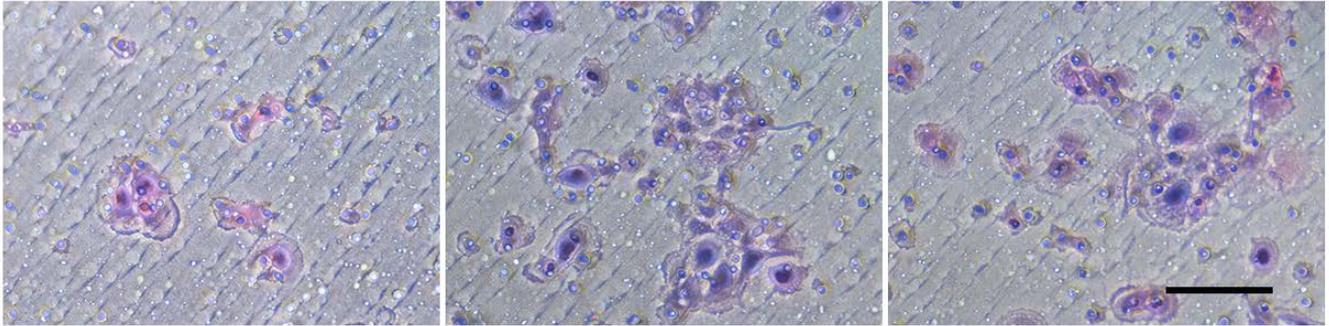
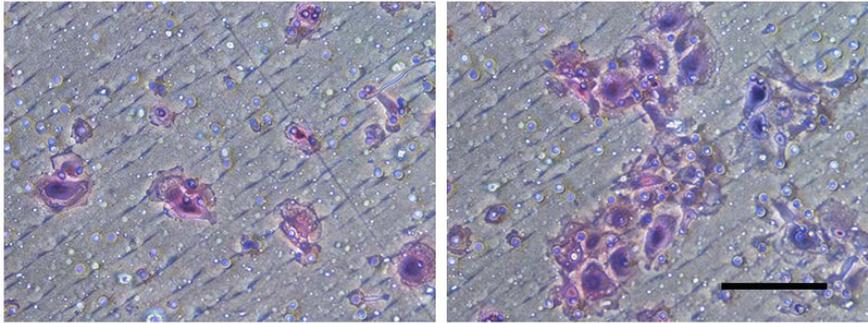
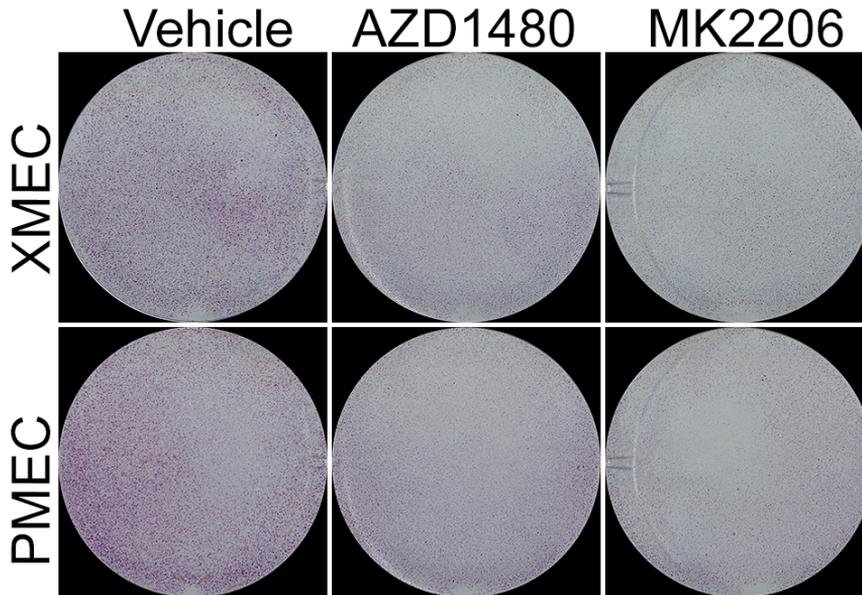


