**METAvivor Progress Report**

**Lay Description of Important Outcomes**

We have made progress in understanding how treatment with a drug that alters gene expression, called an epigenetic modulating drug, changes immune cell function by decreasing immune suppression. This decrease in suppression paves the way for other immunotherapy treatments called immune checkpoint inhibitors, to eliminate tumors. Our understanding of how these drugs work in combination with each other has provided enough evidence to begin planning a phase 2 clinical trial for patients with breast cancer.

In addition, clinical experience and statistics show that incidence, therapy response, and survival rates differ by ethnicity, even when socioeconomic variables are taken into consideration. African Americans and Hispanics face a higher risk of developing more aggressive subtypes of breast cancer than non-Hispanic Whites. A strong possible explanation for differences among ethnicities in relation to breast cancer is variations in the cells that suppress the immune system. Cancer spreads by suppressing the immune system. We are among the first to launch a comprehensive inter-ethnic analysis of Hispanic/ Latina patients as compared to Non-Hispanic White patients to compare the different immune cell types, especially cells that suppress the immune system, to discover how ethnic differences affect breast cancer incidence, treatment, and outcomes. We are investigating immune suppressor cells to better understand the variation in responses to treatment of these different groups of patients. Such information could lead to specific, personalized targets for immunotherapy for different ethnic groups—greatly improving its effectiveness.

One type of immunosuppressive cell that we are investigating is the myeloid-derived suppressor cell (MDSC). Higher levels of such cells are associated with more advanced cancer, poorer outcome, and increased resistance to treatment with immunotherapy in various cancer types, such as breast, pancreatic, colorectal, and non-small cell lung cancer. With the data we have generated and the data we plan to generate over the next year, we are seeking to measure MDSC levels in patients across breast cancer subtypes, stages of disease, and ethnicity. MDSCs could not only serve as a target to sensitize tumors to treatment, making it more effective in patients of various ethnic backgrounds. But could also serve as a marker to help identify patients who are most likely to respond to the therapies we are currently studying. We are developing tiny models—organoids—grown from the cells of patients of different ethnicities to mimic cancer in the body. We will use the organoids to more quickly test the effectiveness of novel combinations of therapies currently in early-phase clinical trials.

As a result of data generated, we have been able to secure three additional grants, one of which is a major grant from the National Institute of Health which will fund our research for the next 5 years. In addition, we now have enough data to being to discuss plans for a phase 2 clinical trial that will be powered to answer if the combination of immunotherapy with an epigenetic modulating drug is more effective than what we currently have to offer. Upon completion of this work we may be able to suggest that Hispanic/ Latina patients are studied as specific cohort for this upcoming clinical trial.