MEMBRANE TYPE 1 MATRIX METALLOPROTEINASE PROTEOLYTIC ACTIVITY IN INITIAL ADHESIVE AND INVASIVE EVENTS OF OVARIAN CANCER METASTASIS

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ABSTRACT

Epithelial ovarian cancer (EOC) metastasis involves detachment of epithelial cells from the primary tumor and dissemination into the peritoneal cavity as single cells and multicellular aggregates (MCA), which then adhere to and anchor in the mesothelial cell monolayer that lines the peritoneal cavity, to subsequently proliferate within the interstitial collagen-rich sub-mesothelial matrix and establish secondary lesions.

Proteolytic activity of membrane type 1 matrix metalloproteinase (MT1-MMP), a transmembrane proteinase that degrades interstitial collagen, has been directly implicated in both the invasion of the sub-mesothelial collagen I matrix and in the shedding of metastatic MCA, but the molecular mechanisms behind these events are not completely understood. The effect of MT1-MMP activity on ovarian tumor cell Mucin16/Cancer Antigen 125 (MUC16/CA-125) ectodomain shedding and the *in vitro* relationship between MT1-MMP and a potential phosphorylator, integrin linked kinase (ILK), on adhesion and invasion were assessed. Results suggest that ILK activity may catalyze phosphorylation of MT1-MMP to promote pro-metastatic events; additionally, MT1-MMP expression may induce MUC16/CA-125 ectodomain shedding.