High grade serous ovarian cancer (HGSOC) is the most lethal gynecological cancer, with a 5-year survival rate of less than 40%. Genomic analysis of HGSOC tumors indicates that there are few mutations that are present in more than 5% of patients, limiting the potential for available molecular-targeted therapies to even be examined in a clinical trial. For the last several years, my laboratory has been working to understand this complex disease to identify new targets that may have broader efficacy and to determine how to better apply existing therapies. In this talk, I will present recent work using tissue engineering and systems biology approaches to study metastasis in HGSOC, with a focus on the impact of the extracellular matrix and immune cells in this process.