The Mechanism of Lymphocytes Heparanase Activation

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Heparanase-1 (HPSE-1) is an endo-beta-glucuronidase encoded by 4q21,3 gene that specifically degrades heparan sulfate (HS) and heparin chains from proteoglycans. HPSE1 increases syndecan-1 shedding promoting angiogenesis, tumor growth and metastasis. The heparanase-2 (HPSE-2) isoform presents no enzymatic activity and the gene is located in the 10q23,24 chromosome. Previous studies have shown that serum or plasma from breast cancer patients enhances both heparanase isoforms expression in the healthy women lymphocytes. The aim of this study is to elucidate the mechanism of lymphocyte activation by tumor cells. In vitro assays demonstrated that co-culture medium obtained from a human breast cancer cell line (MCF-7) with healthy woman lymphocytes or plasma obtained from different types of cancer were able to stimulate both isoforms of heparanases. These results were obtained by immunocytochemistry and flow cytometry techniques. Using specific monoclonal antibody target to heparan sulfate proteoglycan F69-3G10 and digesting conditioned co-culture medium with heparitinases I and II it demonstrated that HS should be involved in the stimulatory effect upon lymphocytes. This data was confirmed using a monoclonal syndecan-1 antibody, MCA681-CD138. The combined results confirmed that lymphocytes heparanase isoforms expression may be stimulated by the presence of tumor. Furthermore, the mechanism of lymphocytes activation possibly involves heparan sulfate signaling that is secreted by tumor cells.

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