東北医科薬科大学

審査学位論文（博士）要旨

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Functional analysis of *N*-acetylglucosaminyltransferase-I: a novel regulator of epithelial-mesenchymal transition

［論文内容要旨］

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平成 31 年 3 月

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Functional analysis of *N*-acetylglucosaminyltransferase-I: a novel regulator of epithelial-mesenchymal transition

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N-Glycans are involved in numerous biological processes such as cell adhesion, migration and invasion. To distinguish their functions of complex high mannose types of *N*-glycans, we used the CRISPR/Cas9 system to establish *N*-acetylglucosaminyltransferase I (GnT-I)-knockout cells (KO). Loss of GnT-I greatly induced cell-cell adhesion, and decreased cell migration. In addition, the expression levels of the epithelial-mesenchymal transition (EMT) markers such as α-SMA, vimentin and N-cadherin were suppressed, while the expression of claudin-1 was promoted, suggesting a mesenchymal-epithelial transition-like phenotype, an opposite process to the EMT, was occurred in the KO cells. The phosphorylation levels of Smad2 and EGFR, as well as those of integrin-mediated FAK were consistently suppressed. Furthermore, the restoration of GnT-I in the KO cells suppressed the cell-cell adhesion and augmented the expression of EMT markers as well as that of FAK activation. The expression levels of integrins were upregulated in the KO cells although their functions were decreased, while their expression levels were downregulated in the rescued cells, which suggested a negative feedback loop between function and expression. Finally, we also found that the expression of GnT-I was important for cell survival, resistance to cancer drugs, and increased colony formation. The results of the present study clearly demonstrate that GnT-I works as a switch to turn on/off EMT, which further supports the notion that on most of surface receptors, the *N*-glycans differentially play important roles in biological functions.

〈参考文献〉主論文，参考論文

Zhang, G., Isaji, T., Xu, Z., Lu, X., Fukuda, T.,Gu, J. *N*-acetylglucosaminyltransferase-I as a novel regulator of epithelial-mesenchymal transition. ***FASEB J***. 2019;33(2):2823-2835

Lu, X., Zhang, D., Shoji, H., Duan, C., Zhang, G., Isaji, T., Wang, Y., Fukuda, T., Gu. J, Deficiency of α1,6-fucosyltransferase promotes neuroinflammation by increasing the sensitivity of glial cells to inflammatory mediators. ***Biochim Biophys Acta Gen Subj***. 2019;1863(3):598-608