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Harnessing novel biomarkers of human embryonic stem cells for cancer diagnosis and therapy

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Human embryonic stem cells (hESCs) are defined as a group of cells at the preimplantation stage of embryo, with the capacity for self-renewal and differentiation to generate different types of cells and tissues. Cancer stem/initiating cells (CSC) also possess the capability of stem cells to multiply and differentiate into their progenies, display resistance to chemotherapy and radiation therapy, and could be the root cause for relapse and metastasis of cancerous tumors. On the cell surface, more than 85% of proteins are glycosylated. Recent studies indicated that glycosphingolipids (GSLs) are ubiquitous components of cell membranes and, similar to surface glycoproteins, can act as mediators of cell adhesion and signal transduction. Therefore, a systematic survey of expression profiles of GSLs and glycoproteins in hESCs and various differentiated derivatives was carried out. Based on MALDI-MS and MS/MS analyses, we have found a number of unique expressions of GSLs in the undifferentiated hESCs and induced pleuripotent stem (iPS) cells, and also a close association of the GSL expressions in hESCs and iPS cells with differentiation. On the other hand, Globo H, a known biomarker for cancers, was highly expressed uniquely in undifferentiated hESCs and iPS cells. This and other ESC signatures unique for hESCs and iPS cells will perhaps be the targets of therapy for cancers. In addition, we had also employed glycoproteomics and glycan analysis to analyze the expression of sialylated N-glycoproteins for hESCs. We have identified seven newly found surface N-linked sialoglycoproteins that are expressed abundantly in hESCs prior to differentiation and their expression levels are many folds higher in breast cancer CSC as compared to non-CSC. For example, silencing of ESC02 leads to decrease in cell proliferation of hESCs and mammary sphere formation of breast cancer, leading to cell arrest. In addition, loss-of-function of ESC02 results in developmental skewing toward endoderm/mesoderm differentiation in vitro and in vivo. These findings warrant the development of ESC02 as target for new therapy. Furthermore, ESC02 sheds to the plasma, resulting in higher level of auto Abs detected in patients with breast cancer. The area under receiver operating characteristic curve (ROC) for these auto Abs in patients was 0.86, indicating excellent discrimination for cancer diagnosis. Therefore, these newly found GSLs and glycoproteins present in hESCs and iPS cells could be candidates for cancer diagnosis and glycan-targeted therapy of tumors.

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