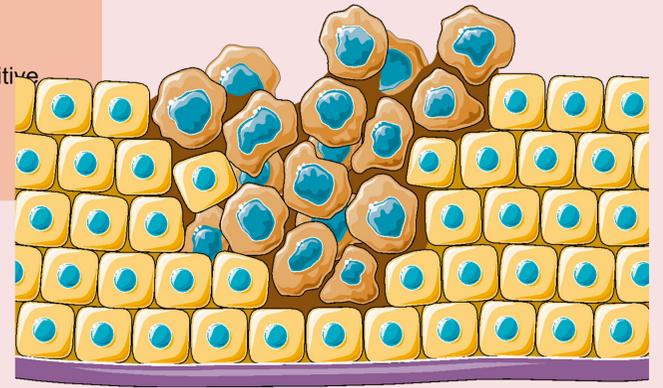


SMAD4's Effect on PDAC

SMAD4 is a gene that codes for a protein which helps run the TGF-β pathway. Without SMAD4, the positive tumor suppressing benefits of TGF-β are lost, resulting in further tumor progression in cancers such as PDAC.

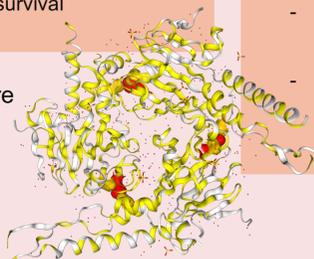


An example of a pre-metastasis tumor

Introduction

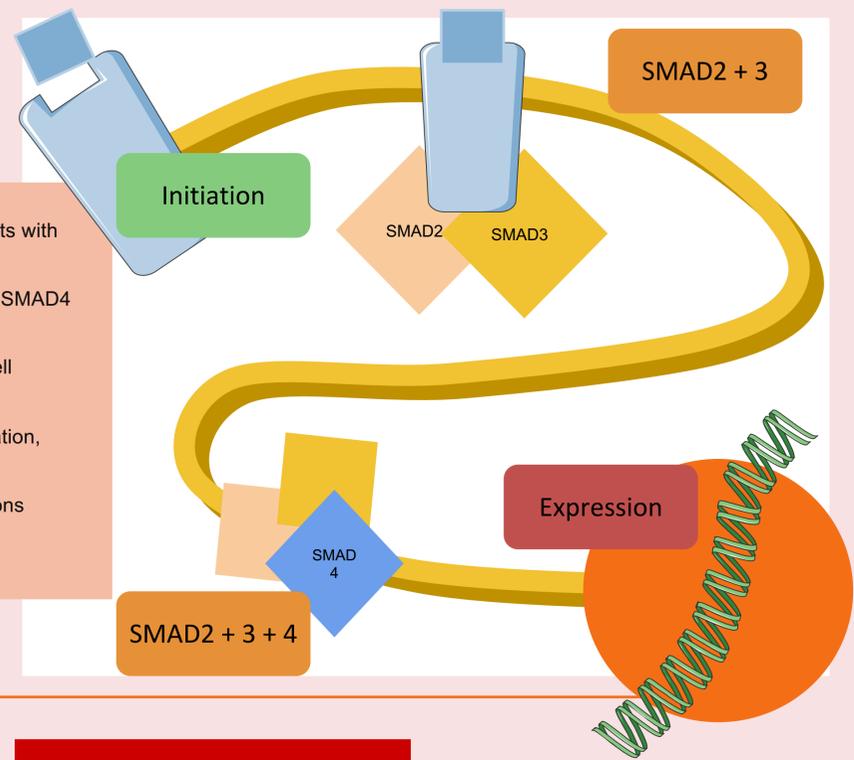
- Within cases of PDAC, malfunction of SMAD4 is a common mutation
- PDAC (Pancreatic Ductal Adenocarcinoma) is a common pancreatic cancer with low survival rates
- Immune resistance and barriers prevent traditional therapy from working properly
- The lack of tumor suppressors such as SMAD4 increases tumor survival

COSMIC3D SMAD4 protein structure



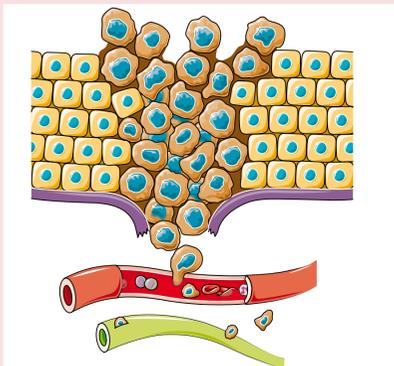
TGF-β

- TGF-β is a protein/ligand that interacts with the TGF-β pathway
- TGF-β pathway is the main pathway SMAD4 interacts with
- TGF-β is involved with a variety of cell functions, especially due to crosstalk
- Can control apoptosis, cell differentiation, regulate genes, initiate EMT
- Loss of SMAD4 hinders these functions



PDAC and SMAD4

- SMAD4 mutations do not directly cause PDAC
- Mutations may increase the aggressiveness of the tumor
- SMAD4 suppresses tumors by helping with apoptosis or increasing other suppressors (PTEN/p21)
- SMAD4 can cause EMT, making the cancer more dangerous in later stages



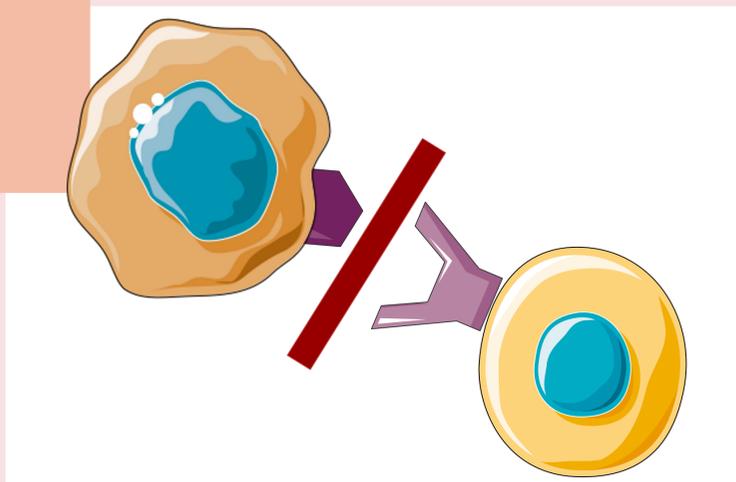
Lack of control/apoptosis leads to cell proliferation

SMAD4 Structure

- SMAD4 contains MH1/MH2 domains, as well as a linking region
- MH1 uses β-hairpins to attach to DNA
- MH2 uses alpha-helices to attach to transcriptional factors

Healthcare

- PDAC comprises of a thick ECM that makes therapy difficult
- Also uses immune suppression
- New immunotherapy + chemotherapy
- Targeting Cancer Stem Cells



Immunotherapy works by blocking tumor anti-immune responses

