Galectin-1

Is a galectin differentially expressed by various normal and pathologic tissues and displays a wide range of biological activities. In oncology, galectin-1 plays a pivotal role in tumor growth and in the multistep process of invasion, angiogenesis, and metastasis. Evidence indicates that galectin-1 exerts a variety of functions at different steps of tumor progression. Moreover, it has been demonstrated that galectin-1 cellular localization and galectin-1 binding partners depend on tumor localization and stage. Recently, galectin-1 overexpression has been extensively documented in several tumor types and/or in the stroma of cancer cells. Its expression is thought to reflect tumor aggressiveness in several tumor types. Galectin-1 has been identified as a promising drug target using synthetic and natural inhibitors. Preclinical data suggest that galectin-1 inhibition may lead to direct antiproliferative effects in cancer cells as well as antiangiogenic effects in tumors [1)].

Benign fibro-osseous lesions (BFOLs) are a diverse group of lesions showing considerable degree of overlap with low grade osteosarcoma (LGOS). Further, de-differentiated osteosarcoma (DOS) is usually indistinguishable from conventional high-grade OS (COS) if LGOS foci are not identified. Thus, there is a need for adjunctive immunohistochemical markers to differentiate OS from benign FOLs as well as DOS from COS. A study of Kaur et al. evaluated the role of immunohistochemical expression of MDM2, CDK4, parafibromin, BCL-2 and Galectin-1 (Gal-1) in accurate characterization of benign FOLs and in differentiating them from OS. They retrieved 101 tissue samples which were diagnosed as osteosarcoma (OS) /ossifying fibroma (OF) / fibrous dysplasia (FD) or fibrous hyperplasia (FH) and examined their immunohistochemical staining pattern with the aforementioned antibodies. MDM2 showed 100% specificity for diagnosing OS. CDK4 and Gal-1 showed linear increase in immunoexpression from benign BFOLs to OS. BCL-2 showed equivocal immunopositivity in OF and OS, but the positivity was higher than that observed in FD. The highest immunoexpression for parafibromin was seen in FD followed by OF and OS cases. Thus, MDM2 is most specific, and Gal-1 is most sensitive of all the markers studied in differentiating OS from benign mimics. Combination of these two markers can be used as an adjunct to conventional imaging and microscopy in accurate characterization of these lesions. Further MDM2 overexpression can differentiate DOS and COS. [2)].

Galectin-1 is a glycan-binding protein, which is involved in the aggressiveness of glioblastoma (Glioblastoma) in part by stimulating angiogenesis. In different cancer models, galectin-1 has also been demonstrated to play a pivotal role in tumor-mediated immune evasion especially by modulating cells of the adaptive immune system. It is yet unknown whether the absence or presence of galectin-1 within the glioma microenvironment also causes qualitative or quantitative differences in innate and/or adaptive antitumor immune responses. All experiments were performed in the orthotopic GL261 mouse high-grade glioma model. Stable galectin-1 knockdown was achieved via transduction of parental GL261 tumor cells with a lentiviral vector encoding a galectin-1-targeting miRNA. We demonstrated that the absence of tumor-derived but not of host-derived galectin-1 significantly prolonged the survival of glioma-bearing mice as such and in combination with dendritic cell (DC)-based immunotherapy. Both flow cytometric and pathological analysis revealed that the silencing of glioma-derived galectin-1 significantly decreased the amount of brain-infiltrating macrophages and myeloid-derived suppressor cells (MDSC) in tumor-bearing mice. Additionally, we revealed a pro-angiogenic role for galectin-1 within the glioma microenvironment. The data provided in this study reveal a pivotal role for glioma-derived galectin-1 in the regulation of myeloid cell accumulation within the glioma microenvironment, the most abundant immune cell population in

high-grade gliomas. Furthermore, the prolonged survival observed in untreated and DC-vaccinated glioma-bearing mice upon the silencing of tumor-derived galectin-1 strongly suggest that the in vivo targeting of tumor-derived galectin-1 might offer a promising and realistic adjuvant treatment modality in patients diagnosed with Glioblastoma [3].

Galectin-1 is involved in pathological disorders like tumor endothelial cell adhesion and migration and therefore presents a relevant target for therapeutic intervention against cancer.

Malignant glioma cells suppress natural killer (NK) immune surveillance by overexpressing the β-galactoside-binding lectin galectin-1. Conversely, galectin-1 deficient glioma cells could be eradicated by host NK cells prior to the initiation of an anti-tumor T-cell response. In vitro experiments demonstrated that galectin-1 deficient GL26-Cit glioma cells are ~3-fold more sensitive to NK-mediated tumor lysis that galectin-1 expressing cells.

This findings suggest that galectin-1 suppression in human glioma could improve patient survival by restoring NK immune surveillance that can eradicate glioma cells [4].

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