Award ID:
RP130553

Project Title:
Exploration of synergistic effects by using a combination of two novel antitumor agents and nano-delivery vehicle to effectively treat resistant solid tumors

Award Mechanism:
Individual Investigator

Principal Investigator:
Zhang, Xiaoliu

Entity:
University of Houston

Lay Summary:

Many solid tumors are routinely treated with chemotherapy and more recently with targeted biotherapy. Despite the enormous progress made in recent years, therapy resistance and/or toxic side effects often limit their benefits. Therefore, new strategies are needed for further improvement. We have made significant progresses on improving both therapies. In our effort to improve chemotherapy, we have synthesized a new class of platinum-based anticancer drugs that exhibit lower cytotoxicity and increased potency than the currently used platinum drugs such as cisplatin. One of these compounds, R,R-D2, has been extensively characterized. It has excellent inhibitory values, not just against cisplatin-sensitive, but also cisplatin-resistant cancers. It possesses diverse antitumor mechanisms, including induction of tumor cell death and inhibition of blood vessel formation. In our efforts at developing novel anticancer biotherapy, we have developed a strategy, a modified T cell designated T-eCAR, that can selectively destroy tumor blood vessels. Our central hypothesis is that combining T-eCAR with R,R-D2 will lead to multi-layer synergy. Layer-1 of synergy will come from the improved delivery of R,R,-D2 via nanoparticles following T-eCAR mediated tumor blood vessel destruction. Layer-2 of synergy will come from the combined effect of T-eCAR mediated tumor blood vessel destruction and inhibition of blood vessel formation by R,R-D2. Together, they will produce a potent therapeutic effect against hard-to-treat tumors, such as ovarian, head and neck, and lung cancers, which are examined in this proposal. We have designed three Specific Aims composed of a series of cell culture (in vitro) and animal (in vivo) experiments to test our central hypothesis. Our ultimate goal is to develop a rationally designated therapeutic regimen that can be translated into the clinics in the near future to benefit patients who suffer from these malignancies.