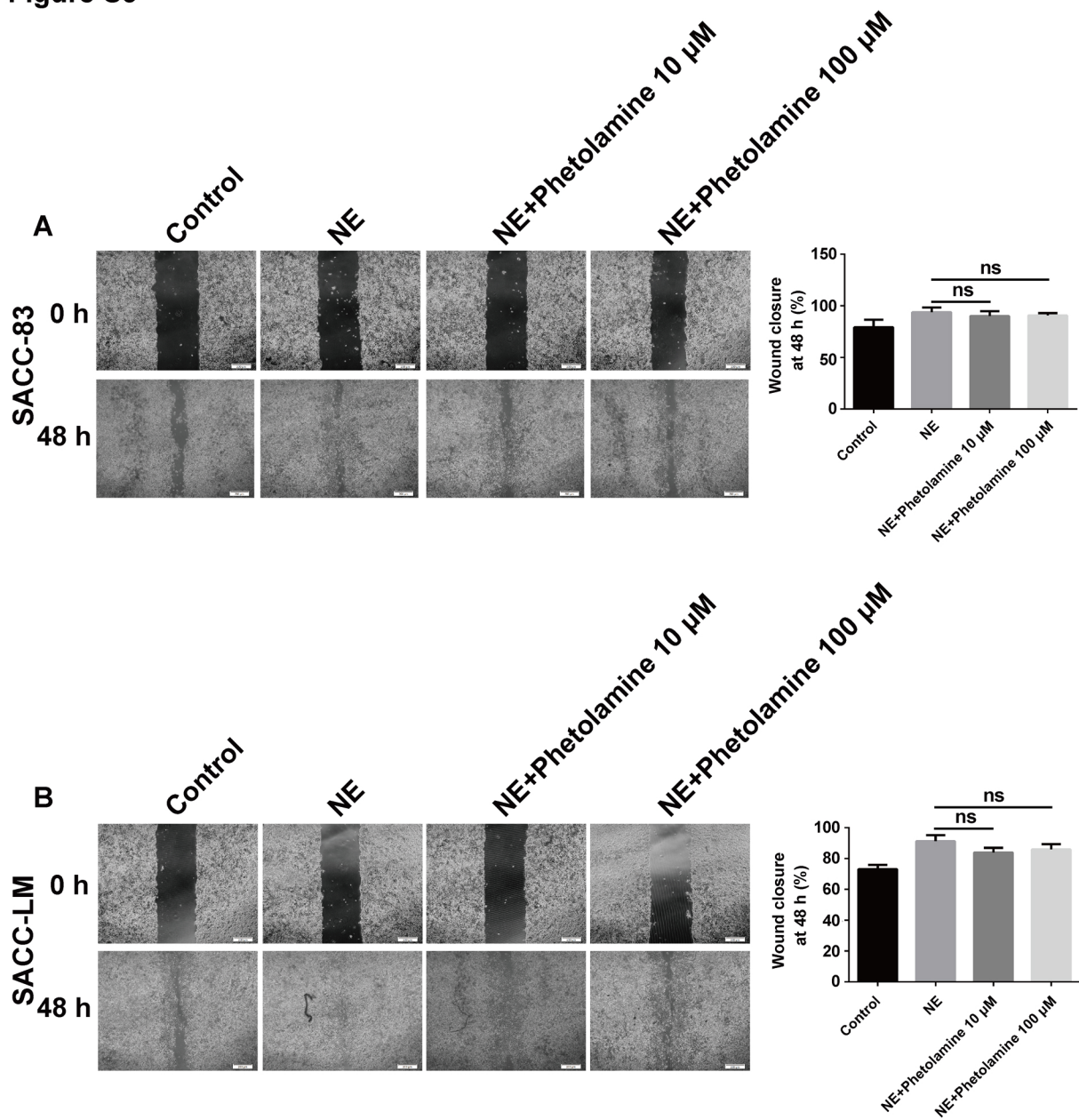
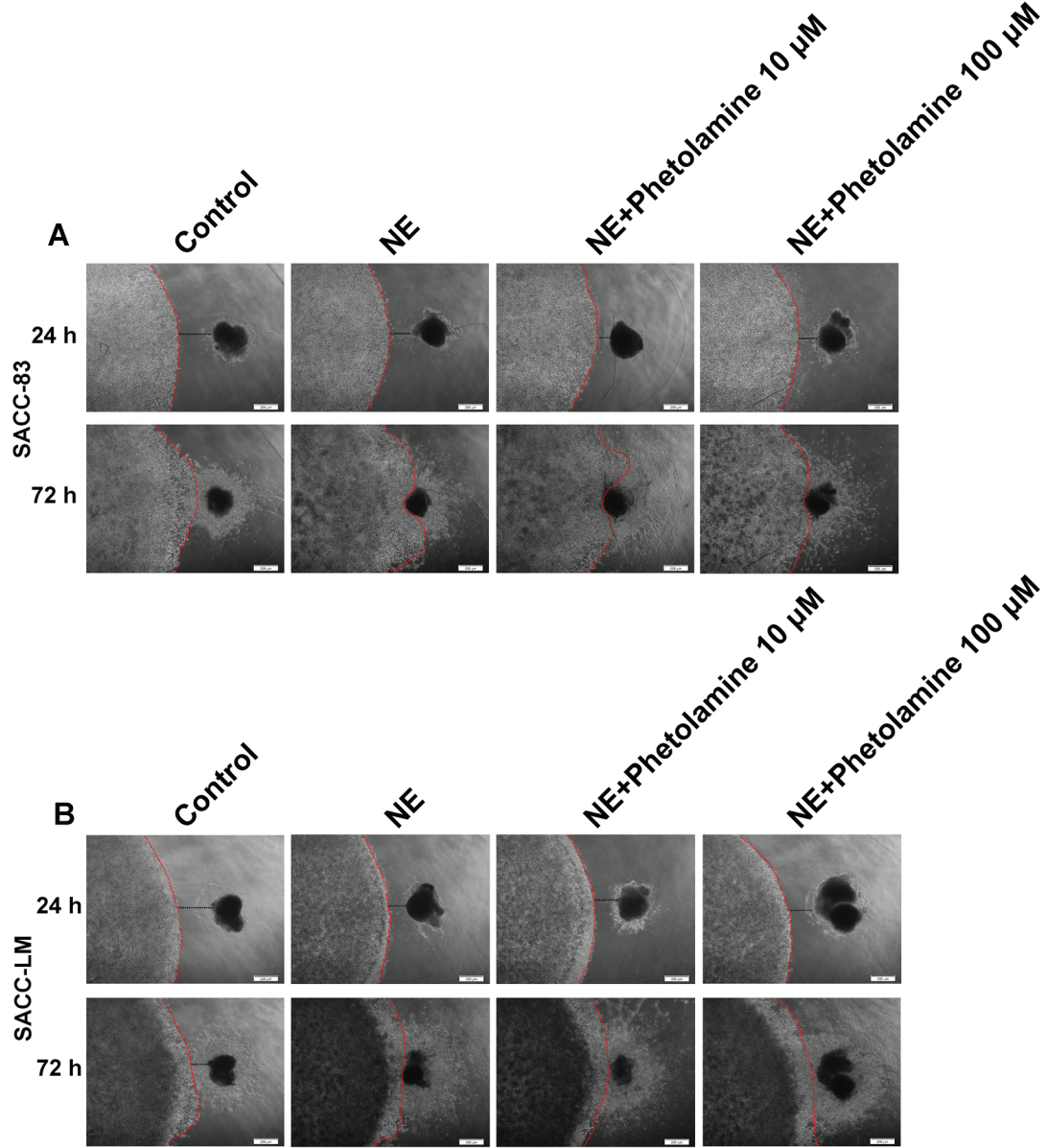


