Prognostic significance of stromal PDGFR expression in cancers of the pancreatic region:

IHC analysis of PDGFRs in cancers of the pancreatic region:

<table>
<thead>
<tr>
<th>PDGFRa</th>
<th>PDGFRb</th>
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<td>HR 0.770 (0.58-1.02) ( p=0.066 )</td>
<td>HR 1.459 (0.79-2.66) ( p=0.025 )</td>
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Background: The most frequent forms of cancer in the pancreatic region are the pancreatic ductal adenocarcinoma (PDAC; 70%) followed by the ampullary adenocarcinoma (AAC; 12%). PDAC is the fourth most common cause of cancer death in Europe. A massive desmoplastic reaction and stroma formation are characteristics for PDAC and AAC with cancer associated fibroblasts being a major component. Recent experimental studies have indicated tumor-supportive as well as -restraining effects of fibroblasts, suggesting the existence of functionally different subgroups. PDGFRα and β are potent regulators of fibroblast biology, both during normal tissue homeostasis and in diseased tissue. Their role in fibroblasts within cancers of the pancreatic region has not yet been identified.

Cohort information: Pancreas embedded sections from 408 patients with cancer in the pancreatic region. 253 patients had pancreatic ductal adenocarcinoma (PDAC) and 155 had ampullary adenocarcinoma (AAC). All cases were stained and analysed for stromal PDGFRα and PDGFRβ expression by IHC.

- PDGFRα were exclusively expressed on stromal cells and scored as low or high expression.
- Kaplan-Meier analysis was performed to determine overall survival.

> We identified an inverse correlation between PDGFRα subset of patients with PDGFRα+/PDGFRβ− stroma cells, that has a significant better overall survival \( p=0.001; \log \text{Rank test} \).

Correlation of stromal PDGFRα with tumoral HMG2α in PDAC:

- In PDAC, PDGFRα shows a negative correlation with HMG2α, while PDGFRβ shows a positive correlation. No significant correlations were found in AAC.
- P value based on Fisher’s Exact test.

Correlation of stromal PDGFRβ with an EMT signature:

- Spearman’s correlation published by Taube et al. (PNAS 2010). This was confirmed on three independent data sets.
- Correlative analysis of stromal PDGFRβ expression with the presence of HMG2α positive tumor cells. HMG2α is a cancer stem cell marker and associated with a bad prognosis.

Conclusions:
- Patients with PDGFRα+/PDGFRβ− expression in stroma cells have a significant worse overall survival.
- A high stromal PDGFRα expression correlates with a well differentiated tumor phenotype.
- The stromal PDGFRα status correlates negatively with the presence of HMG2α expressing tumor cells, while PDGFRβ shows a positive correlation.
- A high stromal PDGFRβ expression correlates positively with the EMT core signature.

> PDGFRα and β marks clinically relevant subsets of cancer-associated fibroblasts in cancers of the pancreatic region. Findings also suggest that these fibroblast subsets play different roles in tumor progression and prognosis.

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