The role of the hypoxic tumor microenvironment on the macrophage-tumor cell interplay

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Aim: The aim of this work is to unveil the role of the hypoxic microenvironment on macrophage-tumor cell interplay, using colorectal cancer (CRC) as a model.

Introduction: Microenvironment, in most cases hypoxic, is composed by cancer cells, extracellular matrix, stromal and immune cells, that cooperate and affect each other activities. Macrophages are one of the most abundant immune cells at the tumor microenvironment, acting as tumor suppressors or promoters. Previous research had shown that both hypoxia and immunosuppressive macrophages are associated with tumor progression. Nevertheless, these studies did not focus on the interplay between hypoxia and macrophage-cancer cell crosstalk.

Methods: To achieve our goal co-cultures of CRC cells and human macrophages, both in normoxia and hypoxia, were established. Macrophages were characterized functionally and phenotypically and their potential to induce cancer cell invasion was evaluated.

Results: Our results suggest that hypoxia, and the presence of cancer cells, decreases the cell surface expression of an anti-inflammatory marker (CD163), however the mRNA expression was not altered. Nevertheless, hypoxia induced an increase in the mRNA expression of the macrophage pro-inflammatory marker (CCR7).

Macrophages metabolic activity was not altered by hypoxia but decreased when co-cultured with cancer cells. In addition, lactate production decrease in co-culture while glucose consumption increased. Notably, macrophages in normoxia presented a more rounded morphology while in hypoxia are more elongated with evident cellular protrusions, suggesting dynamic alterations at the actin cytoskeleton organization. Interestingly, MMP-2 and MMP-9 activity profiles were not altered by the presence of cancer cells or hypoxia. Nevertheless, cancer cell invasion ability increased in the presence of macrophages, suggesting that other MMPs might be involved.

Conclusion: Findings in normoxia regarding macrophage potential to induce cancer cell invasion are consistent with those previously described by our group. Interestingly, we demonstrate now that hypoxia potentiates the invasive behavior of cancer cells and also macrophage pro-invasive ability.

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Ethnopharmacological use of Cymbopogon citratus (DC.) Stapf and Cymbopogon schoenanthus (L.) Spreng.: Anti-inflammatory potential of phenol-rich extracts

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Aim: The aim of this work consisted on expanding the knowledge on the chemical composition of different extracts from Cymbopogon spp., and on the evaluation of their anti-inflammatory potential in cell and cell-free systems.

References