The Role of Heparan Sulfate Proteoglycans in the tumor invasion and metastasis

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Introduction. Metastasis is the spread of cancer from its primary site to other places in the body and is the leading cause for the high mortality of malignant disease, including breast cancer. Cell surface heparan sulfate proteoglycans (HSPGs), syndecans and glypicans, play crucial roles in the functional properties of cancer cells, such as proliferation, adhesion, migration and invasion. The objective of this study is to evaluate the role of Syndecan-1 (Sdc-1) and Glypican-1 (Gpc-1) on the invasiveness and metastatic potential of tumor cells. Material and Methods: The ability of overexpressing wildtype Sdc-1 (WT) or a construct Sdc-1 without the cytoplasmatic domain (392) MDA-MB-231 cells in adhering to and transmigrating through murine endothelial cells (bEnd.3) monolayer was evaluated by static cell adhesion assay and transmigration assay, respectively. Results and Discussion: Comparing both cell lines, it was observed that 392 cells showed higher adhesion to endothelium and a higher number of 392 cells transmigrated through endothelium. In fact, invasive MDA-MD-231 cells have showed lower expression of Sdc-1 in comparison with MCF-7, a non-invasive breast cancer cell, suggesting that sdc-1 on cell surface might somehow impair the interaction between tumor cells and endothelium. However, Sdc-1−/− bEnd.3 cells showed a lower interaction with tumor cells on adhesion assay, suggesting that Sdc-1 from endothelial cells, but not from MDA-MB-231 is relevant for tumor cell-endothelial cells interaction. Conclusions: Previous studies have shown that the expression of Gpc-1 is increased according to the level of tumor invasion. Functional experiments with Gpc-1−/− stably transfected cells are being performed to evaluate the role of Gpc-1 on tumor progression.

Key words: heparan sulfate; glypican-1; syndecan-1; tumor invasion; metastasis

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