Hypoxia affects chemotactic secretome profile in 3D bioprinted co-cultures of glioblastoma multiforme cell lines and human mesenchymal stromal cells

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INTRODUCTION

Glioblastoma multiforme is the most common primary tumor of the central nervous system with the most aggressive clinical outcome. Glioblastoma cells function in a specific microenvironment, in which they exchange numerous physical and biochemical signals with other cells. A proper understanding of this phenomenon is essential for the development of more effective cancer therapies. Nevertheless, classical 2D simple cell culture systems do not sufficiently mimic the complexity of the tumor microenvironment, therefore study *in vitro* 3D models constitutes a more promising approach to studying interactions between different types of cells, therein effectiveness of therapies. The study aimed to evaluate changes in the profile of chemotactic factors secreted by glioblastoma multiforme (GBM) cell lines bioprinted in 3D co-cultures with primary mesenchymal stromal cells (MSCs) in both hypoxic and normoxic environments.

MATERIALS AND METHODS

Glioblastoma multiforme cell lines (DK-MG, U-251) and primary human adipose-derived mesenchymal stromal cells (MSCs) were bioprinted in co-cultures with adequate monoculture control constructs. Cells were mixed with Laminink 111 bioink (Cellink) and bioprinted by extrusion-based technique using BIO X (Cellink). 3D bioprints were cultured for 72 h in DMEM with 4% FBS in hypoxic and normoxic conditions until the Proteome Profilles Array Kit (R&D Systems) was performed.

RESULTS AND DISCUSSION

Under the hypoxic condition, the concentrations of a number chemokines were decreased significantly, especially those of CCL5, CXCL12, CXCL16, and chemerin. However, in GBM-MSC co-cultures in both oxygenic of conditions, but especially in hypoxic ones, we observed a potently increased secretion of such chemokines as CXCL8, fractaline and CCL28.

CONCLUSIONS

The results of our work indicate that the use of the 3D bioprinted method combined with hypoxic conditions is a promising approach to create co-culture models of mimicking the tumor environment. Therefore, this precise technology of the assessment of human tumor biology can significantly bring *in vitro* models closer to the *in vivo* conditions.