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CENTRO DE INVESTIGACION

CIPF Seminar

Stroma redecorates the tumor

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Tumors are much more than just uncontrolled cell growth. A tumor is like an organ where tasks are assigned to specific cell types, and those tasks are part of a common endpoint, which is the continuous dissemination of the malignant cells. When a tumor grows to a certain size it needs to modify the environment where it is growing, in order to continue growing. It is at this point where the tumor cells use the stroma to redecorate this environment. In our lab we focus on the mechanisms that control tumor stroma.

One of the main cell types of the stroma are endothelial cells. Tumor vessels are much more than mere tubes providing nutrients. The number of angiogenic functions are growing every day. In this regard, we have recently described how activation of Notch1 facilitates tumor cell metastasis. We have shown how Notch1 is frequently activated in tumor vessels from patients, and that this activation correlates with bad prognosis and metastasis. We have seen that its activation is linked to senescence, and leads to increased permeability.

To study the role of stromal macrophages we used ovarian cancer as a model. Ovarian cancer is an extremely deadly disease with a poor 5 year survival ratio. There is now a wealth of clinical and experimental evidence that strongly links tumor-associated macrophages (TAMs) with tumor progression. We described recently a mechanism by which epithelial ovarian cancer (EOC) cells reprogram tumor associated macrophages (TAMs) in metastatic ovarian carcinoma. We could name this phenomenon "Feeding the Troll". EOCs need high amounts of cholesterol to build their membranes while they proliferate. EOCs produce hyaluronic acid polymers that, when detected by the TAMs, activate their cholesterol transporters increasing cholesterol efflux. Tumor cells Cholesterol depletion in TAMs translates into a reduction of lipid rafts, which renders them more sensitive to IL4-induced reprogramming.

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