東北医科薬科大学

審査学位論文（博士）要旨

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EpCAM regulates cell adhesion and migration in cancer cells

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The epithelial cell adhesion molecule (EpCAM) is one of the most frequently and intensely expressed of tumor-associated antigens, but the role that EpCAM plays in the proliferation, adhesion and migration properties of cancer cells remains unclear. In the present study, we screened several tumor cell lines and found that colorectal cancer CW-2 and epidermoid carcinoma A431 cells expressed relatively higher levels of EpCAM. In order to assess the biological functions of EpCAM expression in cell adhesion and migration, we established a knock out (KO) of EpCAM genes in both of these types of cancer cells via a CRISPR/Cas9 system. The elongated cell morphology was converted to a rounded morphology in the EpCAM-KO cells. These cells showed decreases in cell proliferation and migration into extracellular matrix proteins, as well as decreases in cellular signaling elements such as phosphorylated focal adhesion kinase (FAK), AKT and ERK. Moreover, the cell growth and the colony formation abilities were significantly decreased in EpCAM-KO cells. Importantly, co-immunoprecipitation analysis revealed that EpCAM associated with integrin β1. Also, the expression levels of integrin α5 were decreased in EpCAM-KO cells, compared with that in the wild-type cells. Taken together, these data clearly demonstrate that EpCAM associates with integrin β1 to regulate FAK/ERK signaling pathways in controlling cell adhesion, migration and proliferation via extracellular matrix adhesion, which provides novel mechanisms for EpCAM-mediated biological functions and cancer phenotypes.

〈参考文献〉　主論文，参考文献

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