Expression of Claudin-4 in Human Urothelial Cancer and Renal Cell Carcinoma

Introduction and Objective: Caludin-4(Cldn4) is a member of Cldns which are the major transmembrane protains among the molecular components tight junctions. They act as a semipermeable barrier to the paracellular transport of ions and solutes, and as barriers in epithelial and endothelial cells by mediating adhesion between cells. In several cancers, abnormal expression and cellular localization of Cldns, particular Cldn3 or Cldn4, were shown to contribute to tumor progression by affecting cell proliferation, cell invasion activities and metastatic behavior. On the other hand, the expression of Cldns are altered, both elevated and downregulated in several cancers, the exact roles of Cldns are still unclear. We examined the correlation between expression of Cldn4 and clinicopathological factors in urological cancers. We also examined Cldn4 effect for cancer cell proliferation and resistance to anticancer drugs *in vitro*.
Materials and Methods: A total of 86 urothelial cancer (UC) and 202 renal cell carcinoma (RCC) were examined. The expression levels of Cldn4 were assayed by immunohistochemistry with scoring the intensity and density. *In vitro* study, bladder cancer cell (T24) viability after treatment of Cldn4 antibody with or without CDDP was assayed by MTS assay.
Results: In UC, 83 cases (96.5%) showed expression of Cldn4, and 62 cases (72.1%) overexpressed compare to adjacent normal urothelia. The expression level significantly correlated with T and N categories. In RCC, 127 cases (62.9%) showed expression of Cldn4, and 34 cases (16.8%) showed overexpression compared to normal tubular epithelium. The expression level did not correlate with TNM categories, however correlated with stage significantly. *In vitro*, T24 growth was inhibited by Cldn4 antibody treatment in a dose dependent manner. Furthermore, the sensitivity for CDDP increased by the Cldn4 antibody treatment.
Conclusion: These data suggested that Cldn4 potentially promoted cancer cell growth. In addition, Cldn4 might play a role as a fence against anticancer drugs. We refer to the cancer cell promotion roles of Cldn4 from the perspective of apoptosis-associated cell signaling pathways in the presentation.