

Harnessing Vascular and Cellular Depots of Nanotherapeutics for the Treatment of Metastatic Breast Cancer

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Breast cancer metastases to distant organs are responsible for the majority of breast cancer deaths. Current breast cancer drugs are very effective at killing cancer cells in a petri dish; yet, they are utterly ineffective at curing metastases in patients. One major reason for their clinical failure is the existence of multiple biological barriers inside the body that block drug access to the disease tissues. A study estimated that less than 0.1% of the total injected drugs could reach the tumor tissue, and the rest drug molecules go to healthy tissues and kill normal cells. That is why most chemotherapy drugs cause severe toxicity to the body, such as hair loss, nausea, internal bleeding, and, in the case of doxorubicin, severe damage to the heart. In a recent article published in *Nature Biotechnology*, we have listed the major biological barriers, and provided strategies to develop new drugs and drug formulations to overcome such barriers. Following this design map, we have developed a multi-component, multi-functional drug that accumulates at the major metastatic sites of breast cancer. In preclinical studies, we have demonstrated long-term survival in about 50% of the tumor-bearing mice in two murine models of triple negative breast cancer metastases to the lung and liver. In the current study, we will develop strategies to further block drug entrapment by the normal cells, and divert drug accumulation to the tumor cells inside these organs.