GLIOMA - MACROPHAGE CROSSTALK MODULATES THE PURINERGIC SIGNALING AND AFFECTS MACROPHAGE CELL VIABILITY

Azambuja, H.J.¹; Carvalho, R.T.¹; Silveira, F.E.¹; Pedra, N.S.¹; Beira, F.T.²; Spanevello, R.M.¹; Braganhol, E³.

¹Programa de Pós Graduação em Bioquímica e Bioprospecção, Centro de Ciências Químicas, Farmacêuticas e de Alimentos, Universidade Federal de Pelotas.
²Departamento de Farmacologia e de Fisiologia, Universidade Federal de Pelotas.
³Departamento de Ciências Básicas da Saúde, Universidade Federal de Ciências da Saúde de Porto Alegre.

Glioblastoma multiforme is the worst and most common primary brain tumor. In addition to tumor cells, the microenvironment is composed by a population of non-transformed cells, including fibroblasts, neutrophils, macrophages and its secretion products. Although the inflammatory process contributes to tumor progression by promoting angiogenesis and immunesuppression the molecular and cellular mechanisms involved in cancer-related inflammation remain unknown. Purinergic signaling has emerged as an important mediator of immune and inflammatory responses and alterations in this pathway has been related to cancer progression.

The objective of this study was evaluate the ectonucleotidases activities and cell viability on macrophages exposed to glioma-conditioned medium (GCM) or co-cultured with mouse GL261 glioma cell line.

Methods: Macrophages were collected by lavage of peritoneal cavity from C57/BL6 mice and treated with GCM or directly co-cultured. Following 24h of treatment the ATP, ADP and AMP hydrolysis were determined by the malachite green method. For cell viability analysis, macrophages were exposed to GCM or co-cultured in absence or in presence of ATP (0.1-1mM) for 24h and the sulfarodaminaB was performed. Data were analyzed by ANOVA followed by Tukey post-hoc. The treatment with GCM promoted a decrease of 40% ATP hydrolysis while ADP and AMP hydrolysis remained unchanged. When macrophages were co-cultured, it was observed a decrease of ATP, ADP and AMP hydrolysis by 45%, 40%, and 40%, respectively. Based in these results, we investigated the effects of ATP in the cell viability and the results showed that the treatment with ATP in co-culture promote a significant increase of 33% in cell viability when compared to control (P<0.05). These results suggest that the glioma-macrophage crosstalk modulate the purinergic signaling by decreasing the ectonucleotidase activities which may favor ATP accumulation in the microenvironment. This nucleotide increases the macrophage cell viability and could play an important role in the cancer-related inflammation.

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