1-Slide U54 summary received from the NCI

Pancreatic Cancer ARTNet Center

Pancreatic Cancer ARTNet Center (PCAC)

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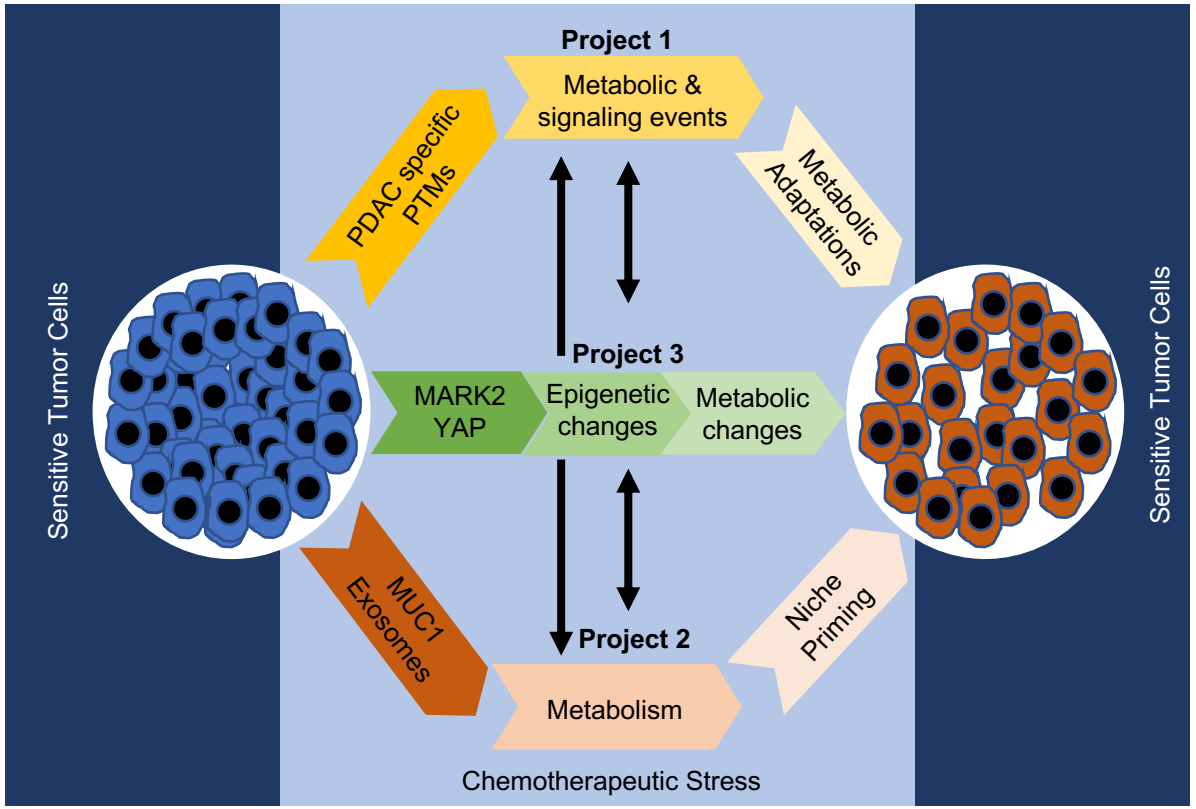
- Tumor-Stroma Dynamics
- PTM- & Exosome-Mediated Metabolic Reprograming & Fibrosis (PTMs axis)
- Rapid Autopsy Program



(PDAC)

- ➢ *Signaling mechanism underlying tumor metabolite-mediated signaling and epigenetic regulation of stroma & TiME*
- ➢ *Tumor metabolite-derived intrinsic tumor mechanisms modulating response to SOC*
- ➢ *Mechanisms of CT-MUC^{+}-derived exosomes modulating therapy response*

- **P1 Metabolic regulation of SOC acquired resistance**
  - ✓ *PDAC-specific PTMs mediated regulation of metabolism*
  - ✓ *Matched paired models of acquired resistance (pre-post therapy)*
  - ✓ *PDX, organoids, patient samples*

- **P2 MUC1 in therapy resistance**
  - ✓ *MUC1 regulation of HIF1a-anabolic glucose metabolism axis*
  - ✓ *CT-MUC1-dependent exosome cargo loading (proteins & metabolites)*

- **P3 Targeting MARK2-HDAC signaling to overcome resistance**
  - ✓ *MARK2-mediated regulation of HDAC4-YAP axis and serine metabolism*
  - ✓ *Inform Vorinostat combination clinical trials*

- **Metabolism and Tissue Cores**
  - ✓ *Leverages metabolomics and rapid autopsy program for longitudinal sample collection*