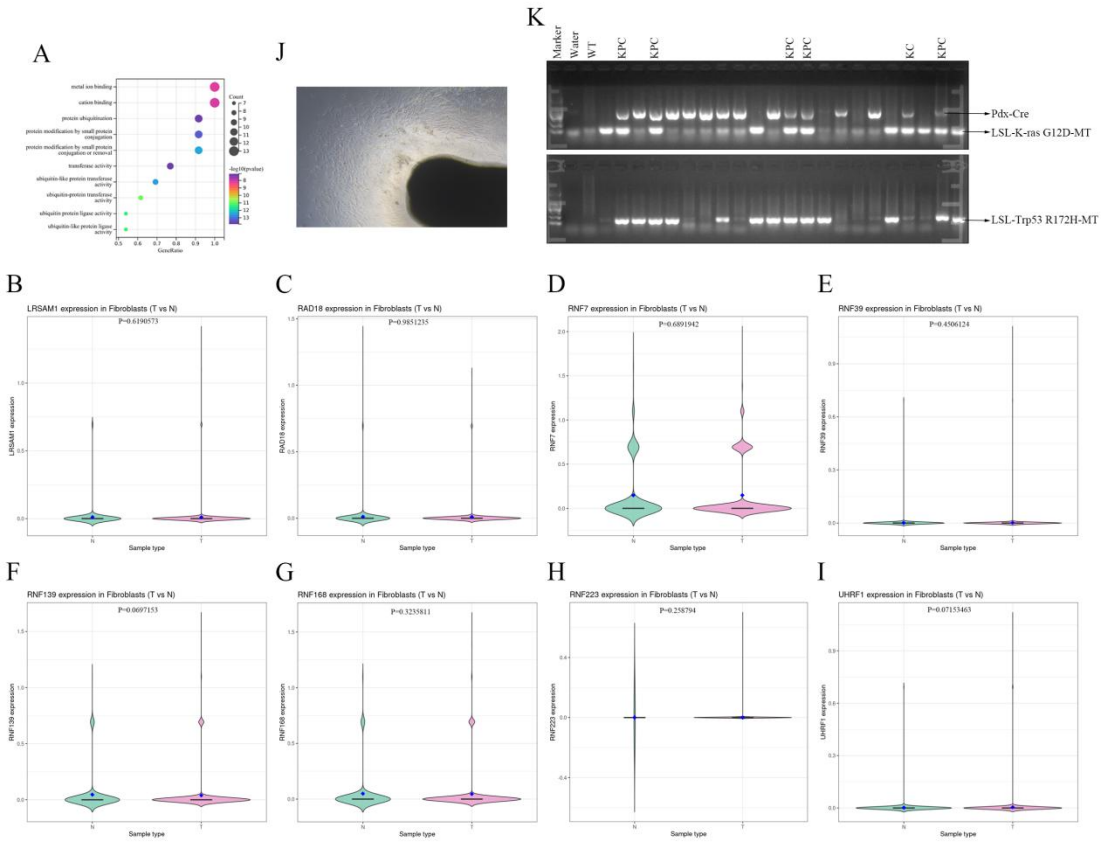


Figure S1. Functional enrichment analysis, primary cell morphology, other E3 ligases and genotyping validation of genetically engineered mouse models. (**A**) Gene Ontology (GO) enrichment analysis of candidate genes. (**B–I**) Violin plots show the expression differences of E3 ligases with no significant differential expression in PAAD tumor (T) and normal (N) fibroblasts. (**J**) Representative bright-field image of primary pancreatic tumor-derived cells cultured in vitro. (**K**) Genotyping validation of genetically engineered mouse models (GEMMs) by PCR.

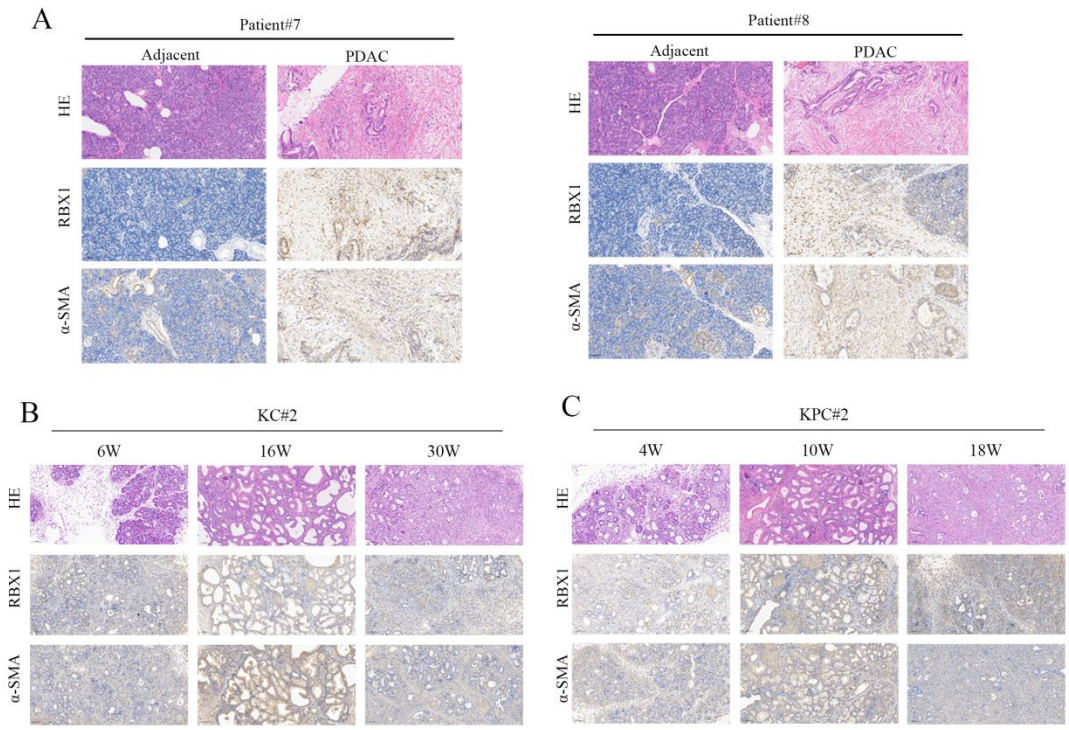


Figure S2. Immunohistochemical staining of various samples from different patients and mice. (**A**) Immunohistochemical staining of patient samples. (**B**) Longitudinal study in KC mice. (**C**) Longitudinal study in KPC mice.