NT-06. PHOSPHATIDYLSERINE-SELECTIVE TARGETING AND ANTICANCER EFFECTS OF SapC-DOPS NANOVESICLES ON BRAIN TUMORS
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Despite significant advances in our understanding of the biology of CNS tumors, the translation of such knowledge to novel and effective therapeutic strategies has been slow. Consequently, both primary (e.g., glioblastoma multiforme) and secondary (metastatic) brain tumors remain among the most intractable and fatal of all cancers. We have shown that nanovesicles consisting of saposin C (SapC) and dioleylphosphatidylserine (DOPS) effectively target and kill brain tumor cells both in vitro and in vivo. These actions are a consequence of the affinity of SapC-DOPS for phosphatidylserine (PS), an acidic phospholipid abundantly present in the outer membrane of a variety of tumor cells and tumor-associated vasculature. Here, we characterize SapC-DOPS bioavailability in a human glioblastoma orthotopic mouse model and reveal a time-dependent, tumor-specific extravascular accumulation of fluorescently labeled SapC-DOPS. Glioblastoma targeting by SapC-DOPS is abrogated after in vivo exposure to lactadherin, a protein that binds PS with high affinity. We also demonstrate that SapC-DOPS selectively targets brain metastases-forming cancer cells both in vitro, in co-cultures with human astrocytes, and in mouse models bearing brain metastases derived from human breast or lung cancer. We finally that SapC-DOPS cytotoxic activity against metastatic breast cancer cells in vitro, and prolongs the survival of mice with breast cancer brain metastases. Taken together, these results suggest that surface-exposed PS can be potentially useful as a novel lipid marker for diagnosis, monitoring, and therapy of central nervous system cancer, and highlights the potential of SapC-DOPS in the diagnosis and treatment of primary and metastatic brain tumors.