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Galectin-1 as a potent target for cancer therapy: Role in the tumour microenvironment

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Galectin-1 is a hypoxia-inducible β-galactoside binding lectin protein produced by a wide range of cancer cells and plays a number of significant processes within the tumour microenvironment. In the present study, we investigated novel mechanisms for galectin-1-induced immunosuppression, tumour angiogenesis and metastasis, and further examined whether blocking galectin-1 carbohydrate recognition domains (CRDs) using thiodigalactoside (TDG) or knocking down the expression of galectin-1 (G1KD) by shRNA would exhibit tumour suppressive effects. We firstly observed that TDG significantly inhibited galectin-1 binding to the endothelial substratums and surfaces of human endothelial cells associated with reduced endothelial cell proliferation and formation of capillary-like tubes in Matrigel. We further investigated in vivo effects of inhibiting galectin-1 using the B16F10 melanoma, 4T1 breast and CT26 colon carcinoma models. TDG treatment or G1KD significantly reduced tumour angiogenic activities as well as increased both $CD4^+$ Th cell and $CD8^+$ CTL tumour infiltration, resulting in enhanced responses of effector T cells within the tumour microenvironment. In combination with either doxorubicin, anti-cytotoxic T lymphocyte antigen-4 (CTLA-4) mAb (9H10), adenosine receptor ($A_{2A}R$) antagonist (SCH58261) or B7.1 expressing cancer cell vaccine, galectin-1 inhibition prolonged overall survival of the tumour bearing mice. Moreover, anti-metastatic effects of targeting galectin-1 were also confirmed by using 4T1.2 mCherry+ breast cancer and CT26 colon cancer cell lines. Metastatic foci were significantly reduced by either TDG or shRNA galectin-1 knockdown (G1KD), associated with increased $CD4^+$ and $CD8^+$ T cell levels in the peripheral blood. Interestingly, the expression of cancer stem cell markers, CD44 and CD326 in breast and colon cancer and CD271 and ABCB5 in melanoma were correlated with galectin-1 expression in the lung metastatic lesions, suggesting an association of galectin-1 with cancer stem cells. In conclusion, the present study confirmed that targeting galectin-1 could represent a novel and effective novel anti-cancer and anti-metastatic strategy.

Biography

Koichi Ito is currently a third year of his Ph.D in School of Medical Science, Griffith University, Australia. He has published total six publications during his Ph.D. His current interests in cancer research are roles of glycan recognizing proteins in cancer progression and metastasis.

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