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Identificación del proyecto:

Superar la resistencia a la terapia inducida por los fibroblastos asociados al cáncer colorectal

Descripción del proyecto:

Cancer-associated fibroblasts display diverse characteristics and functions in primary and metastatic tumors, influencing tumor aggressiveness and treatment sensitivity. Moreover, evolving cancer-associated fibroblasts heterogeneity during cancer progression and treatment can alter the tumor microenvironment, transitioning from an effector immune landscape to an immunosuppressive one. This proposal centers on comprehending the heterogeneity and dynamic nature of cancer-associated fibroblasts in colorectal cancer and its implications for cancer progression and therapy response. To achieve a comprehensive characterization of cancer-associated fibroblasts heterogeneity dynamics, we will employ a multiomic approach (whole tumor, single-cell and spatial transcriptomics, and immunohistochemistry) performed on colorectal cancer patients treated with chemotherapy. This will help us characterize distinct subpopulations of cancer-associated fibroblasts in colorectal cancer and comprehend their functional roles and plasticity during cancer progression and treatment. Additionally, we will develop fully humanized ex vivo models derived from colorectal cancer patient samples, replicating the immunocompetent tumor microenvironment of colorectal cancer. These models will enable us to investigate the influence of specific cancer-associated fibroblasts subsets on the anti-cancer response to therapy and immunity, identifying those that contribute to resistance against systemic and targeted therapy. We will identify new compounds capable of overcoming the tumor microenvironmentinduced resistance to treatment in patients with colorectal cancer. To that end, we will combine our unique patient-derived cancer-in-a-dish models with a two-step pharmacological screening strategy. Studying the mechanisms underlying cancer-associated fibroblasts heterogeneity and utilizing humanized ex vivo models together with a drug screening approach will provide critical insights that can drive advancements in cancer treatment strategies and personalized oncology for colorectal cancer patients.

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199.634,00€

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