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Identification of CAF-Derived Ligands inducing Tumor Progression in Colorectal Cancer

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Cancer-associated fibroblasts (CAFs) are recognized as major components of the tumor microenvironment, playing a pivotal role in promoting colorectal cancer (CRC) progression by mediating complex paracrine signaling. Despite their significance, the precise ligand-receptor interactions between CAFs and CRC cells that drive these tumor-promoting effects remain inadequately understood. To address this gap, we performed a comprehensive analysis using publicly available single-cell RNA sequencing data to identify and prioritize candidate ligand-receptor pairs that could mediate the communication between CAFs and CRC cells. By analyzing the expression patterns of ligand-receptor pairs in single-cell RNA sequencing data, we mapped potential cell-cell interactions between CAFs and cancer cells. From this analysis, we identified a set of ligand-receptor pairs where the ligand was highly expressed specifically in CAFs, suggesting their role in CAF-driven tumor-promoting pathways. Among these candidates, we prioritized ten key CAF-derived ligands, including INHBA, POSTN, SPARC, and seven others, which are highly expressed in the tumor stroma and may critically influence CRC tumor growth, invasion, and metastasis.

To validate the role of these ligands, we plan to conduct in vitro experiments using colorectal cancer cell lines, followed by in vivo evaluation in organoid-based xenograft models. These studies will help elucidate the mechanistic role of CAF-derived ligands and their potential as therapeutic targets in CRC.

Our findings highlight the critical role of CAFs in shaping the CRC tumor microenvironment through specific ligand-receptor signaling pathways. Ultimately, this study lays the groundwork for future therapeutic strategies that could disrupt CAF-tumor cell interactions and mitigate tumor progression in colorectal cancer.