

Gemcitabine-Ukrain Combination Affects MMP9 Expression in Primary Pancreatic Adenocarcinoma Cell Cultures (PPCCs)

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Context Pancreatic ductal adenocarcinoma (PDAC) is among the most lethal tumors mostly because of its invasive behavior and resistance to most chemotherapy regimens. Our previous results suggested that NSC-631570 (ukrain) modulates extracellular matrix remodeling of PDAC cell lines [1]. This study investigates the modulation of key determinants of invasive behavior such as MMP9 protein by gemcitabine-ukrain, using appropriate preclinical models. **Objective** This study investigates the modulation of key determinants of invasive behavior such as MMP9 protein by gemcitabine-ukrain, using appropriate preclinical models. **Methods** Two PPCCs and two cell lines of PDAC were seeded in multi-well chamber slides (8,000 each/well) and exposed to gemcitabine (10 nM), ukrain (1 µM) and their combination. After 48-h treatment the cells were stained with the polyclonal antibody (CST-Euroclone) for MMP9. Untreated cells were used to evaluate the basal level of MMP9, and while non-stained cells were employed as negative control. Protein expression levels were evaluated with novel software for image analysis,

checking both nuclei and cytoplasm staining intensity. Differences in expression values were compared by t-test/ANOVA analyses. **Results** We observed a significant reduction of MMP9 expression in both PPCCs treated with gemcitabine-ukrain combination with respect to their controls and to cells treated with gemcitabine or ukrain alone (P<0.01). Moreover, drug combination significantly reduced the number cells, and modified the structure of most nuclei with respect to untreated cells. **Conclusion** New approaches to reduce the metastatic behavior of PDAC are warranted, and gemcitabine-ukrain showed promising results in our preclinical studies. The new computerized approach to evaluate MMP9 staining at ICC is an ease-to-use and rapid method that should be further developed both in preclinical models and for IHC analyses of PDAC tissues.

Reference

1. Funel N, Costa F, Pettinari L, Taddeo A, Sala A, Chiriva-Internati M, et al., Ukrain affects pancreas cancer cell phenotype in vitro by targeting MMP-9 and intra-/extracellular SPARC expression. *Pancreatol* 2010; 10:545-52.