Metabolic Reprogramming of Host Cells Induced by Cancer Cells: Implications for Premetastatic Niche Formation

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I. Introduction

Tumor cells undergo metabolic changes during metastasis to survive in different microenvironments, while spreading to distant organs (1). Glutamine (Gln) emerges as a pivotal component, playing an important role in fueling ATP production and cell survival (2). Mesenchymal cells and cancer-associated fibroblasts (CAFs) exhibit heightened Gln requirements, known as “Glutamine addiction” (3). In this study we aimed to investigate the effect of cell-cell interactions in promoting metabolic alterations and transition of normal fibroblasts to CAFs.

II. Materials and methods

We employed the Mimetas OrganoPlate™ 3-lane 40 platform to investigate the interactions between MDA-MB-231 metastatic breast cancer cells and MRC5 cells (normal lung fibroblasts). MDA-MB-231 (30000 cells/well) and MRC5 cells (15000 cells/well) were cultured in the top and bottom channels, respectively. After 48 hours of cell-cell interactions the media was collected for metabolomics analysis.

Results.

Metabolomics analysis revealed a significant decrease in Gln concentration, deemed to be consumed by MRC5 cells, and increase in L-glutamic acid production by MRC5 cells following cancer cell-lung cell crosstalk.

Conclusion. The observed metabolic shift suggests the potential transition of normal lung fibroblasts towards a CAF phenotype, indicating their contribution to creating a favorable environment for hosting cancer cells before their arrival. These findings shed light on the intricate interplay between cancer and host cells in shaping the metabolic landscape of premetastatic niches, and tumor cells may induce metabolic alterations within secondary tumor sites, establishing a premetastatic niche crucial for cancer progression.

Conflict of Interest

The authors declare that they have no conflict of interest.

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