Abstract 466: Clinical Genomic Implications of Transcriptional Subtypes in Pancreatic Cancer

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Background/Methods:
• Transcriptional profiling of pancreatic cancers (PC) has defined classical and basal subtypes
• Basal subtypes have worse prognosis
• Post therapy Mesenchymal (MES) and neural–like progenitor (NRP) states have been defined
• Initial clinical data suggests differential response of transcriptional subtypes with FOLFIRINOX vs. Gemcitabine-nab-Paclitaxel (Gem/nab-P) in PC.
• Basal tumors may preferentially response to Gem/nab-P

Methods:
• Genomic cohort: 7,250 PCs profiled by Caris Life Sciences
• Clinical cohort: 1,623 PCs with additional clinical data available. Survival data was obtained from insurance claims data. Kaplan-Meier estimates were used for survival analysis.
• Transcriptional cell states were identified using RNA-seq

Results:
• 3,063 tumors (42.2%) were strongly classical (SC), 2,015 tumors (27.8%) were strongly basal (SB)
• MES and NRP marker genes were significantly co-expressed with each other, with basal genes, and anti-correlated with classical genes.

Basal tumors have worse overall outcomes

Upfront FOLFIRINOX seems to mitigate worse prognosis of Basal tumors

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Classical tumors have significantly lower rates of KRAS, TP53 & ARID1A mutations & significantly higher rates of SMAD4 mutations:

Basal Tumors display higher levels of PD-L1 and markers of immune exhaustion:

Quantiseq RNA deconvolution identifies potential TME differences:
<table>
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<tr>
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<th>SC</th>
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<th>SB</th>
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<tbody>
<tr>
<td></td>
<td>n = 3,063</td>
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<td>n = 2,015</td>
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<tr>
<td>KRAS</td>
<td>88.0%</td>
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<td>93.5%</td>
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<td>TP53</td>
<td>71.8%</td>
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<td>SMAD4</td>
<td>22.9%</td>
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<tr>
<td>ARID1A</td>
<td>7.9%</td>
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