

ABSTRACT:

The present dissertation addresses two main objectives.

First, the interaction between four pancreatic ductal adenocarcinoma (PDAC) cell lines and conditioned media from normal/healthy fibroblasts was investigated, HF) and cancer-associated fibroblasts (CAFs) derived from PDAC (PDAC-derived CAFs, PANFs), cells derived from ascitic fluid of patients with end-stage PDAC and primary PDAC tumor. Subsequently, the genome-wide profile of PANFs was determined.

The second aim was to differentiate squamous cell carcinoma (SCC) cells, surgical resection margin (MSR) cells and normal mucosa (NM) cells in patients operated for head and neck squamous cell carcinoma (HNSCC) by immunohistochemistry, using detection of tenascin (Ten), fibronectin (Fn) and galectin-1 (Gal-1), and to correlate these results with their clinical characteristics. Subsequently, whole-genome profiling of SCC, MSR and NM samples was performed based on Ten expression stratification.

Results

Cultivation of the four PDAC lines under the influence of conditioned media from HF and PANF was heterogeneous. After stimulation, the most aggressive behavior was obtained in the Panc-1 cell line while the PaTu-8902 line was rather inhibited by the media. The PANF transcriptome showed increased expression of some genes (e.g. IL-6, IL-8, MFG8, periostin) that may contribute to tumor progression and aggressiveness.

There was a statistically significant difference in co-expression of Ten, Fn, Gal-1 between SCC, NM and MSR samples ($p < 0.01$ and $p < 0.05$, respectively). Microarray analysis of gene expression revealed increased expression of several genes related to tumor progression in Ten⁺ (tenascin positive) SCC and strong activity of genes related to lipid metabolism in MSR Ten⁻ (tenascin negative) SCC.

Conclusion

TME significantly affects the behavior of PDAC cells. Based on their high variability and their differential interaction with TME, the likely future of treatment lies in the establishment of an individualized tumor-specific treatment protocol. Gene analysis showed significant and specific changes based on Ten stratification in SCC patients, however, without affecting disease prognosis.