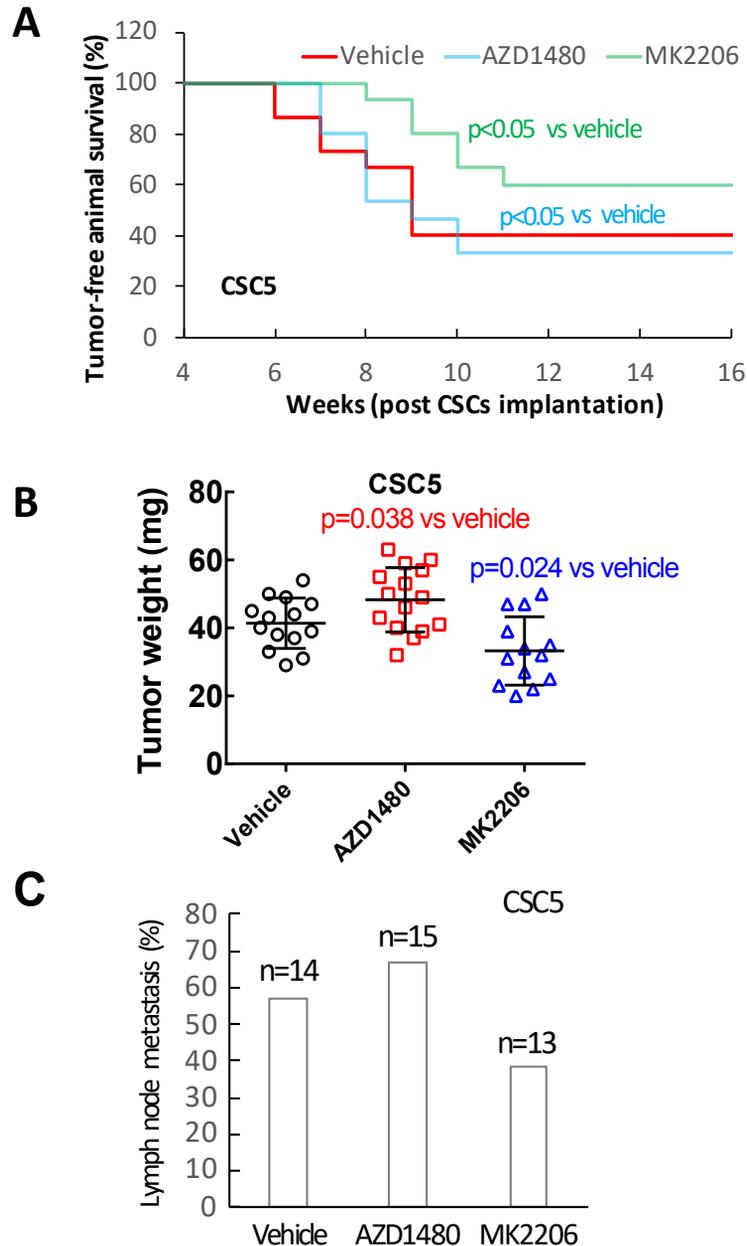
**A****MTSC****XMEC1****XMEC2****B****HTSC****PMEC**

Supplementary Figure S1. **PTC tumor stromal cells enhanced CSC invasiveness.** **A** Patient-derived xenograft tumor stromal cells increased CSC2 cell invasive activities in Boyden chamber invasion assays. **B** Patient primary tumor stromal cells increased CSC2 cell invasive activities. Mouse normal thyroid stromal cell culture (MTSC), xenograft tumor microenvironment stromal cell culture (XMEC), patient non-tumor thyroid stromal cell culture (HTSC), patient primary tumor microenvironment stromal cell culture (PMEC). Scale bar: 100  $\mu$ m

**CSC2**

Supplementary Figure S2. **PI3K/Akt and JAK/STAT3 signaling engaged in the effects of tumor stromal cells on CSC clonal growth.** The blockades of PI3K/Akt and JAK/STAT3 signaling decreased the enhancement of patient-derived xenograft tumor stromal cells (top panel) and patient primary tumor stromal cells (bottom panel) on CSC2 clonal growth. Xenograft tumor microenvironment stromal cell culture (XMEC); patient primary tumor microenvironment stromal cell culture (PMEC).

### Supplementary Figure S3



Supplementary Figure S3. **Inhibition of PI3K/Akt signaling reduced CSC tumorigenesis and tumor progression.** **A** Akt inhibitor MS2206 treatment decreased CSC tumor formation efficiency compared with vehicle and JAK/STAT3 signaling inhibitor AZD1480 treatment in a subcutaneous xenograft tumor model. **B, C** MS2206 treatment reduced PTC tumor growth (B) and lymph node metastasis (C) compared with vehicle and AZD1480 treatment in an orthotopic xenograft tumor model.