Ovarian cancer is the deadliest gynecological malignancy and the fifth leading cause of cancer death. Due to the lack of early symptoms, ovarian cancer is most commonly diagnosed in the distant stages, drastically reducing the 5 year survival rate from 92% in early stage diagnoses to 29% in advanced stage cases. This large difference is thought to be linked to the high rate of recurrence and development of drug resistance to chemotherapeutics in ovarian cancer patients. First-line therapy includes a combination of tumor resection surgery and chemotherapy regimen including cisplatin, a DNA-alkylating agent, and paclitaxel, a microtubule stabilization agent. However, treatment becomes more complex upon recurrence due to the development of drug resistance. Drug resistance has been linked to many mechanisms, including efflux transporters, dysregulation of apoptosis, autophagy, cancer stem cells, epigenetics, and the epithelial-mesenchymal transition. Due to the wide variety of mechanisms involved in resistance, developing and choosing effective therapies is extremely complex.

Liposomes demonstrate potential as delivery systems to combat drug-resistance in cancer due to their versatility in loading. Liposomes possess the ability to load multiple therapeutics to re-sensitize resistant cancer cells while simultaneously treating those cells with a chemotherapeutic agent. Here, a liposomal carrier for both paclitaxel and siRNA was designed and synthesized to provide a combinatorial therapy to re-sensitize drug-resistant ovarian cancer cells to paclitaxel and thereby increase the efficacy of paclitaxel. A custom siRNA array was developed, and we identified three possible gene targets, ABCB1, JAK2, and CFLAR, involved in the development of drug resistance in paclitaxel-resistant OVCAR3-TR ovarian cancer cells.

Two combinatorial, cationic liposomal delivery systems were designed and synthesized via the lipid film hydration method. Liposomes were characterized for size, surface charge, stability, and loading efficiencies. We demonstrated efficient loading of paclitaxel and protection of bound siRNA in both liposome formulations. Cellular uptake of the liposomes was confirmed using fluorescence microscopy. Overall, the liposomes show promise in loading both paclitaxel and siRNA to target genes involved in drug-resistance development in ovarian cancer cells.