Figure S6



## Supplementary Figure Legends

**Figure S1** SACC tissues stained with hematoxylin and eosin to confirm PNI.

**Notes: (A-F)** Nerve fibers were invaded by tumor cells in SACC tissues with PNI (invaded tumor cells are indicated with red arrowheads). Original magnification, 400×; scale bar=50 μm.

**Abbreviations:** PNI, perineural invasion; SACC, salivary adenoid cystic carcinoma.

**Figure S2** Negative controls for immunofluorescence assay in SACC-83 and SACC-LM cells.

**Notes: (A and B)** PBS and rabbit IgG isotype control were used as negative controls for immunofluorescence assay in SACC-83 and SACC-LM cells, respectively. Original magnification, 400×; scale bar=20 μm.

**Abbreviations:** SACC, salivary adenoid cystic carcinoma.

**Figure S3** The effect of phentolamine on proliferation of SACC-83 and SACC-LM cells.

**Notes: (A and C)** MTT assay showed that incubating SACC-83 and SACC-LM cells with different concentrations of phentolamine (0.1-50 μM) for 48 hours did not inhibit the proliferation of SACC cells. **(B and D)** 50 μM phentolamine failed to abrogate the NE-dependent increase in SACC-83 and SACC-LM cell proliferation. ns, no significance. The error bars indicate the SD.

**Abbreviations:** SACC, salivary adenoid cystic carcinoma.

**Figure S4** Treatment with 10-50 μM ICI118,551 significantly inhibited the NE-induced proliferation of SACC-83 and SACC-LM cells.

**Notes: (A and C)** MTT assay showed that incubating SACC-83 and SACC-LM cells with

different concentrations of ICI118,551 (1-100  $\mu$ M) for 48 hours inhibited the proliferation of SACC-83 and SACC-LM cell in a concentration-dependent manner. **(B and D)** Treatment with 10-50  $\mu$ M ICI118,551 significantly inhibited the 10  $\mu$ M NE-induced proliferation of SACC-83 and SACC-LM cells. The error bars indicate the SD.

**Abbreviations:** MTT, methyl thiazolyl tetrazolium; NE, norepinephrine; SACC, salivary adenoid cystic carcinoma.

**Figure S5** 10-100  $\mu$ M phentolamine failed to abrogate the NE-dependent increase in SACC-83 and SACC-LM cell migration.

**Notes: (A and B)** Wound-healing assay comparing the migration abilities of SACC-83 and SACC-LM cells treated with 10  $\mu$ M NE and 10-100  $\mu$ M phentolamine. The wound-closure percentage was quantified at 48 hours after scratching relative to that at 0 hour. Original magnification, 40 $\times$ ; scale bar=200  $\mu$ m. ns, no significance. The error bars indicate the SD.

**Abbreviations:** SACC, salivary adenoid cystic carcinoma.

**Figure S6** 10-100  $\mu$ M phentolamine failed to abrogate the NE-induced PNI in SACC-83 and SACC-LM cell.

**Notes: (A and B)** DRG coculture models comparing the PNI abilities of SACC-83 and SACC-LM cell treated with NE and 10-100  $\mu$ M phentolamine. The red lines indicate the edge of SACC colonies and the black lines indicate the total distance between the DRGs and the cancer colonies. Original magnification, 40 $\times$ ; scale bar=200  $\mu$ m.

**Abbreviations:** DRG, dorsal root ganglia; NE, norepinephrine; PNI, perineural invasion; SACC,



salivary adenoid cystic carcinoma.