Advances in early detection have improved patient outcomes for many types of cancer. However, for cancers that are typically diagnosed at advanced stages, such as ovarian cancer, the tumor cells have widely disseminated and therapeutic options are limited. Standard of care for ovarian cancer is surgical debulking followed by combination chemotherapy with platinum and taxane agents such as cisplatin and paclitaxel. While many patients initially respond to treatment, 20-30% of patients are resistant to the chemotherapy, as indicated by aggressive recurrence within six months of completing treatment. The lack of a method to rapidly predict a patient’s responsiveness to chemotherapy is a major challenge in clinical management of the disease. In this talk, I will describe an approach involving single cell immobilization in stiff silica-based biomaterials to distinguish chemoresistant ovarian cancer cells. Tumor cells selected for resistance to cisplatin or taxane are more readily able to transition to a non-proliferate state upon experiencing the stress of physical confinement, while most cancer cells die within days once immobilized. RNA-seq analysis of cells that survive immobilization has provided mechanistic insight into the signaling pathways enabling enhanced survival of chemoresistant cells. In addition, when compared to chemoresistant patient cohorts, immobilized cells share differentially expressed genes associated with platinum-resistance pathways. Current efforts are focused on validation of this diagnostic platform with patient tumor samples. Finally, I will discuss development of biomaterials that can associate with disseminated tumor cells within the body such that these cells can be ablated as an alternative treatment option for chemoresistant patients.