Binding of galectin-1 to CA125 promoted tumor invasion and progression in ovarian cancer

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BACKGROUND: Ovarian carcinoma is the second most common gynecological cancer but the leading cause of death from gynecological malignancies in the world. The 5-year survival rate of epithelial ovarian cancer (EOC) patients has improved very little in the past decade, only 20% - 30% with the standard treatment of debulking surgery followed by paclitaxel and platinum (TP) chemotherapy. Therefore, the development of novel molecular approaches is of particular importance for combined modality treatments of EOC. CA125 is one of the most commonly used diagnostic antigens of ovarian cancer, although its biochemical nature has long been elusive. Only recently, its primary structure was elucidated, demonstrating that CA125 shows several unusual features. Galectin-1 is a prototype galectin that share a conserved carbohydrate recognition domain of about 130 amino acids. There is direct evidence that galectin-1 expression is necessary for the initiation of the transformation into malign phenotypes and for immunobiology. It has been implicated that CA125 represents a novel counter receptor for galectin-1.

HYPOTHESIS: This study is aimed at investigating the functional role, clinical implication and novel molecular mechanism of this interaction in EOC.

METHODS: Immunoprecipitation and immunofluorescence were used to show the specific binding of galectin-1to CA125 in EOC cell lines. The role of this interaction in EOC progression was evaluated in vitro by over-expression or knockdown galectin-1 in EOC cell lines. To elucidate the molecular mechanisms underlying the interaction-mediated tumor progression, we analyzed the expression and activities of some signaling molecules associated with galectin-1 and CA125 by Western blotting. A tissue microarray containing samples from EOC patients was used to examine the relationship of galectin-1 and CA125 expressions in EOC.

RESULTS: We demonstrated that galectin-1 bound to CA125 in a specific manner in EOC cells. This binding promoted EOC cell invasion and migration, and CA125 releasing from OVCAR-3 cells. Blocking this interaction with anti-CA125 antibody resulted in the reduction in cell invasion and migration in vitro, which could be caused by high COX1 expression and MAPK/NF-kB activation. Finally, we show that CA125 and galectin-1 were co-expressed in advanced grade EOC. Taken together, our data indicated that galectin-1 was a novel CA125-binding protein and that the interaction of CA125 and galect-1 could contribute to the invasion and migration of EOC.