Proyecto PID2019-104698RB-I00 financiado por MCIN/ AEI /10.13039/501100011033

Identificación del proyecto:

Diseccionado la acción del estroma sobre la progresión de los tumores epiteliales (ESCAN)

Descripción del proyecto:

Epithelial tumors are the most common neoplastic alteration in humans. It is becoming progressively clear that the tumor microenviroment (TME), also called the tumor stroma, is crucial for tumor development and provides to epithelial cells signals that potentiate their invasiveness and accelerates the acquisition of other tumors traits, such as the resistance to the immune attack. TME is composed by different types of not-transformed cells that surrounds and infiltrates the epithelial tumor cells. Among them, cancer-associated fibroblasts (CAFs) are particularly relevant but the TME also contains endothelial and immune cells and in some cases adipocytes. All these cells exhibit significant differences with respect to the non-tumorigenic, naïve cells since they are activated by the neighbor tumor cells. We have previously described that Snail1 transcription factor is required for CAF activation and function: CAFs-deficient in Snail1 are unable to enhance the invasion of tumor cells when co-cultured and do not prevent the attack of immune cells. This project is a continuation of the previous research of the group with four major goals: 1) investigate the mechanism of CAF activation particularly analyzing the role of Snail1 as transcriptional activator and as an effector of the alternative splicing of mesenchymal genes; 2) identify and characterize inhibitors of CAF activation either by precluding alternative splicing or preventing Snail1 protein stabilization; 3) analyze the inhibition by CAFs of the immune attack with a particular emphasis on macrophages; and 4) investigate the activation of adipocytes by tumor cells and the contribution of adipocytes to CAF activation and epithelial tumor cells growth and invasion. We think that this research will explain how TME facilitates tumor growth and invasion and metastasis development and identify new drugs with a potential antineoplastic use.

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266.200,00€