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Title: Potassium Ionophore-Based Lipid Nanoparticles for Treatment of Solid Tumors with Necrosis

Necrosis is a feature of many solid organ tumor types that correlates with poor prognosis of cancer patients. Necrotic cells spew their intracellular contents into the extracellular space of tumors and induce various adverse effects. K+ released from necrotic cells profoundly suppresses the function of effector T cells in the tumor microenvironment. This seminal discovery provides new insights into the mechanism of cancer persistence and offers a potentially new therapeutic target and strategy for cancer treatment. In this project, we seek to develop a generic nanoparticle platform for the imaging of K+ in a tumor, the absorption of excess K+, and the release of chemotherapeutic drugs triggered by K+. Optical imaging of tumor K+ will provide molecular-level information on the tumor status and will facilitate personalized cancer therapy. Additionally, the sequestration of immune-suppressive K+ into nanoparticles will unleash the immune system to fight cancer. The sequestration process can further trigger the localized release of drugs such as doxorubicin for targeted cancer chemotherapy.