Key Proteins and Mechanisms in Pancreatic Cancer

Protein / Gene	Role	Mechanism in Pancreatic Cancer
KRAS	Oncogene	Mutations (e.g., G12D, G12V) lock KRAS in an active GTP-bound state → continuous activation of MAPK and PI3K-AKT pathways → uncontrolled cell proliferation and survival.
TP53 (p53)	Tumor suppressor	Normally induces DNA repair or apoptosis under stress; mutations lead to loss of tumor suppression and sometimes gain-of-function that promotes metastasis.
CDKN2A (p16INK4A)	Cell cycle regulator	Inhibits CDK4/6 to block G1→S transition; loss of function removes this checkpoint → uncontrolled cell division.
SMAD4 (DPC4)	TGF-β pathway mediator	Transduces TGF-β tumor-suppressive signals; loss of SMAD4 disrupts growth inhibition and enhances metastatic behavior.
BRCA1 / BRCA2	DNA repair (homologous recombination)	Mutations impair DNA double-strand break repair → genomic instability → cancer development; tumors may respond to PARP inhibitors.
PALB2	DNA repair cofactor	Works with BRCA2 in homologous recombination repair; mutations increase susceptibility to pancreatic cancer.
HER2 / ERBB2	Receptor tyrosine kinase (RTK)	Overexpression activates MAPK and PI3K-AKT signaling → cell proliferation and tumor aggressiveness.
EGFR	Receptor tyrosine kinase	Ligand binding activates downstream proliferative and survival pathways (MAPK, PI3K, JAK/STAT); overactivation promotes tumor growth.
NF-κB	Transcription factor	Chronic activation (via inflammation or KRAS signaling) upregulates anti-apoptotic and pro-inflammatory genes → survival and metastasis.
STAT3	Signal transducer & transcription activator	Activated by cytokines/growth factors → induces proliferation, invasion, and immune evasion genes.
MUC1 / MUC4	Cell surface glycoproteins (mucins)	Overexpression alters cell adhesion, signaling, and immune interactions → promotes metastasis and chemoresistance.
CD44	Cancer stem cell marker	Supports self-renewal, migration, and resistance to therapy through interaction with extracellular matrix and signaling molecules.
ALDH1	Cancer stem cell enzyme	Enhances detoxification and stemness → contributes to chemoresistance and tumor recurrence.
VEGF	Angiogenesis regulator	Stimulates endothelial proliferation and new blood vessel formation → tumor vascularization and nutrient supply.
HIF1α	Hypoxia-response transcription factor	Stabilized under low oxygen → activates VEGF and glycolytic genes → promotes angiogenesis and metabolic adaptation.