Supplementary Figures

Supplementary Figure 1 Transcriptomic analysis of Panc1 and Panc89 cell variants revealed differences in their pathways activities. Comparative Gene Set Enrichment Analysis (GSEA) on the differential effect sizes of the reactome pathways in **A)** parental Panc1 and Panc89 cells, **B)** Panc1 Holo- and Paraclone cells and **C)** Panc89 Holo- and Paraclone cells. GSEA on the shrunken log2 fold changes from apeglm (52) was performed using GAGE (v2.48.0) (53) against Hallmark, Reactome and Gene Ontology Biological Processes (GOBP) gene sets extracted from the msigdbr R package (v7.5.1). **D)** RNA sequencing-based subtyping of parental Panc1 and Panc89, Holo- and Paraclone cells. according to the classical-like and basal-like PDAC cell subtypes of Moffit et al. (56). Data are presented from 3 independent replicates.

Supplementary Figure 2 Pan-Cytokeratin staining of Panc1 and Panc89 tumors and cyst formation in Panc89 Paraclone tumors. SCID beige mice were inoculated intrasplenically with either 1×10^4 Panc1 Holo- or Paraclone cells or Panc89 Holo- or Paraclone cells (10 mice/group). Resected tissues and tumor lesions were stained for **A)** Pan-cytokeratin. Scale bars in the representative images: left = 500 µm; right = 100 µm. **B)** Representative images of cyst formation in two different Panc89 Paraclone tumors. Scale bar = 200 µm.

Supplementary Figure 3 Immunohistochemical analysis of L1CAM and Sox2 expression in Panc89 Holoclone tumors. SCID beige mice were inoculated intrasplenically with either 1×10^4 Panc89 Holoclone cells (10 mice/group). Extracted tumors were stained for L1CAM and SOX2. Data of the comparative analysis of L1CAM and SOX2 expression in all Panc89 Holoclone tumors (left) and of Panc89 Holoclone tumors exhibiting high L1CAM expression (right) are presented as median with range in violin plots. $p \leq 0.033$= *.