Impact of Hyperglycemia on Immunomodulation of Colorectal Cancer

Mantuano, N,R[1] ; Vasconcelos-dos-Santos, A.[1]; Rodrigues, L.S.[1]; Oliveira, A-C[1]; Todeschini, A.R.[1]; Dias, W.B.[1]

[1]IBCCF-UFRJ- Instituto de Biofísica Carlos Chagas Filho- Universidade Federal do Rio de Janeiro

Introduction: During malignant transformation, cell glycosylation is strongly altered when compared to adjacent healthy tissue with differential expression of glycosyltransferases, glycosidases and monosaccharide transporters besides the increased glucose. Besides, The biosynthesis of glycoconjugates depends on the availability of activated sugars, generally derived from glucose and glutamine (augmented in cancer cells) through, the hexosamine biosynthetic pathway (HBP).
Recent work suggests that the metabolite availability to the hexosamine pathway induces aberrant cell glycosylation and cell migration (Plos One, 8: e60471, 2013). These results put forward the hypotheses that glycosylation acts a metabolic sensor and, in turn, modulates cell plasticity (cell survival and proliferation).
Aims: With the main purpose of studying the role of cellular glycosylation in tumor progression, in this work we analyzed the impact of hyperglycemia (HG) in immunomodulation and tumor progression of murine colon carcinoma cells (MC38) in vivo, analyzing tumor growth and infiltrating cells.
Materials and methods. In this model, metabolite availability to the HBP is induced by selective destruction of β-pancreatic cells through treatment of C57BL/6 with streptozotocin (STZ) leading hyperglycemic mice (HG mice). MC38 cells were injected subcutaneously, tumor size was measured for 28 days. The blood was collected in 14º e 28º days. Tumors were dissected, digested in collagenase and DNAse, and inflammatory cells were analyzed in a FACScalibur cytometer.
Results: HG mice showed subcutaneous tumors with increased area and mass. Histochemistry of tumors from HG mice demonstrated an increment of glycoconjugates containing α2-6sialic acid. STZ treated mice presented hypersialylated $CD8^+$ T cells, which were less activated than $CD8^+$ T cells from control mice. Noteworthy is that tumors of STZ treated mice also showed a higher number of M2 polarized macrophages. Taken together, our results allow us to infer that an increase of glucose levels induces the biosynthesis of aberrant glycoconjugates, and increases tumor progression of murine colon carcinoma cell MC38.

Key words: Hyperglycemia, tumor, glycosylation
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