Public/Lay Abstract (1-page limit)

Breast cancer affects 1 in 8 women over a lifetime with about 310,000 new cases per year. Despite years of advances, a stubborn 20% are afflicted with metastatic breast cancer—which accounts for 90% of deaths. The triple negative breast cancer subtype (TNBC) accounts for about 20% of all breast cancer, but the rate of TNBC metastatic disease is 40%. A major impediment to improved survival of metastatic breast cancer patients are fatal central nervous system (CNS) metastases, which are comprised of metastases to the brain parenchyma and/or to the leptomeninges. Currently, metastases at extracranial sites are held at bay with maintenance treatment, but the irony of better treatment of extracranial metastases is an increase in CNS metastases due to longer survival and that treatments do not cross the blood brain barrier. Fatal CNS metastases are estimated at 20% in all metastatic breast cancer patient with 40% in TNBC patients. Unquestionably, effective treatment for CNS metastases will greatly advance metastatic patient outcomes.

A solution to be improved. Immune checkpoint inhibitors (ICI) (e.g. anti-PDL1 and Anti PD1) re-engage the local tumor immune environment to enact tumor destruction and would be excellent for the metastatic patient. Soberingly, only about 25% of cancers have excellent results with a glaring 75% with modest to no results, including TNBC. The non-responsive tumors (denoted “cold”) have features that escape immune-mediated destruction and ICI action. Essentially, cold tumors do not respond to ICI, whereas hot tumors do respond. The degree of cold-to-hot (C-H) is a property of the cancer. Borrowing from other cancers, there have been great outcomes that we would like to import for breast cancer patients. Former president Jimmy Carter was diagnosed at age 90 in 2015 with melanoma and brain metastases and was one of the first patients to receive the Keytruda ICI for his “hot” tumors. He remains alive today at age 99. We seek to make “Jimmy Carter” outcomes for the metastatic breast cancer patients. TNBC and most breast cancers are cold tumors, so drugs that enact C-H reprogramming (or C-H drugs) would improve ICI susceptibility. A potential C-H drug would have wide ramifications for all cancer patients, especially the 75% with no-to-modest responses. We at Cha Therapeutics have discovered a first in class C-H drug for TNBC. Cha 1 is a proprietary combination of the principal compound in green tea and epigenic disruptor decitabine. Our studies show pre-clinical efficacy for endowing anti-PDL1 efficacy for TNBC and a subset of brain metastases and first-in-human safety. We hypothesize that judicious combination of Cha1 and anti-PDL1 may prime CNS metastatic disease for ICI destruction, thus increasing efficacy for TNBC and otherwise fatal brain metastases and with improved safety. This grant is a comprehensive investigation for TNBC and brain metastases and a road map for expedited path to patient application. We prioritize science and safety in our studies and engage patient advocates in the design of patient-friendly therapeutics. If successful, we would advance life-saving treatment for metastatic breast cancer patients and dramatically increase survival. This Metavivor project is a joint venture between Tufts and Cha Therapeutics leveraging the strengths of each partner for the ultimate benefit of the breast cancer patients.