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Ovarian cancer is the deadliest gynecologic cancer with a high mortality rate that has remained unchanged in the past four decades. Epithelial ovarian cancer, the most common type of ovarian cancer, initially responds to cisplatin therapy, but most patients acquire drug resistance and eventually succumb to the disease. New strategies to overcome drug resistance are urgently needed to improve prognosis.

The discovery of small interfering RNA (siRNA) by Fire and Mello in 1998 has provided new avenues of combating resistant cancers. Small interfering RNAs ma be able to Silence the genes that are involved in cisplatin resistance. But this strategy requires the development of novel vehicles that can specifically and effectively deliver cisplatin to cell nuclei and siRNAs to cell cytoplasms, respectively. [WHY?] We report here the first use of nanoscale metal-organic frameworks (NMOFs) for the co-delivery of cisplatin and pooled siRNAs.

Metal-organic frameworks (MOFs) are an emerging class of self-assembled, porous materials whose properties can be readily tuned by varying the molecular building blocks. Nano-sized MOFs have been used as nanocarriers for imaging contrast agents and chemotherapeutics. We hypothesized that the large pores of NMOFs could be used to load drugs such as cisplatin while the metal ions on the NMOF surfaces could be used to simultaneously bind siRNAs. We suspect that UiO NMOFs protect siRNAs from nuclease degradation, enhance siRNA cellular uptake, and promote siRNA escape from endosomes. In this work, we sequentially loaded into **UiO** NMOFs (by covalently attaching to bridging ligands inside the NMOFs and coordinating to metal sites on the NMOF surfaces, respectively). We found that co-delivery of cisplatin and siRNAs with NMOFs increased in vitro chemotherapy efficacy by 10-fold, as indicated by a cell viability assay, DNA laddering, and Annexin V staining.