Talk

The role of macrophages in cancer progression

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ABSTRACT

In recent years, it has been demonstrated that the tumor microenvironment is a fundamental piece in the progression of cancer and thus, it emerges as a potential therapeutic target. This microenvironment contains non-malignant cell lines, including tumor-associated macrophages (TAMs), which play a key role in the control or promotion of tumor growth, metastasis and angiogenesis. Therefore, understanding how TAMs interact with tumor cells is critical to understand cancer development.

The fruit fly Drosophila melanogaster is an excellent genetically tractable model system to address the complex cell interactions and genetic cooperation that lead to tumor formation and progression. In this respect, Drosophila embryonic macrophages (hemocytes) have emerged as a powerful system to study the innate immune response against the early stages of tumor development. Deriving from the head mesoderm, hemocytes are highly migratory cells, achieving an even distribution throughout the embryo by the end of embryogenesis.

The aim of this study is to create a tumor in an embryonic tissue and analyse the response of embryonic macrophages to the presence of tumor. To do so, we have used the Gal4/UAS system to test several of the most representative oncogenes in human cancers, such as Ras, Notch, EGFR, PI3K or Yorkie, for their ability to generate a tumor in the salivary glands. The choice of this tissue relies on the fact that salivary glands develop in the head region of the embryo, the place where embryonic macrophages emerge from. Thus, one could test whether tumors recruit macrophages by analysing if they halt at salivary glands containing a tumor. Our analysis in fixed tissue shows that indeed macrophages stop their migration at salivary glands-containing tumors and wrap them. We are now in the process of analysing this behaviour at the cellular level in vivo by confocal microscopy.

This project also proposes to compare at a genetic level the behaviour of wild type and TAMs macrophages. To perform this a protocol for the isolation of macrophages by flow cytometry is being established. Once control and experimental macrophages are isolated, RNA-seq will be carried out to analyse the gene expression profile of both types of macrophages.This will allow us to identify genes and pathways involved in the regulation of tumor progression by macrophages.

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