that ZnT5 and ZnT6 heterodimers are required to activate several proteins that play important roles in tumorigenesis, infiltration, and metastasis. However, the functions of ZnT5 and ZnT6 heterodimers in breast cancer remain unknown. Therefore, in this study, we first immunolocalized ZnT5 and ZnT6 in 113 pathological specimens of breast cancer. We then analyzed the interaction between ZnT5 and ZnT6 in breast cancer tissue using proximity ligation assay (PLA). Further, we evaluated cell migration and the expression of epithelial mesenchymal transition (EMT) markers as well as vimentin and E-cadherin in ZnT5 knockdown MCF-7 cells using siRNA. Next, we utilized human phosphorylation multipathway profiling array to explore the underlying mechanism of ZnT5 knockdown-induced cell migration. Immunohistochemical analysis revealed that the number of ZnT5-positive breast cancer cells was significantly higher in patients with a low pathologic N factor, and the number of ZnT6-positive breast cancer cells was significantly higher in patients with a low histological grade. The number of ZnT5 and ZnT6 double-positive breast cancer cells was significantly higher in patients with low Ki-67 expression than those with ZnT5-positive and ZnT6-negative breast cancer cells. In addition, ZnT5 and ZnT6 heterodimers were detected using PLA in breast cancer tissues with high expression of both ZnT5 and ZnT6. Treatment with 100 μM ZnCl 2 inhibited migration of MCF-7 cells, but ZnT5 knockdown promoted cell migration. ZnT5 knockdown induced higher levels of vimentin and lower levels of E-cadherin and activated SMAD1 in the presence of 100 μM ZnCl 2 . These results indicate that the involvement of ZnT5 in the inhibition of EMT through SMAD1 inactivation. These results also indicate that the role of ZnT5 and ZnT6 heterodimers differs from that of the ZnT5 homodimer in cell proliferation. However, further studies are required to clarify the role of zinc transporters and zinc signaling in breast cancer.

Presentation: No date and time listed

Abstract citation ID: bvac150.1815

Tumor Biology

ODP562

ZnT5 Involvement in EMT in Breast Cancer

Yasuhiro Miki, DVM, PhD, Erina Iwabuchi, PhD, Junyao Xu, MD, Takanori Ishida, MD, PhD, and Hironobu Sasano, MD, PhD

The zinc levels in breast cancer tissue are reportedly higher than in normal tissue. In addition, the expression levels of zinc transporters, including ZnT5 and ZnT6, in breast cancer tissue are higher than in normal breast tissue. Moreover, ZnT5 and ZnT6 contribute to the formation of heterodimers and are involved in different biological functions. In vitro studies using chicken DT40 cells showed