POSTER 115

MODELING PERITONEAL METASTASES OF OVARIAN CANCER

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The majority of women with ovarian cancer (EOC) are diagnosed with disseminated ip metastasis leading to a poor prognosis. Ovarian cancer is the most deadly gynecological cancer in the US due primarily to late diagnosis with already wide spread presence of metastases. The mechanism by which EOC are shed ip and anchor in the peritoneal mesothelium is poorly understood. Our goal is to establish in vitro organotypic and ex vivo models to better understand mechanistic aspects of EOC metastasis. We have developed a modified 3D in vitro model of the peritoneum to investigate this process. To generate “meso-mimetics”, primary peritoneal mesothelial cells (human, mouse, pig) or a mesothelial cell line (LP9) are layered upon a collagen I gel with embedded fibroblasts. Ex vivo studies use murine peritoneal tissue explants pinned to silastic resin. In both models, fluorescently labeled EOC cells are seeded onto the meso-mimetic or tissue explant as single cells or multi-cellular aggregates, and adhesion is monitored using confocal microscopy and relative fluorescence. Preliminary results show rapid robust adhesion of EOC to meso-mimetics and explants. Analysis of explants by scanning EM confirms these data and show mesothelial invasion by tumor cells within 24 h. Similar results were obtained using mice injected ip with fluorescently labeled ovarian cancer cells: adherent fluorescent cells were visible atop the peritoneum after 24 h, with tissue invasion observed after 72 hours. We have developed a comprehensive suite of assays for mechanistic analysis of key events that regulate EOC tumor progression to metastasis.