**Lay Summary**

Three manuscripts reporting on findings funded, at least partially, by METAvivor were published in 2021. Three additional manuscripts which leverage some of the studies funded by METAvivor were also published.

**Funding support obtained with METAvivor data if any, and goal of the support**

We’ve initiated collaborations with Dr. Isidore Rigoutsos at Thomas Jefferson University to explore the role of the tRNA fragments in TNBC and other breast cancer metastasis. The results from his lab and ours have been pooled together and formed the basis for multiple submitted proposals that are still to be reviewed.

**Summary of important findings**

The main goal of this project was to begin defining the mechanism of action for a metastasis suppressor, BRMS1. That information is essential for future development of therapeutics from based upon BRMS1. We were able to demonstrate that a modification of the BRMS1 protein affects the effectiveness of metastasis suppression. This study also showed the portion of the BRMS1 molecule which needs to remain intact if we are to use BRMS1 as a metastasis suppressing therapy. Another intriguing, though replicated, finding is that a 16 amino acid fragment of BRMS1 may indeed be sufficient to block metastasis.

A second major finding which will be critical for translating our laboratory experiments into clinical practice is that the proteins with which BRMS1 interacts are altered, depending upon the protein modification mentioned above. We also obtained preliminary structural information regarding the BRMS1 protein and the portion of the BRMS1 molecule from which drugs could be modeled.

Unfortunately, COVID19 policies severely limited progress. The scope of our research has been modified. However, we will continue this line of investigation as long as Ms. Zimmermann is still in the laboratory. She is expected to defend her dissertation in spring 2022.

 **Clinical relevance of findings i.e., upcoming/in progress trials, impact on MBC treatment**

 Our hope is based upon clinical data showing that BRMS1 expression is decreased as many cancer types, including breast, gain the ability to metastasize. We predict, therefore, that restoring or replacing BRMS1 will prevent new metastases and may, in fact, stop the outgrowth of seeded metastases. If we are lucky, getting BRMS1 back into metastatic cells may result in the elimination of already established metastasis.

We have begun discussions with colleagues to develop nano delivery mechanisms in order to get BRMS1 and/or the BRMS1 fragment into breast cancer cells. These discussions are at an early stage and we hope that by the next progress report we will have a fully fleshed out plan.