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cxcr4 promotes oral squamous cell carcinoma migration and invasion through inducing expression of mmp-9, 13 via the erk signaling pathway

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The increased migration and invasion of oral squamous cell carcinoma cells are key events in the development of metastasis to the lymph nodes and distant organs. Although the chemokine receptor CXCR4 and its ligand, stromal-cell-derived factor-1α, have been found to play an important role in tumor invasion, its precise role and potential underlying mechanisms remain largely unknown. In this study, we showed that knockdown of CXCR4 significantly decreased Tca8113 cells migration and invasion, accompanied with the reduction of MMP9 and MMP13 expression. Inhibition of ligand binding to CXCR4 by a specific antagonist TN14003, also led to reduced cancer cell migration and invasion. Because the degradation of the ECM and the basement membrane by proteases, such as matrix metalloproteinases (MMPs) is critical for migration and invasion of cancer cells, we investigated the expression of several MMPs and found that the expression of functional MMP9 and MMP13 was selectively decreased in CXCR4 knockdown cells. More importantly, decreased cell migration and invasion of CXCR4 knockdown cells were completely rescued by exogenous expression of MMP9 or MMP13, indicating that the two MMPs are downstream targets of CXCR4-mediated signaling. Furthermore, we found the level of phosphorylated extracellular signal-regulated kinase (ERK) was significantly decreased in CXCR4-silenced cells, suggesting that ERK may be a potential mediator of CXCR4-regulated MMP9 and MMP13 expression in Tca8113 cells. Taken together, our results strongly suggest the underlying mechanism of CXCR4 promoting Tca8113 migration and invasion by regulating MMP9 and MMP13 expression perhaps via activation of the ERK signaling pathway.

Biography

Yingying Wu is a Ph.D student at the age of 27 years from Sichuan University, China. She has published more than 5 papers in reputed journals.