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Pro-inflammatory Cytokine Secretion In The Tumor Microenvironment Is Triggered By CD74 Activation In Tumor Cells In Pancreatic Ductal Adenocarcinoma

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Background : Pancreatic Ductal Adenocarcinoma (PDAC) is an aggressive cancer characterized by high mortality and morbidity. The five-year survival rate is less than 5%, due to a lack of therapeutic agents and biomarkers for early detection. Therefore, it is critical to identify and develop new therapeutic targets for PDAC therapy. Here, we highlight the evidence for an interactive mechanism between CD74 activation in cancer cells and the release of pro-inflammatory cytokines by cancer associated fibroblasts (CAFs) in the tumor microenvironment (TME) in PDAC.

Methods : By suppressing the expression of CD74 in pancreatic cancer cells, we found that CD74 triggered TRAF6-mediated activation of the NF-kB pathway, leading to the expression and secretion of various inflammatory factors into the TME as confirmed by ELISA secretion assay. Furthermore, we found that these secretory factors bind to the receptors on CAFs to induce release of pro-inflammatory cytokines by the TME. Expressions of pro-inflammatory cytokines in CAFs were upregulated as verified by western blot.

Results : Here, we highlight the evidence for an interactive mechanism between CD74 activation in cancer cells and the release of pro-inflammatory cytokines by cancer associated fibroblasts (CAFs) in the tumor microenvironment (TME) in PDAC.

Conclusions : Taken together, our findings are by far the first to present a supportive role of CD74 in constituting a more pro-inflammatory condition in the TME in PDAC.

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