Ovarian cancer is the leading cause of death in women with gynecological malignancies. This is due to the fact that the cancer is most often found at late stages at which point it has already metastasized to other regions of the body. The omentum is a primary attachment site for ovarian cancer metastasis, accounting for 80% of serous papillary ovarian cancers. Recently, studies examining the omental tumor microenvironment have cited macrophages as a significant component in tumor cell migration and invasion.

Previous models for tumor cell and macrophage interaction have often been limited and fail to accurately represent \textit{in vivo} conditions.

We hypothesize that tumor associated macrophages (TAMs) play an integral role in the ovarian cancer microenvironment to enhance attachment and invasion onto the omentum surface.

We propose using a novel ovarian cancer model mimicking the omental microenvironment in order to study the interaction between macrophages and ovarian cancer during metastasis.

**Hypothesis**

We hypothesize that tumor associated macrophages (TAMs) play an integral role in the ovarian cancer microenvironment to enhance attachment and invasion onto the omentum surface.

**Novel in vitro co-culture models**

![Figure 1](image1.png)

**Figure 1** (A) Schematic of novel \textit{in-vitro} co-culture device. (B) Schematic of metastatic adhesions model with adherent ovarian cancer cells (green) in device on top of mesothelial cells (blue) conditioned with TAMs (white). (C) Schematic of metastatic clearance with adherent ovarian cancer cell spheroid (grey) in device on top of fluorescently-labeled mesothelial cells (green) conditioned with TAMs (white).

**Ovarian cancer spheroid characterization on collagen I**

![Figure 2](image2.png)

**Figure 2.** Spheroids seeded on top of 2.4 mg/mL collagen I for 48 hours with treatments listed. OVCAR5 and CaOV3 cell lines showed most invasive behavior, with the greatest dissemination of cells from the spheroid body.

**TAMs increase ovarian cancer adherence to mesothelial barrier**

![Figure 3](image3.png)

**Figure 3.** (A) Metastases adhesion model with adherent ovarian cancer cells (green) in device on top of mesothelial cells (blue) that have been conditioned with TAMs (white). (B,C) Conditioning of mesothelial barrier with TAMs increases ovarian cancer cell adherence (OVCA433, OVCAR5) onto mesothelial barrier compared to cell-free control by three hours. *p<0.05

**TAMs may increase ovarian cancer spheroid clearance through mesothelial barrier**

![Figure 4](image4.png)

**Figure 4.** (A) Model of metastases clearance through omental barrier with ovarian cancer cell spheroid (grey) in device on top of fluorescently-labeled mesothelial cells (green) that have been conditioned with TAMs (white). (B) Conditioning of mesothelial cell layer with TAMs before spheroid addition may facilitate spheroid clearance of mesothelial cell barrier in OVCA433 cell line. *p<0.05

**Conclusions**

We found that macrophage presence in the tumor microenvironment enhanced single-cell adhesion, as well as multi-cellular aggregate clearance of a mesothelial cell barrier, representative of the omentum.

**Future Directions**

Studies using these \textit{in vitro} metastatic microenvironment models can be expanded to study specific ligands secreted by macrophages that affect attachment and clearance, and eventually determine target treatment of these factors in the metastatic environment.

**References**


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