

METAvivor Final Report, Lay Summary

Early Career Investigator Award

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The goal of the proposed studies was to evaluate the potential use of extracellular vesicles (EVs) as therapeutic carriers in breast cancer brain metastases. We used super paramagnetic iron oxide nanoparticles (SPIONs) to label the EVs (FeEVs), which enabled them to be imaged by magnetic particle imaging (MPI). In culture, we found an increased uptake of FeEVs into cancer cells, versus SPION only. In a mouse model, the FeEV were retained in primary mammary fat pad tumors (80% retention), over 72h, whereas the group which were injected with SPION only had a significant decrease in iron content over time (10% retention). This suggests that the EV coating played a role in retention, perhaps through cellular uptake or other interactions with the tumor microenvironment. Further, FeEV were able to cross the blood-brain-barrier, and were identified using MPI in the brain of mice which had brain metastases, but not those which were healthy. No MPI signal was detectable in mice with brain metastases injected with the SPION only. Further, there was no evidence of BBB disruption; each of these findings suggest that the EVs mediated crossing of the intact blood-brain-barrier, resulting in brain accumulation in mice burdened with brain metastases. These findings will allow for, and encourage further studies using EVs to carry therapeutics, targeting hard to treat breast cancer brain metastases.