東北医科薬科大学

審査学位論文（博士）要旨

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Importance of *O*-GlcNAcylation in cell adhesion and migration

［論文内容要旨］

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Importance of *O*-GlcNAcylation in cell adhesion and migration

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O-GlcNAcylation is a post-translational modification of protein serine, or threonine residue catalyzed by *O*-GlcNAc transferase (OGT) in the nucleus and cytoplasm. *O*-GlcNAcylation plays critical roles in the cellular signaling that affects the different biological functions of cells depending upon cell type. However, the molecular mechanisms that how the *O*-GlcNAcylation regulates cell migration remains unclear. Here, we used the doxycycline (DOX) inducible short hairpin RNA (shRNA) system to establish an OGT knockdown (KD) HeLa cell line and found that *O*-GlcNAcylation is a key regulator for cell adhesion, migration, and focal adhesion (FA) complex formation. The expression levels of OGT and *O*-GlcNAcylation were remarkably suppressed 24 h after induction of DOX. Knockdown of OGT significantly promoted cell adhesion, but it suppressed the cell migration on fibronectin. The immunostaining with paxillin, a marker for FA plaque, clearly showed that the number of FA was increased in the KD cells compared with that in the control cells. The *O*-GlcNAcylation levels of paxillin, talin, and focal adhesion kinase (FAK) were downregulated in KD cells. Interestingly, the complex formation between integrin β1, FAK, paxillin, and talin was greatly increased in KD cells. Consistently, levels of active integrin β1 were significantly enhanced in KD cells, while they were decreased in cells overexpressing OGT. Taking together, these data suggest a novel regulatory mechanism where loss of O-GlcNAclyation may promote focal adhesion complex formation, thereby affecting integrin-mediated functions such as cell adhesion and migration.

＜参考文献＞主論文，参考論文

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