The tumor microenvironment in pancreatic cancer — new clinical challenges, but more opportunities

Lei Zheng, MD, PhD
Executive Director, Mays Cancer Center
UT Health San Antonio MD Anderson Cancer Center
Professor, Department of Medicine
UT Health San Antonio, USA

Abstract:
Advancements in our understanding of the tumor microenvironment (TME) in pancreatic ductal adenocarcinoma (PDAC) can present new challenges, but can also provide more opportunities for effectively treating PDAC. By dissecting the desmoplastic stroma and both the intra- and inter-tumoral heterogeneity of PDAC, with an emphasis on cancer-associated fibroblasts and their surrounding immune cell niches, we identified new approaches in converting the “cold” PDAC TME into a “hot” one by priming T cell activation, overcoming T cell exhaustion, and unraveling myeloid-mediated immunosuppression. Furthermore, by exploring integrated targets in the TME such as points of convergence in tumor, stromal, immune cell metabolism and oncogenic KRAS signaling, combined with improved preclinical models of PDAC, advancements in single-cell, spatial multi-omics and machine-learning-based models, recent studies have provided novel approaches to untangle the complexities of the TME. Finally, building on our experience with failed clinical trials in the past, this evolving, comprehensive understanding of the TME will ensure future success in developing more effective therapies for PDAC.