Metavivor Inc. 2022 PI: Welch, D.R.

## **PUBLIC ABSTRACT**

Metastasis remains the most life-threatening property of cancer cells. Yet still relatively little is known about what drives cancer cells to become metastatic and deadly. Even less is known about why some people's cancer becomes metastatic while others with the same risk factors do not. We know disparities, based upon ancestry or race, do exist. But why? Our preliminary data, using a unique mouse model we developed, identified molecules that could explain racial disparities in metastasis in addition to fundamental knowledge about how metastases develop. Those molecules are fragments from a transfer RNA (tRNA) encoded in the mitochondria (an organelle usually associated linked with energy production within cells). Like with different human races, the sequences of the mitochondrial genes vary in different mouse strains. Similarly, the tRNA fragments (tRF) derived from the tRNA reflect those genetic differences. This project takes first steps to map out the exact nature or features the of tRNA/tRF. Once we do that, we will begin testing how they work. In a series of biochemical studies, we will address these questions: How are the tRF made? Are they differently modified, expressed, or localized? Do those modifications affect how they work? What other molecules do the tRF interact with or work with? Are there analogous human tRF that similarly change in human cancer? Where are the tRF found inside or outside cells? Is tRF expression tissue specific?

Once these basic questions are answered, we will have the critical information required to test directly whether the racially distinct mitochondrial tRF are responsible for controlling metastasis. If they are, as our preliminary data suggest, then the tRF could become anti-metastatic targets for treating (and possibly preventing) metastasis. Also, the tRF could become markers to monitor whether treatments are successful or when recurrence might be imminent.