The Effect of Fluid Shear Stress on Ovarian Cancer Cell Viability and Organization
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Ovarian cancer cells are exposed to physical stress in the peritoneal cavity both during tumor growth and dissemination. Here we investigate how ovarian cancer cells of increasing aggressiveness respond to < 1 dyne/cm² of fluid-induced shear stress. While this biophysical stimulus significantly reduced cell viability in all cells, benign ovarian cells proved to be most sensitive. In more tumorigenic cell lines, fluid shear stress induced spheroid formation, associated with a more invasive phenotype and significantly altered cytoskeleton organization. Together, our findings suggest that shear stress can significantly impact ovarian cancer metastasis.

Introduction: All cells exist in a physiological environment that is impacted by chemical and physical factors. These stimuli affect tissue growth, organization and function but also contribute to diseases such as cancer.1 Epithelial ovarian cancer (EOC) has a 5-year survival rate below 30% since the majority of cases are diagnosed after metastasis where cells disseminate throughout the peritoneal cavity and are exposed to physical stresses.2 While neoplastic progression is a topic of much interest, there are few investigations in vitro into the effects of fluid-induced shear stress on EOC. We utilized our mouse ovarian surface epithelial (MOSE) model for this investigation since it uniquely transforms and progresses in vitro from a premalignant, non-tumorigenic (MOSE-E) to a slow-developing, malignant (MOSE-L) and finally, to a highly aggressive, fast-developing phenotype (MOSE-LFFL).3 We hypothesize that even at relatively small, physiological values of shear stress, long-term exposure to this shear force will significantly and differently impact the various stages of EOC cell survival, spheroid formation and cell cytoskeleton structure.

Materials and Methods: We first estimated the shear stress for our system to be ~0.14 dyne/cm² which is physiologically relevant.4 Cells were seeded and placed immediately (imm-) onto or allowed to adhere (adh-) before placement onto a Lab Rotator. MOSE cell viability (hemocytometer count), spheroid formation (imaging) and cytoskeleton structure (indirect immunofluorescence) were assessed at each, successive 96h time period (3 total). ANOVAs were used to determine significance (* indicates p <0.05 significance).

Results and Discussion: Shear stress significantly impacts cell viability at all stages of disease. In particular, shear stress induces spheroid formation in malignant cells (Figure 1) and induces cell death in benign cells (Figure 2). In addition, cytoskeleton structure is heavily impacted by fluid shear stress (results to be presented).

Conclusions: Physiological magnitudes of shear stress significantly impact MOSE cell viability at all stages of disease. Additionally, the continual fluid shear stress induces cell death in benign cells. Shear stress induces spheroid formation in the slow-developing and fast-developing stages of ovarian cancer. Lastly, cytoskeleton structure is heavily impacted by continual fluid shear stress.

Acknowledgements: This work was supported by NSF IGERT Grant 0966125.